HEMATOLOGY, TRANSFUSION AND CELL THERAPY

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POSTER PRESENTATIONS

ADULT HEMATOLOGY
ACUTE LEUKEMIAS

PP 01

Hypercalcemia due to the interaction between all trans retinoic acid and posaconazole used for acute promyelocytic leukemia treatment

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Objective: All-trans retinoic acid (ATRA), a physiological metabolite of vitamin A, has revolutionized acute promyelocytic leukemia (APL) treatment. Most APL cases show a t(15;17) (q22 q21) chromosomal translocation from which a PML/retinoic acid receptor a (RARa) fusion gene originates. The maturation of APL cells during myeloid differentiation is blocked at the promyelocyte stage, and ATRA induces the terminal differentiation and apoptosis of leukemia cells. Although very high rates of complete remission have been achieved using ATRA in APL patients, side effects associated with systemic ATRA treatment have also been reported in the literature. Hypercalcemia associated with ATRA has been reported among rare side effects of the drug. We report a case of hypercalcemia that resulted from the interaction of ATRA and posaconazole used in the treatment APL.

Case report: A 49-year-old woman was diagnosed with APL by tests and studies to investigate the etiology of pancytopenia, and was started on a combination of daunorubicin 60 mg/m^2/day (3 days), cytosine arabinoside 100 mg/m^2/day (7 days) plus ATRA 45 mg/m^2/day. Due to febrile neutropenia, piperacillin/tazobactam treatment and posaconazole treatment at a dose of 300 mg/day were added. She developed difficulty breathing and weight gain on the 6th day of therapy, which was attributed to the ATRA syndrome; thus, ATRA was stopped and dexamethasone was started. As she developed hyperbilirubinemia during her follow-up, posaconazole and prophylactic drugs were stopped. The patient entered remission after induction therapy, and ATRA plus idarubicin 5 mg/m^2/day (4 days) chemotherapy regimen, and prophylactic posaconazole were planned as the first consolidation therapy. Having a normal calcium level (9.79 mg/dL; normal range 8.6–10.2 mg/dL) prior to treatment, the patient developed a progressive rise of serum calcium (10.3 to 10.6 to 10.8 to 11.1 mg/dL) with the start of posaconazole and ATRA. Her Vitamin D level and PTH, both of which were in the normal range. Considering that hypercalcemia might have been caused by posaconazole and ATRA, both drugs were stopped. When the calcium level returned to normal by four days, ATRA but not posaconazole was reinstituted, and the patient developed no calcium elevation thereafter.

Conclusion: It is known that ATRA is metabolized by Cytochrome P450 pathway, and closely associated with the enzymes CYP 2C9 and CYP3A4. Azole antifungals have been shown to be strong inhibitors of the cytochrome P450 enzyme system. A case of hypercalcemia developing as a result of the addition of voriconazole to ATRA was reported in the literature, and another case of hypercalcemia developing as a result of combined use of itraconazole and ATRA. To reduce the incidence of side effects during ATRA treatment, it may be prudent to limit the use of any drug with the potential of inhibiting the cytochrome P450 enzyme system. A review of the literature has not provided any clear evidence as to when ATRA can be reinstituted after the cessation of a drug belonging to the azole group. This case highlights the importance of monitoring ATRA's side effects when it is used in combination with drugs inhibiting the cytochrome P450 enzymes.

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PP 02

Acute cerebellar syndrome after high dose cytosine arabinoside treatment: case report

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Objective: Cytosine Arabinoside (cytarabine, ARA-C) discovered in the early 1950s from crptathetia crpta which is a type of sponge. It is a chemotherapeutic agent that is an analogue of primidine from the group of antimetabolites and it is used in AML (acute myeloid leukemia), ALL (acute lymphoblastic leukemia), CML (chronic myeloid leukemia), relapse or refractory hodgkin lymphoma, non-hodgkin lymphoma, primary central nervous system lymphoma treatment. The most common side effect is cytopenias due to the bone marrow suppression. In addition; side effects may occur such as nausea, vomiting, diarrhea, abdominal pain, hepatic dysfunction, neurological side effects. Beside many neurological side effects such as peripheral neuropaty, convulsion, cerebral dysfunction can be seen in systemic and intrathecal treatments, classical cytarabine neurotoxicity is acute cerebellar syndrome caused by high-dose systemic therapy.

Case report: A 61 year-old man who had lung cancer history and not suitable for allogeneic stem cell transplantation; was planned HyperCVAD A/B chemotherapy protocol with the diagnosis of B-ALL. Dysarthria and impaired coordination of hand and foot movements occurred on the sixth days of second cycle of HyperCVAD-B chemotherapy. In neurologic examination, dysarthric speech, measured and sequential motion tests for cerebral examination was failed and no motor deficits. No mass or vascular pathology were detected in imaging examinations that could explain the patient's complaint. As a result, the patient was evaluated acute cerebellar syndrome caused by high dose cytosine arabinoside side effect by neurology department. From the eleventh day of treatment patient's complaints was regressed and come back to normal at fifteenth days of treatment.

Conclusion: Acute cerebellar syndrome begins 3–8 days after the start of drug administration. Cerebellar symptoms such as dysarthria, dysdiadokokinesia, dysmetry and ataxia greatly improved after stopping the drug however these symptoms may not full recover in approximately 1/3 of patients. Therefore there is not any treatment for neurological side effects, it should be kept in mind in chemoterapy treatment planning. While planning treatment, dose adjustment considering side effects as performance and age of patient. Nearly monitored is most important for early diagnosed of neurological symptoms.

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PP 03

An unusual case report: myeloid sarcoma presented with appendicitis

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Objective: Myeloid sarcomas (MS) also called as granulocytic sarcomas, myeloblastoma or chloromas are the representatives of extramedullary infiltrates of immatur myeloid cells. According to 2016 revısıon to the World Health Organization classification of myeloid neoplasms and acute leukemia; it is classified a subgroup of Acute myeloid leukemia (AML) and related neoplasms. MS has more aggressive clinical course than AML. MS may present simultaneously with or precede bone marrow disease or may be seen in relapse. Isolated myeloid sarcoma involvement is most frequently detected in the bone, periosteum, soft tissues and lymph nodes. Herein we reported an unusual case of a 44 year old man who presented to appendicitis and diagnosed with MS with appendicitis pathology report.

Case report: A 44 year-old man who had no history of smoking, alcohol or any chronic disease, was admitted to the hospital with sudden abdominal pain, nause and vomiting. The patient, who was diagnosed with appendicitis and was underwent appendectomy. The patient's appendectomy result was reported as MS. In the blood test examination; white blood cells (WBC): $43.2 \times 10^3/\mu L$; neutrophil: $36.3 \times 10^3/\mu L$; monocyte: $2 \times 10^3/\mu L$, hemoglobin:11.5 g/dL, and plateletes:$100 \times 10^3/\mu L$ were detected. Peripheral smear was applied to the patient due to leukocytosis. Blastic cell infiltration was detected in peripheral smear and the patient underwent bone marrow biopsy. More than 20% monoblasts were observed in bone marrow aspiration. Flowcytometric examination was performed and immunfenotypic finding MS of the patient were interpreted of AML M5. Remission induction chemotherapy (daunorubucin 60 mg/m^2 110 mg/daily throughout 3 days and ARA-C 100 mg/m^2 180 mg/daily, throughout 7 days) was planned.

Conclusion: Hematological malignancies could involve extramedullary soft tissue in relatively rare cases. MSs are rare extramedullary tumors, most commonly occur in patient with acute or chronic myeloid leukemia (1–3). De novo MS may represent the first sign of systemic disease. Untreated MS usually progress to AML in about 1 year. The clinical presentation of MS depends on location, size of mass. In the current case a sudden right lower abdominal pain, nause and vomiting due to blastic infiltraion and obstruction of appendix were initial symptoms. Total excision of the mass is to gold standard for diagnosis. In the current case, appendix patology results showed that monoblastic and localize inflitration of cell form of monocytoid with large nucleolus, prominent nucleoli, wide cytoplasm, Ki 67 proliferative activity >. There is no consensus of MS treatment. Recommended treatment regimen for isolated MS or MS with AML is conventional AML protocols. In conclusion, MS is a subgroup of AML present with myeloblastic

infiltration of soft tissue. MS may present at any time of disease process and any localization. It should be kept in mind that hematological malignancies may be seen all over the body and may be present atypically because early diagnosis and treatment are very important cause of MS's aggressive clinical course.

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PP 04

Postdural puncture superior sagittal sinus thrombosis during remission induction therapy for acute lymphoblastic leukemia

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Objective: Superior sagittal sinus thrombosis (SSST) during the course of acute lymphoblastic leukemia (ALL) may arise during or even after treatment. Majority of the cases are either directly attributed to ALL or considered as a consequence of using chemotherapy agents including prednisone, vincristine, cytarabine and especially L-Asparaginase. Post-lumbar puncture intracranial hypotension is a rarely encountered cause of SSST in ALL.

Case report: A 27-year-old man was admitted with fatigue and following bone marrow aspiration and biopsy, he was diagnosed as having B-ALL. He received HyperCVAD regimen as remission induction therapy, which included doxorubicine, vincristine and cyclophosphamide, dexamethasone and intrathecal administration of methotrexate. Cranial computerized tomography (CT) prior to intrathecal methotrexate was normal. Cerebrospinal fluid analysis was acellular and showed no ALL infiltration. He complained of mild postural headache intrathecal treatment. Eight days after intrathecal administration of methotrexate on day 13 of HyperCVAD, he complained of newly developing non-postural headache and vomiting.

Methodology: At the time of symptoms, complete blood count showed the following: WBC: 5480/uL, Hgb: 12.3 g/dL and PLT: 148,000/uL. Coagulation profile studies showed prothrombin time of 13 s, partial thromboplastin time (PTT) of 30.9 s, and normal concentrations of fibrinogen. Neurologic examination including evaluation of his mental status, sensory, motor, and reflex functions of his extremities. Coronal plane contrast enhanced T1-weighted MRİ demonstrated a nonenhancing superior sagittal sinus with the empty delta sign, compatible with a diagnosis of SSVT. Enoxaparin 2×1 mg/kg was initiated. Platelet transfusions were given to keep platelet count over 50,000/uL during the course of anticoagulant therapy.

Results: SSST in the context of ALL has been ascribed to lymphoblastic infiltration of the superior sagittal sinus wall or to the chemotherapeutic agents used. L-Asparaginase decreases plasma antithrombin, plasminogen, and fibrinogen concentrations while prednisone may increase the levels of factor VIII. These hemostatic changes may predispose to thrombosis, especially in the setting of the turbulent flow in the superior sagittal sinus. Our patient harbored none of the aforementioned risk factors except for the use of corticosteroids. Any cause of intracranial hypotension, which induces a downward shift and traction of the brain, may disrupt the veins/sinus and hence may lead to venous dilatation and thrombosis.

Conclusion: Our patient most probably developed intracranial hypotension due to lumbar puncture, which resulted in SSST. The possibility of a dural venous thrombosis should be suspected in patients with ALL who had treatment with L-asparaginase and prednisone. However, SSST thrombosis should also be an important consideration in patients with dural puncture who report a changing pattern of their headache (postural headache becoming nonpostural in character) and severe nausea and vomiting.

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PP 05

Retrospective analysis of all patients single center experience

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Objective: The aim of study was to evaluate the demographic, clinical, laboratory, genetic and pathological features of the patients followed with the diagnosis of adult ALL in our center and to evaluate their contribution to the prognosis, treatment responses and overall survival rates of the patients and to contribute to the literature.

Methodology: A total of 116 patients diagnosed with ALL in our center between 2006–2018 were included in the study. Patients under 18 years of age and patients with active solid organ malignancies were not included in our study. The data of the patients were obtained by scanning the hospital computer automation system and patient files.

Results: Sixty-two of our patients are male and 54 are female. The mean age of the patients was 43.1 years. Twenty patients were T-ALL and 96 patients were B-ALL. In a quarter of patients, the Philedelphia chromosome was positive. 22 of our patients had standard risk and 94 had high risk class. Total survival rate was 52.6%. The mean total survival time was 41,4 months. 83.6% of the patients were in remission with induction therapy. Forty patients underwent allogeneic stem cell transplantation. There was no statistically significant difference between B-ALL, T-ALL and Ph+ ALL patients in terms of remission induction and survival. Tyrosine kinase inhibitors improved the prognosis of Ph+ ALL patients. In patients who received TKI treatment, the decrease in PCR values at the 3rd month was found to be a good prognostic factor. PCR monitoring is important in predicting prognosis in patients receiving

TKI. The presence of severe fibrosis in the bone marrow (Grade 2–4) was found to be poor prognostic.

Conclusion: In our study, although the overall survival rate is consistent with the literature, it is evident that it is still insufficient. Therefore, more study and innovation are needed in the treatment of adult ALL.

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PP 06

Case report: acute lymphoblastic leukemia with bone involvement

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Objective: ALL is the most common type of acute leukemia in children, after AML in adults. At the time of diagnosis, there may be weakness due to anemia, signs of bleeding due to thrombocytopenia, signs of infection related to neutropenia. There may be bone pain due to expansion of the medullary cavity by the leukemic process. However, low back pain due to vertebral body collapse is one of the rare symptoms at the time of diagnosis. We are reporting an adult male patient with acute lymphoblastic leukemia who presented with paraparesis and multiple osteolytic lesions in lomber and thoracal vertebra.

Case report: A 63-year-old male patient had a complaint of back pain for 4 months, spreading to the left leg, accompanied by numbness and loss of strength. The patient without incontinence and painful walking was operated by the neurosurgery department. The patient with pancytopenia was consulted to us. In physical examination peripheral LAP was not detected and spleen size was determined as 16.5 cm by ultrasound. In the laboratory examination was remarkable for Hb: 9 g/dL, MCV: 79 fL, plt: $13*10^3$/uL, sedim 76 mm/h LDH: 1092 u/L. Other biochemical tests are normal. The L2 corpus pathological fracture biopsy result was determined as CD45+, Cd19+, Cd10+, TDT+, PAX 5+, c myc 30%+, Kİ 67% 50+, and was compatible with B lymphoblastic lymphoma infiltration. In bone marrow biopsy, 98% cellularıty, 99% blastic infiltration was detected. Blasts were CD34+, CD19+, PAX 5+, 80% CD10+, 80% TDT+, 50% CD22+, 30% CD20+, CD123+, respectively. Cytogenetics and fluorescence in situ hybridization (FISH) panel for ALL were normal; Philadelphia chromosome was not present. HyperCVAD chemotherapy was started for the patient who was diagnosed with B-ALL+ bone involvement. Intrathecal chemotherapies were given. After Hyper CVAD 2B chemotherapy, the patient was clapped due to sepsis.

Conclusion: Skeletal lesions can occur in a variety of malignant hematological conditions. In diseases such as multiple myeloma and waldenstrom macroglobulinemia, bone involvement is a common finding in diagnosis. Acute lymphoblastic leukemia and lymphomas can rarely present with osteolytic lesions and neurological involvement. ALL is a chemosensitive tumor, so chemotherapy is the main treatment option. In patients with bone involvement, radiotherapy and surgical resection are the other treatment options that can be applied.

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CHRONIC LEUKEMIAS

PP 07

Chronic lymphocytic leukemia presenting as pulmonary involvement in an elderly patient: a case report

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Objective: A significant part of chronic lymphocytic leukemia (CLL) cases receive a diagnosis during the examination of routinely detected lymphocytosis or the investigation of the causes of lymphadenopathy or hepatosplenomegaly. Apart from these, CLL cases may rarely manifest as pulmonary involvement, which can include broncho-pulmonary infiltration, pleural effusion, or an endobronchial lesion. In the literature, cases presenting with CLL-associated broncho-pulmonary infiltration are extremely rare. Here, we present an elderly case with CLL presenting as pulmonary involvement.

Case report: An 82-year-old male patient presented to our hospital with progressive dyspnea, non-productive cough, and weight loss, which had persisted for one month. Chest X-ray radiography revealed opacity in the lower zone of the right lung. Contrast computed tomography (CT) of the chest visualized a soft-tissue density measuring approximately 74 mm × 75 mm in maximal axial dimensions in the inferior segment of the right middle lobe with surrounding ground-glass density and some air bronchogram localized near the medial hilum. Laboratory test results were as follows: hemoglobin level, 13.4 g/dL; total leukocyte count, 174×10^9/L; lymphocyte count, 148×10^9/L; platelet count, 192×10^9/L. Peripheral blood smear showed diffuse mature small lymphocytes and smudge cells. Peripheral blood flow cytometry revealed strong positivity for the CD5, CD20, CD19, and CD23 markers, consistent with CLL. A bronchoscopy was performed for diagnostic purposes and a transbronchial biopsy was taken from the lung parenchyma, and bronchoalveolar lavage (BAL) was performed. BAL cytology and microbiological tests were not diagnostic. On immunohistochemical examination of the parenchymal biopsy, neoplastic cells showed a CD20(+), CD5(+), CD23(+), CK(−), CK7(−), CK20(−), CD56(−), synaptophysin(−), chromogranin-A(−), CD3(−), TTF-1(−), Napsin A(−), and P63(−) staining pattern. The Ki67 proliferation index was 10%. The pathology clinic reported the result to be consistent with a chronic lymphocytic leukemia/small lymphoma infiltration. Cervical and abdominopelvic CT results of the patient were also considered and the CLL stage was determined as RAI 2

(moderate risk) and Binet B (moderate risk). However, in consideration of his weight loss and symptomatic extranodal involvement, a chemotherapy protocol with bendamustine and the CD20 antibody rituximab (BR) was initiated. BR treatment was administered every 28 days for up to 6 courses. The patient's symptoms demonstrated marked improvement after two cycles of chemotherapy. After a total of 4 courses, lymphocytosis in the peripheral blood showed complete remission and the involvement that had been visualized on direct chest radiography and CT showed nearly complete remission. After 6 cycles of chemotherapy, the patient was considered in complete remission and follow-up was started.

Conclusion: Pulmonary complications and involvement in CLL typically occur after the diagnosis, in the course of the disease, while there are cases who present as pulmonary involvement (broncho-pulmonary infiltrates, hilar and mediastinal lymphadenopathies, pleural effusion, etc.), although much less frequently. Pulmonary involvement must be considered in patients diagnosed with CLL who have symptoms associated with the respiratory system. Particularly in patients diagnosed with broncho-pulmonary lesions based on peripheral blood analysis or lymph node biopsy, CLL-associated involvement should certainly be included in the differential diagnosis when the most common causes are excluded.

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PP 08

Frequency of brucellosis and hepatitis b virus seropositivity in patients with chronic lymphocytic leukemia

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Objective: Chronic lymphocytic leukemia (CLL) is a disease characterized by an increase in mature neoplastic lymphocytes in tissues with a lymphoid component, such as peripheral blood, bone marrow, lymph node, spleen, and liver. Patients with CLL show defective cellular and humoral immune responses. Although such immune failure is known to be associated with an increase in the frequency of particularly gram-positive and -negative bacterial infections, data on the increase in the frequency of zoonoses such as brucellosis and viral infections such as the hepatitis B virus (HBV) are inconclusive. This study aims to investigate the frequency of brucellosis and HBV seropositivity in patients diagnosed with CLL.

Methodology: Patients followed-up for CLL between 2005 and 2019 were evaluated. Results of patients who were tested for HBsAg and anti-HBs serology using the ELISA assay and for Brucellosis using the serum (Wright) agglutination test were recorded. Demographic data and laboratory results of all patients included in the study were evaluated.

Results: This study included 188 patients diagnosed with CLL, of whom 56 (29.8%) were female and 132 (70.2%) were male. The median age was 62 (range: 33–92) years. Complete blood count parameters at diagnosis were as follows: median leukocyte count, 54.4×10^9/L; median lymphocyte count, 42.3×10^9/L; median platelet count, 148×10^9/L; median hemoglobin level, 13.4 g/dL. HBsAg and anti-HBs were tested in 142 patients. A total of 16 (11.27%) patients were HBsAg-positive; with 5 (3.52%) positive cases in females and 11 (7.75%) in males. A total of 105 (73.95%) patients were anti-HBs-positive; with 32 (22.54%) positive cases in females and 73 (51.41%) in males. The Wright agglutination test was performed on 82 patients. A total of 4 (4.88%) patients reacted positively to the Wright test; with 3 (3.66%) positive cases in females and 1 (1.22%) in males.

Conclusion: The immune system disorders that develop due to the nature of CLL make the patient more vulnerable to infections. Accordingly, many patients lose their lives due to a clinical picture of severe infection. Based on the present study, compared with the epidemiological studies conducted in the same region; the rate of positive reactions to the Wright agglutination test was consistent with the literature data; however, a higher rate of HBsAg positivity was determined. This may be linked to the increase in the risk of HBV transmission due to the immune defect caused by CLL or the immunosuppressive picture induced by the medication used in the treatment, or viral reactivation.

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PP 09

Epidemiological spectrum and diagnosis patterns of hematological malignancies in the republic of moldova

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Objective: Hematological malignancies (HM) are the relatively frequent nosological entities within the structure of morbidity by malignant tumors, exhibiting a severe evolution, restrained prognosis and negative socio-economic impact in the advanced stages and phases. The objective of the study was to analyze the incidence and diagnosis patterns of HM in Moldova.

Methodology: The following research methods were used: epidemiological, descriptive statistics, clinico-analytic. The type of HM was identified according to the Revised 2017 WHO Classification of Tumours of Hematopoietic and Lymphoid Tissues. The diagnosis was proved by histopathological, cytological, cytogenetic, molecular and immunophenotyping examinations. The quantitative real-time PCR was used in order to assess the expression of BCR-ABL p210 and p190 transcripts for CML diagnosis. The quantitative detection of JAK2 V617F mutation served as a major criterion for diagnosis of polycythemia vera (PV) and primary myelofibrosis (PMF).

Results: The number of newly diagnosed and followed-up patients with HM at the Institute of Oncology in 2016, 2017, 2018 and 2019 amounted respectively to 725, 802, 613 and 628, the incidence (new cases per 100,000 population) being 17.6,

19.5, 14.9 and 17.7. In 2019 Hodgkin lymphoma was diagnosed in 9.4% of cases, non-Hodgkin lymphomas – in 36.4%, multiple myeloma and plasma cells neoplasms – in 8.6%, lymphoid leukemias – in 13.7%, myeloid leukemias – in 8.3%, monocytic leukemias – in 1.7%, and other leukemias – in 19.8%. The male's rate was 51.5%, the female's rate – 48.5%. The age of 50–79 years prevailed in both genders (males – 65%, females – 72.5%). The children constituted 4.0% of newly diagnosed cases and 4.8% of those under the follow-up at the end of the year. Regarding the chronic myeloproliferative neoplasms (CMN), prefibrotic stage of PMF was confirmed in 42.1% of cases, fibrotic stage – in 57.9%. The diagnosis of CML was asserted in chronic phase in 89.3% of patients and in accelerated phase in 10.7%. PV was diagnosed in erythremic stage in all cases: II A – in 87.1% of cases, IIB – in 12.9%. The age group of 60–69 years proved to be more numerous in PV (80.6%), as compared with CML (53.4%) and PMF (52.6%) cases. The disease span range from the onset to diagnosis was 1.4–7 months (median – 3.5 ± 0.63 months) in PMF, 1.5–12 months (median – 2.1 ± 0.37 months) in CML, and 1–8 months (median – 3.8 ± 0.54 months) in PV. The clinical onset and addressability of patients with CML and PMF did not significantly differ, the absolute majority (over 90%) being consulted by the family doctors because of the appearance of fatigue, left upper hemiabdomen heaviness and pain. The majority of PV patients (67.7%) addressed for the medical care by reason of a stable arterial hypertension and astheno-vegetative syndrome.

Conclusion: The incidence of malignant lymphomas and leukemias in Moldova emerged rather lower than in the majority of European countries mainly due to the migration of a workable population. Mostly the 50–79 years old males proved to be affected. PV yielded to be less frequently registered CMN, diagnosed more tardily due to the resemblance with cardiovascular disorders.

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PP 10

A rare case: coexistence of small cell lung cancer and chronic lymphocytic leukemia

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Objective: The most common type of leukemia in adults; chronic lymphocytic leukemia (CLL), which is detected in 25% of all leukemias. In epidemiological studies in western societies, its incidence was found to be 4/100,000. CLL is an advanced age disease and its incidence increases with age. While some of the patients are followed up asymptomatically and with lymphocytosis without any treatment indications, others may show aggressive clinical course, appear with cytopenia and cause chemotherapy indications. Suppression of immunity and B cell dysfunction in CLL can cause secondary malignancies. In a much rarer group of patients, the diagnosis of CLL and solid organ cancer is made simultaneously. In such cases, pathological or cytogenetic common mechanisms or common risk factors such as smoking and radiation may play a role in etiology. We also wanted to present the coexistence of small cell lung cancer (SCLC) and CLL, which are rarely diagnosed simultaneously, and may contribute to the literature.

Case report: In the examination of a 82-year-old male with a history of smoking 30 packs/year, who suffered from ongoing loss of balance for approximately 1 month, an irregular limited mass with a size of 3×2 cm was detected in the upper left lobe. The fine needle biopsy result from the mass was reported as SCLC and was considered Stage 3 in the evaluation. The patient was started on cisplatin 75 mg/m^2 + etoposide 100 mg/m^2 chemotherapy protocol treatment by department of pulmonary diseases. During the diagnosis process, the patient, who was found to have had long-standing lymphocytosis, was also asked for flow cytometry examination upon monitoring of mature lymphocyte infiltration and basket cells in the peripheral smear examination. In flow cytometric examination, CD5, CD19, CD20, CD23 were positive and CD10, CD103 were negative and these findings were reported as B-lymphoproliferative disease (CLL). The patient, who was evaluated as stage 1 CLL with detailed blood tests and imaging, was followed up without treatment. During follow-up, in the evaluation of the patient with deep anemia, the direct coombs test was positive (IgG) and the biochemical markers were compatible with hemolysis, 60 mg/day (1 mg/kg/day) methylprednisolone treatment was started for the patient who was diagnosed with autoimmune hemolytic anemia. With the initiation of corticosteroid therapy, a significant increase in both hemoglobin value and improvement in hemolysis parameters of the patient was observed and treatment was continued by decreasing the dose. The patient, whose steroid treatment is completed and hemogram parameters are monitored within normal limits, is followed up without treatment by the hematology department in terms of CLL. At the same time, the third cycle of chemotherapy has been completed with the diagnosis of SCLC and is followed by the department of pulmonary diseases.

Conclusion: CLL constitutes a high risk factor for many solid tumors such as lung, breast, colon and prostate cancer. In a study in which 4.869 CLL patients were screened for secondary malignancy, 33 lung cancers were detected and SCLC was 6% among all lung cancers.

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PP 11

Stevens–Johnson syndrome secondary to rituximab administration in a chronic lymphocytic leukemia patient

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Objective: Stevens–Johnson syndrome (SJS) is an acute hypersensitivity reaction that compromises the integrity of mucous membranes and cutaneous tissue. Chronic

lymphocytic leukemia(CLL) is a chronic B-lymphoproliferative neoplasm that is one of the most often appearances in daily hematological practice. The CD20 antigen is an attractive target in CLL as it is present on the surface of mature B-cells. Rituximab is a highly specific chimeric mouse/human anti-CD20 antibody that is widely used in the treatment of CLL and other B-lymphomas. The aim of this abstract is to describe the occurrence of Stevens-Johnson syndrome as a result of the administration of Rituximab to a patient with CLL

Case report: We report the case of a 49 years old caucasian male that four years previously was diagnosed with CLL stage A Binet. The "watch and wait" strategy was adopted at that time. But the patient disappeared from the current supervision of the hematologist and returned after 4 years with B symptoms, giant splenomegaly, hepatomegaly, peripheral lymphadenopathy, and bicytopenia (anemia and thrombocytopenia) that accompanied the lymphocytosis in peripheral blood. Stage C Binet was established, and for this patient was proposed the initiation of treatment with chemoimmunotherapy type FCR according to guidelines. But, the patient refused to administer any type of chemotherapy and in the absence of new targeted therapeutic alternatives, the most plausible solution was to initiate monotherapy with Rituximab 375 mg/m^2 weekly. On the 3rd day after the second administration of rituximab, he experienced a febrile episode 38.5 °C, fatigue, and weakness, moderate pain all over the skin, which were aggravated by a slight touch and a non-pruritic widespread maculopapular rash, which affects the oral mucosa and also the skin in the genital area, palmar and plantar region. SJS was diagnosed affecting 12% of total body surface area according to the Lund-Browder Burn calculator. Rituximab therapy was stopped and immediate treatment of SJS has started. Patients received supportive care measures including hydration, wound debridement, systemic and topical antibiotics, topical and systemic corticosteroids, nutritional support, and pain management for 4 weeks with a total recovery of skin and mucosal lesions.

Conclusion: Although SJS is a rare complication of Rituximab therapy (0.01% in a series of 167,000 patients), it remains a dreaded complication with a 30% mortality rate among patients who develop it. Recognition of clinical signs and prompt diagnosis along with complex therapy can ensure adequate recovery of the case.

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CHRONIC MYELOPROLIFERATIVE DISEASES

PP 12

Concomitant essential thrombocythemia and mature B-lymphoproliferative disorder in a patient

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Objective: ET and B-LPD are two distinct, clonal hematologic malignancies with their concomitant existence in a single individual being exceedingly rare.

Case report: A 64-year-old male was admitted with cough, weight loss, maculopapular rash and elevated platelet counts. The rash was present on his face and trunk for 20 days and he had non-productive cough for the past two weeks. On examination, he was found to have cervical lymphadenopathy and splenomegaly (5 cm below left costal margin). His blood counts were as follows: hemoglobin 10.8 g/dl, hematocrit 37.2%, RBC mass 5.34×10^{12}/L, WBC 62.1×10^9/L, platelets 1169×10^9/L. LDH was found to be 816 IU/L and C-reactive protein was 2.43 mg/dl. Peripheral blood film showed anisocytosis, poikilocytosis, elliptical cells, tear-drop cells, nucleated red blood cells, myelocytes and metamyelocytes. Platelets were markedly increased on film. Leucoerythroblastic blood picture was noted. Suspecting a myeloproliferative disorder, additional investigations were sent while the patient was started on hydroxyurea 1gm daily and allopurinol 100 mg daily in addition to antibiotics. Bone marrow aspirate depicted increase in lymphoid cells that constituted around 35% of the total nucleated non-erythroid cell population. M:E ratio was 4:1. Bone trephine showed hypercellularity for age with overall cellularity 90 to 95%. Cellular areas exhibited increase in myeloid precursors along with prominent lymphoid cells and abundant megakaryocytes. Pan-T (CD03) and Pan-B (CD20) marker by immunohistochemistry was applied on bone trephine biopsy specimen which was interpreted as increase in B-lymphocytes. Reticulin stain showed grade MF-2 reticulin fibrosis. Overall findings were suggestive of essential thrombocythemia. In view of increased CD20 positive cells, immunophenotyping by flow cytometry was recommended. CD45 positive lymphoid cells population was 31%. This population showed reactivity to Pan-B-markers i.e. CD19 (26%), CD20 (27%), CD22 (26%), CD23 (11%) and cCD79a (30%) along with HLA-DR (12%) and CD45 (35%). Double bright positivity of CD19 and CD5 typical of CLL was absent. This population also showed positivity to lambda light chains restriction (kappa 0%, lambda 13%). Results were consistent with mature-B-lymphoproliferative disorder (B-LPD). JAK2 mutation was detected by PCR while BCR-ABL1 translocation was not detected by fluorescence in situ hybridization (FISH). Since double bright positivity for CD19 and CD5 was absent along with absence of FMC7, a diagnosis of mature-B-lymphoproliferative disorder was made. Cyclin D1 was applied on bone trephine, which was negative, and the infiltration did not reveal a follicular pattern. Ki67 was approximately 30%. A diagnosis of ET progressing to myelofibrosis and B-LPD was made. Patient was discharged in a stable condition and followed up on an outpatient basis. Ruxolitinib at a dose of 5 mg twice daily was initiated while hydroxyurea was reduced to 500 mg daily and then later to alternate day dosing. A wait and watch approach was adopted for the B-LPD Ruxolitinib was later increased to 10 mg twice daily. After a few months, ruxolitinib was switched to 15 mg daily with the counts remaining stable. The patient remains stable and asymptomatic two and half years later. The most recent blood counts show hemoglobin at 10.9 g/dl, WBC 31.1×10^9/L, and platelets 445×10^9/L.

Methodology: Retrospective review of case.

Conclusion: We report a rare case of ET with concomitant B-LPD. The patient is stable on Ruxolitinib and is on wait and watch approach for B-LPD.

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PP 13

Acute phase reactants in chronic inflammation leading to secondary myelofibrosis in polycythemia vera and essential thrombocytosis

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Objective: Polycythemia vera and essential thrombocytosis are chronic and progressive myeloproliferative neoplasms characterized by a clonal increase in hematopoietic stem cells in the bone marrow. Myelofibrosis in the bone marrow has been shown to be secondary to an inflammatory process.

Methodology: To investigate the association between the secondary myelofibrosis and acute phase reactants in patients with polycythemia vera and essential thrombocytosis. Fourty-six PV and 28 ET patients without myelofibrosis above Grade 1 were included in the present study. Bone marrow evaluations were performed retrospectively. C-reactive protein, ferritin, and albumin levels were measured.

Results: C-reactive protein (0.55 ng/L vs. 4.2 ng/L, $p < 0.001$) and ferritin (18.5 ng/mL vs. 118 ng/mL, $p = 0.001$) levels in patients with secondary myelofibrosis were found to be increased compared to baseline levels. Mean albumin levels in patients with secondary myelofibrosis, and CRP, ferritin, and albumin levels in patients without secondary myelofibrosis were similar at the diagnosis and at last visit. There were also similar the baseline levels of CRP, ferritin, and albumin between the patients with and without secondary myelofibrosis.

Conclusion: The increase in CRP and ferritin, which are indicators of chronic inflammation, may be used to show the inflammation and relevant secondary fibrosis in the bone marrow. Due to the similar CRP, ferritin, and albumin levels at the diagnosis, the prediction for the development of the secondary myelofibrosis is not possible in the present study.

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PP 14

Polycythemia vera: updates in diagnosis and treatment outcomes

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Objective: The objective of the study was to analyze the contemporary clinical and laboratory features of polycythemia vera (PV), as well as to evaluate the short- and long-term results of different treatment options.

Methodology: The clinico-hematological evolution features, complications, short- and long-term results of cytoreductive treatment were evaluated in a group of 114 PV patients, aged at 28–78 years old, who were followed up at the Institute of Oncology of Moldova between 1987–2019. The diagnosis was proved by the bone marrow biopsy and quantitative detection of JAK2 V617F mutation in pending cases. Physical and histopathologic examinations were associated with the repeated complete blood counts and abdominal ultrasound scan. The treatment included phlebotomies and cytoreductive chemotherapy with busulfan (56 patients) and hydroxycarbamide (58 patients) in standard doses. The life-table method was used for Kaplan–Meier Survival Analysis in order to evaluate the long-term results of treatment.

Results: The disease was commonly diagnosed in males – 66 (57.9%) patients. The females prevailed in the age groups of 40–49 years (31.3% versus 24.6% in males) and 60–69 years (25% versus 19.8% in males). The disease span from the onset of the initial clinical manifestations until the diagnosis lasted 4–9 months (median – 5.8 months) in the majority of patients (86.8%), that led to the development of thromboembolic complications in 28.1% of cases. The diagnosis was proved in stage IIA disease in 105 (92.1%) patients, IIB in 9 (7.9%) patients. The skin hiperemia was registered in 112 (98.3%) cases, scleral congestion – in 109 (95.6%), splenomegaly – in 77 (67.5%), erythromelalgia – in 71 (62.2%), aquagenic skin itching – in 68 (59.6%), hepatomegaly – in 61 (53.5%), vascular thrombosis – in 32 (28.1%). The complete blood count revealed the increase of hemoglobin (18.0–23.5 g/dL) and red cells (5.5–6.7 × 1,000,000 [MICRO]/L). The platelets range was 180–1690 × 1000 [MICRO]/L, leukocytes range – 5.1–21.3 × 1000 [MICRO]/L. Leukocytosis occurred in 69 (60.5%) patients, thrombcytosis – in 61 (53.5%). The bone marrow biopsy detected a hyperplasia due to the proliferation of erythroid, granulocyte and megakaryocyte cell lines. The study of short-term results asserted the complete remissions in all cases under chemotherapy combined with phlebotomies. The overall one-, 5-, 10- and 15 year was 100%, 98.6%, 85.9% and 67.1%, respectively. 73 (64.04%) patients remain in stage II disease after the treatment during 5–26 years of follow-up. The survival median was not reached.

Conclusion: The reluctant evolution, progressive growth of hemoglobin and red cell count, gradual increase of blood hyperviscosity and the lack of hemato-oncological vigilance of primary care physicians may lead to the development of

thrombotic and vascular complications in some PV cases. Chemotherapy improves significantly the patient's quality of life, reduces the rate of thromboembolic events and extends the life-span, comparable with that of total population of Moldova.

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PP 15

Disease and clinical characteristics of patients with chronic myeloproliferative neoplasms: 11-year single center experience

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Objective: BCR/ABL-negative myeloproliferative neoplasms are characterized by over-production myeloid lineages in the bone marrow. Polycythemia vera, essential thrombocythemia and primary myelofibrosis are the most common myeloproliferative neoplasms. Diagnosis is made according to the WHO diagnostic criteria from clinical data, hematological and biochemical analysis and BM histology. The aim of this study was to analyse patient demographic characteristics, clinical features, laboratory findings, mutational status together with complications, clinical course and survival.

Methodology: This study was conducted on patients diagnosed with myeloproliferative neoplasms between 2008 and 2019. Hemogram and biochemical parameters, demographic information, mutation analysis, management, complications and follow-up periods were recorded for all patients. Survival rates were calculated and the effect of the parameters on overall survival was analyzed.

Results: Evaluation was made of 247 patients, comprising 105 polycythemia vera, 126 essential thrombocythemia and 16 primary myelofibrosis patients. The overall frequency of driver mutations was 96.1% for PV, 71.4% for ET and 75% for PMF. Hydroxyurea was the most commonly used first-line treatment agent and the most common indication for switching to second-line treatment in all disease subgroups was the development of side-effects. During follow-up, 11 polycythemia vera, 14 essential thrombocythemia and 2 primary myelofibrosis patients developed thromboembolic complications. Median overall survival could not be reached in polycythemia vera and essential thrombocythemia patient and determined as 70.3 months in primary myelofibrosis patients. Age, LDH, ferritin and platelet/lymphocyte ratio at the time of diagnosis and thromboembolic complications were determined to have a statistically significant effect on survival in all patients.

Conclusion: Lower survival rates were seen in the primary myelofibrosis patients although thromboembolic complications were observed at similar rates in all 3 disease subgroups. In addition to known risk factors such as age and thromboembolic complications, parameters such as LDH, ferritin and PLR, which may be considered to indicate disease activity and inflammation, can also be used as prognostic markers.

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PP 16

The frequency of calreticulin and mpl gene mutations in bcr-abl and jak2 unmutated chronic myeloproliferative neoplasms and its effect on the outcome

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Objective: The World Health Organization (WHO) embedded calreticulin receptor (CalR) and myeloproliferative leukemia virus (MPL) gene mutation in diagnostic criteria for primary myelofibrosis (PMF) and essential thrombocythemia (ET), since 2016). We aimed to identify the frequency of CalR and MPL gene mutations and their effects on clinical outcomes in bcr-Abl and Jak2 unmutated chronic myeloproliferative neoplasms (MPNs).

Methodology: We screened bcr-abl negative and Jak2 unmutated MPNs diagnosed and treated between March 2004 and January 2013 at İstanbul Medical Faculty. We revised the MPN diagnosis according to the latest WHO classification. The association of CalR and MPL mutation with thrombotic complications, leukemic transformation, and survival was was defined.

Results: A total of 46 ET ($n = 34$) and PMF ($n = 12$) patients enrolled in the study. The demographic characteristics were similar between the two disease groups. Patients' mean age was 53.5 years (range 23–93 years) and gender distribution as 18 male to 28 female. A total of 18 patients (39.1%) had CalR mutation, and 4 (8.69%) patients MPL mutation. None of the ET patients had MPL mutations. CalR positive PMF patients' mean age was lower compared to patients without the mutation (p: 0.028). During the follow-up period, 8.3% of PMF and 5.9% of ET patients experienced leukemic transformation. None of the leukemic transformed patients had gene mutations. Among thrombosis complications, six patients developed thrombosis. All of them were ET patients, and 3 of them had CalR mutation two as CalR type 1 and one as CalR type 2. The mortality ratio was higher in patients in PMF, regardless of mutational status (p: 0.006).

Conclusion: Our study cohort is small to make a definite conclusion. Apart from the diagnostic guide, CALR mutations seem to have a prognostic effect is different in PMF and ET. This prognostic significance of CALR could be different among the MPN categories.

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PP 17

Study of JAK2V617F gene allele burden in polycythemia vera

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Objective: In recent years, it became necessary to identify a new clinical form of polycythemia vera – latent polycythemia vera (LPV). Considering the significant role of the JAK2V617F gene in the pathogenesis of LPV, we investigated the relationship between the allele burden of the JAK2V617F gene and clinical and laboratory parameters of the disease.

Case report: Patient G.N., at the age of 64, complained of pain in the legs, itching during bathing, weakness, headaches. He had been ill for several years. He suffered from glaucoma, as a result of which he acquired blindness. For a long period paresthesias, erythromelalgia and a gradual impairment of movement in the lower extremities had been observed. The patient was observed by a neurologist with a diagnosis of sensory neuropathy. Recently pain in the legs intensified and there were difficulties in walking. Due to changes in the hemogram, the patient was sent for a consultation to a hematologist. During examination, hyperemia on the face, traces of scratching were visible on the skin. On palpation, the spleen was enlarged by 1.5 cm. In laboratory analysis in the hemogram Hb-185 g/L, RBC-6.96 $\times 10^{12}$/L, Ht-58.5%, WBC-13.4 $\times 10^{9}$/L, PLT-471 $\times 10^{9}$/L. Taking into account the clinical and laboratory data, the patient underwent trepanobiopsy and molecular genetic analysis for the JAK2V617F mutation. As a result of histological examination of the trepanobioptate, three-branch proliferation in the bone marrow was revealed. The allele burden of the JAK2V617F gene was 79.5%. The patient was diagnosed with PV. After phlebotomy 4 times at a dose of 500 ml + LDA, the patient's condition improved, the pain in the legs disappeared, and independent movement without the help resumed. Control parameters of the hemogram: Hb-131q/L, RBC-4.5 $\times 10^{12}$/L, Ht-40%, WBC-9.69 $\times 10^{9}$/L, PLT-394 $\times 10^{9}$/L.

Methodology: The data of 193 patients were analyzed: hemogram parameters, allele burden of the JAK2V617F gene, analysis of the risk groups of patients were carried out. The WHO classification of 2008 and 2016, the prognosis of the risk of thrombohemorrhagic complications (TC) according to the Marchioli scale was used.

Results: Out of 193 patients, 127 were with classic polycythemia vera (CPV), and 66 were with LPV. The age of the patients (M ± m) with CPV was 57.01 ± 1.1 years, with LPV – 55.03 ± 1.6 years ($p > 0.05$). 97% of patients had the mutation of JAK2V617F gene. Laboratory parameters of patients with CPV and LPV were compared (M ± m): hemoglobin – 182.66 ± 2.1 g/L and 157.97 ± 2.2 g/L ($p < 0.05$), hematocrit – 71.85 ± 1.4% and 63.5 ± 1.8% ($p < 0.05$), erythrocytes – 6.18 ± 0.1 $\times 10^{12}$/L and 5.46 ± 0.1 $\times 10^{12}$/L ($p < 0.05$), platelets – 526.85 ± 30.9 $\times 10^{9}$/L and 429.3 ± 34.7 $\times 10^{9}$/L ($p < 0.05$), leukocytes 11.92 ± 0.6 $\times 10^{9}$/L and 10.79 ± 0.7 $\times 10^{9}$/L ($p > 0.05$), allele burden of the JAK2V617F gene – 55.0 ± 6.4% and 27.0 ± 6.9% ($p < 0.05$). Allele burden was divided into quartiles. In CPV 21.78% of patients belonged to the 1st, 20.16% to the 2nd, 18.55% to the 3rd, 39.51% to the 4th quartile. In LPV – 20% of patients belonged to the 1st, 80% to the 2nd quartile, in the 3rd and 4th quartiles there were no patients. In CPV the highest leukocyte count was in the 4th quartile. In LPV patients with an allele burden of the JAK2V617F gene above 40% had higher leukocyte and platelet counts, while the allele burden did not exceed 50%. We did not find any more relationship between allele burden and other hemogram parameters in patients with CPV and LPV. TC risk groups in CPV-low – 56.34%, intermediate – 38.03%, high – 5.63%, in LPV- low – 51.3%, intermediate –16.2%, high – 32.5%. In the analysis of JAK2V617F gene allele burden in the 1st and 2nd quartiles, no differences were found between the risk groups of LPV patients.

Conclusion: Out of PV patients 65.8% were with CPV, and 34.2% with LPV. In LPV the allele burden was lower than in CPV and did not exceed 50%. In CPV and LPV more than 51% of patients were at low risk of TC. CPV patients with JAK2V617F allele burden >75% had higher leukocyte count. LPV patients with JAK2V617F allele burden >40% had higher leukocyte and platelet counts.

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COAGULATION DISEASES

PP 18

Clinical and anamnestic signs of hypercoagulation in patients with β-thalassemia

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Objective: Hypercoagulation in β-thalassemia patients is known to manifest as arterial and/or venous thrombotic complications. Along with the clinical assessment of thrombotic complications (TC), it is also important to study latent (masked) hypercoagulation (LH) hypercoagulable state (HS) in patients with β-thalassemia. HS assessment is possible based on the analysis of various clinical symptoms and patient history.

Case report: In the National Centers of Hematology and Transfusiology, we studied 315 women aged 18–40 years: 130 with β-thalassemia Major (TM), 95 with β-thalassemia intermedia (TI), 60 with β-thalassemia minor (Tm), 30 blood donors (BD).

Methodology: The data were analyzed retrospectively and as a result of our survey on the increased thrombotic tendency. Statistics: data input system MS Excel, data processing using the program Statistics 6.

Results: In 10.0 ± 2.6% of TM patients and in 14.7 ± 3.6% of TI patients, various TCs were revealed: arterial thrombosis, venous thrombosis, chronic venous insufficiency (varicose nodes of the lower extremities, telangiectasia, trophic ulcer, venous eczema, swelling of the feet and lower legs). Such complications was not detected in patients with Tm and in the control group. Out of 60 splenectomized patients with

TM, arterial thrombosis was observed in 2 (3.3%) patients, venous thrombosis in 3 (5.0%) patients, and signs of chronic venous insufficiency in 4 (6.7%) patients. Out of 70 non-splenectomized patients with TM, venous thrombosis was observed in 1 (1.4%) patient, and signs of chronic venous insufficiency in 3 (4.3%) patients. Of the 40 splenectomized TI patients, arterial thrombosis was observed in 2 (5.0%), venous thrombosis in 3 (7.5%), and signs of chronic venous insufficiency in 4 (10%). Of 55 non-splenectomized TI patients, venous thrombosis was observed in 2 (3.6%), and signs of chronic venous insufficiency in 3 (5.4%). Assessment of thrombotic tendency was conducted among non-splenectomized patients. HS (the total score for the PTT questionnaire >30) was detected in 36.0 ± 6.8% of TM patients and 40.0 ± 7.7% of TI patients. In patients with TI and in BD, increased thrombotic tendency was not detected (the sum of the scores for the PTT questionnaire is <30).

Conclusion: TCs detected in patients with homozygous β-thalassemia was more common in patients with TI compared with patients with TM ($p \geq 0.05$). In patients, cases of venous thrombosis were detected 2 times more often than arterial thrombosis ($p \geq 0.05$). Chronic venous insufficiency was detected identically in patients with TM and TI. TCs was observed more often in splenectomized patients with TM and TI compared with non-splenectomized patients ($p \geq 0.05$). It was established that some patients with β-thalassemia who did not have clinical thrombotic complications had prethrombotic state. A study of clinical and anamnestic risk factors revealed a tendency to HS in 1/3 of patients with β-thalassemia. Based on the results of the survey, the risk factors (predictors) of HS were determined. The tendency to form blood clots in patients with anemia was associated with two groups of clinical and anamnestic symptoms: “comorbidity” and “chronic stress conditions”.

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PP 19

Factor XIII deficiency case with posttravmatic subcutaneous bleeding

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Objective: Factor XIII deficiency; is a rare hereditary bleeding disorder caused by heterogeneous mutations that can lead to life-threatening bleeding. Hereditary factor XIII deficiency's inheritance is autosomal recessive and its incidence is about 1–3/1,000,000. The form of bleeding can be seen in a wide spectrum, from life-threatening bleeding (such as intracranial bleeding) to skin bleeding. Umbilical cord hemorrhage and soft tissue hematoma is the most common and often first symptom of factor XIII deficiency (1). Lifelong bleeding diathesis can be seen in hereditary FXIII deficiency. Especially subcutaneous bleeding (57%), delayed umbilical cord bleeding (56%), muscle hematoma (49%), postoperative bleeding (40%), intracerebral bleeding (34%) and recurrent abortion can be seen. Bleeding after trauma or surgery (12–36 h) is pathognomonic in factor XIII deficiency. (2) Diagnosis of factor XIII deficiency is difficult due to its rarity. Because standard clotting screening tests including prothrombin time (PT), activated partial thromboplastin time (aPTT), thrombin time (TT), platelet count or bleeding time are normal; therefore, specific factor XIII assays are required. For all these reasons, factor XIII deficiency remains one of the least diagnosed rare bleeding disorders (1).

Case report: 34-year-old male patient applied to the emergency department due to the swelling that developed after hitting his right arm on the door. He stated that he had a history of factor 13 deficiency. Fracture or fissure line was not observed in the patient's physical examination and direct radiography. Bleeding observed in skin and subcutaneous region. In the anamnesis, the patient stated that he had a history of skin-subcutaneous bleeding and hematoma after trauma. In hospital records, it was observed that he had posttraumatic intramuscular hematoma two times in the last 5 years (the largest is 75 mm × 25 mm × 40 mm). In these hematomas treatment; there was no need for factor XIII concentrate, it was regressed with fresh frosen plasma replacement. In the laboratory tests performed in emergency department; leukocyte value 12,370/μL, neutrophil 6720/μL, hemoglobin 16.7 g/dL, platelet 315,000, PT: 9.12 s, aPTT 23.2 s, INR 1.02 was detected. Fresh frozen plasma was replaced at a dose of 15 mL/kg. The patient, who did not have any additional systemic problem, was discharged by recommending polyclinic control.

Conclusion: Hereditary factor XIII deficiency is an autosomal recessive bleeding disorder with a serious course (4). Unlike other hereditary hemostatic protein deficiencies, clotting tests and platelet function tests are normal in factor XIII deficiency. For this reason, specific factor XIII assays should be performed and the factor XIII level should be checked. The basis of treatment is replacement of the missing factor with plasma, cryoprecipitate and FXIII concentrates (2). However, in cases where there is a serious decrease in factor XIII levels, prophylaxis strategies with factor XIII concentrate can be applied to minimize bleeding events (5). In cases with recurrent delayed bleeding after trauma, factor XIII deficiency should be considered if the clotting profile is normal (2).

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PP 20

Acute ischemic stroke presentation of otherwise asymptomatic covid-19 patient

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Objective: Coronavirus disease 2019 (COVID-19), first identified in Wuhan, China in December 2019, become widespread and may be mortal, especially in some high-risk group. Most of the reported experiences suggested that COVID-19 is associated with a distinct coagulation disorder resulting in fibrin thrombi within small vessels and capillaries. Data focusing on arterial thrombotic events is few. In milder COVID cases, both hemorrhagic and ischemic stroke may occur. Acute ischemic stroke seems to be higher than the rate identified among patients who visited the emergency departments (ED). On the other hand, SARS-CoV-2 has the potential for neurotropism. We here present a case who had neurological symptoms during pandemic days and has been diagnosed with imaging-proven ischemic stroke with COVID-19.

Case report: A 40-year-old female patient presented to the ED with an articulation of speech and numbness in the right arm and leg. She is not a smoker and denied any environmental exposure. Physical examination revealed fever and hypotension with a respiratory rate was 18 breaths/min. She had dysarthria, hypoesthesia, and frustrated hemiparesis on the right arm and leg. Oxygen saturation was 98% on room air. Mild normocytic anaemia and lymphopenia associated with a mild elevation in transaminases (AST 73 U/L, ALT 103 U/L) and in D-Dimer (1440 ng/ml) associated the clinical picture. Thoracic CT showed bilateral multifocal peripheral ground glass infiltrations (Picture-1). Conventional MRI imaging is consistent with acute ischemia of millimetre in size on the left parietal lobe (Picture-2). The patient was accepted as having COVID-19 and acute ischemic stroke. She commenced on hydroxychloroquine and azithromycin with enoxaparin. Nasopharynx swab sample was found to be severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) positive by RT-PCR. She did not progress to the hyperinflammation phase and discharged on 10th day of admission. One month later on, outpatient visit her neurological findings resolved, no weakness was detected.

Conclusion: For each patient with an acute stroke clinic, thoracic CT and SARS-CoV-2 PCR should be performed before transferring to stroke or neurointensive care unit. For our patient, she did not have apparent risk factors for stroke. She was nearly asymptomatic apart of the stroke-related clinic, which points to the direct effect of coronavirus on vascular endothelial cells apart of the relationship between inflammation and coagulopathic complications in COVID-19.

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LYMPHOMA

PP 21

Isolated primary spinal mucosa-associated lymphoid tissue (malt) lymphoma: a rare case report

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Objective: Mucosa-associated lymphoid tissue (MALT) lymphoma, also known as extranodal marginal zone lymphoma (MZL), is a subtype of indolent B-cell non-Hodgkin's lymphoma (NHL). MALT lymphomas are encountered mainly in mucosal organs such as the stomach, however, they can also be found in non-mucosal organs and tissue regions. MALT lymphoma of the spinal dura is a very rare condition. Here, we present the clinical presentation pattern, histopathologic and radiographic findings, treatment options, and response to treatment in a rare case of isolated primary spinal MALT lymphoma.

Case report: A 74-year-old male presented to our hospital with progressive weakness and loss of sensation in bilateral lower extremities, and fecal and urinary incontinence. Spinal MRI examination visualized an extra-axial mass lesion of approximately 45 mm × 11 mm between the vertebral levels T5 and T7. The lesion markedly compressed the spinal cord, severely narrowing the spinal canal and bilateral neural foramina. In order to ensure early decompression of the spine and histopathological diagnosis of the epidural mass, a total laminectomy of T6 and a subtotal resection of the mass were performed. On immunohistochemical examination of the mass, neoplastic cells showed: LCA(+), CD20(+), CD79a(+), PAX5(+), bcl-6(−), fascin(−), CD3(−), CD5(−), cyclin D1(−),CD23(−), CD138(−), kappa (−), lambda (−), MUM1(−), CD10(−), tdt(−), CD15(−), CD30(−), reticulin(−), and a Ki67 proliferation index of 20%; and the pathology department reported the findings to be consistent with MALT lymphoma of the dura. Following mass resection, FDG-PET CT) was performed to determine the extent of the disease, and other regions of the body did not show 18-FDG uptake. Bone marrow aspiration and biopsy showed that there was no infiltration. Only systemic chemotherapy was planned as the patient refused to undergo radiotherapy. A systemic combination therapy with R-CHOP protocol every 3 weeks and central nervous system prophylaxis with intrathecal cytarabine and dexamethasone were carried for the patient. After

two chemotherapy cycles, there was a significant improvement in motor weakness and the fecal and urinary function impairment. After a total of 6 cycles, spinal MRI and FDG-PET CT showed complete disappearance of the lesion. The patient remains in remission, at 1-year follow-up.

Conclusion: This report presents a case of primary spinal MALT lymphoma, which is extremely rare. Lymphoma should be considered in the differential diagnosis of patients who present with a spinal mass and the subtype of the lymphoma must be identified. The management of MALT lymphomas is quite heterogenous and there exist no universally-accepted therapeutic guidelines for this rare condition. A treatment option must be selected in consideration of the disease subtype, stage, and the clinical characteristics of the patient. In spinal MALT lymphoma, both local and systemic treatment options are available. Local treatments such as surgical resection or radiotherapy can achieve complete remission in patients with MALT lymphomas confined to a single site or at early stages. Systemic treatment is an option for patients who are not suitable for local treatment and appropriate patients may be administered systemic chemotherapy regimens that include anti-CD20 monoclonal antibodies.

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PP 22

Ir2 leading to complete remission in r/r richter syndrome – a case report

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Introduction: Relapsed and refractory diffuse large B Non-Hodgkin lymphoma (r/r DLBCL) is a severe condition with fatal outcome for the majority of the patients. (1) Richter Syndrome is defined as a transformation of chronic lymphatic leukemia in a highly aggressive B-Non-Hodgkin lymphoma, mainly DLBCL. 20% of Richters Syndromes are de novo DLBCL, implying comparable prognosis to other aggressive Non-Hodgkin Lymphoma, whereas 80% are clonally related to the CLL cells and imply a poor prognosis of one-year median overall survival. (2) Despite huge efforts that have been achieved recently by implementing CAR-T Cells for r/r DLBCL and transformed Follicular Lymphoma, treatment of r/r Richter syndrome remains desperate with poor outcome. Allogenic stem cell transplantation is recommended for eligible patients. The combination of Anti CD 20 Antibody Rituximab with IMiD Lenalidomide and Bruton-kinase inhibitor Ibrutinib iR2 has shown safety and efficacy in a breaking phase II study. (2)

We present the rare case of a patient with refractory DLBCL after CLL (Richter Transformation) who achieved complete remission with iR2 and was successfully transplanted.

Case report: Our by now 74-year old patient was first diagnosed with CLL in 08/2014. He showed ubiquitous lymph nodes and evidence of p53 mutation, Binet stage B & RAI I.

He was treated with Ofatumumab + Bendamustine in the first line, Rituximab + Idelalisib in first relapse and Ibrutinib in second relapse before evolving to highly aggressive B-NHL in 10/2019. Richters Syndrome was first treated with Standard Immunochemotherapy (R-CHOP), before switching to Rituximab + Ifosphamid + Etoposid + Carboplatin (R-ICE) for refractory disease. There was further progress (clearly progressive lymph nodes cervical) after first cycle R-ICE chemotherapy, we decided to treat with a combination of immunotherapy with the Anti CD 79a-Antibody Polatuzumab in combination with Rituximab. Unfortunately, we saw again progressive disease after three cycles, that lead to the decision of experimental application of Ibrutinib in combination with Rituximab and Lenalidomid.

We saw an immediate effect as Lactat-dehydrogenase normalized very soon and lymph nodes disappeared completely.

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PP 23

Primary spinal extramedullary diffuse large B-cell lymphoma presenting with initial spinal cord compression: a case report

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Objective: Extranodal lymphomas, by definition, can involve any organ or tissue. Brain parenchyma, spinal cord, eyes, cranial nerves, and meninx are extranodal regions that show involvement at much lower rates. It is quite rare for lymphoma patients to present to the hospital with symptoms and findings associated with spinal cord compression as the initial presentation. This condition can lead to irreversible autonomic dysfunction, and motor and sensory loss. Here, we present a rare primary spinal intradural extramedullary diffuse large B-cell lymphoma (DLBCL) case who presented with acute neurological symptoms and no findings of cerebral involvement or involvement at any other site.

Case report: A 41-year-old male patient presented to our hospital with thoracic back pain and progressive complaints of weakness, numbness and difficulty in ambulation in bilateral lower extremities. On spinal MRI examination, a well-circumscribed intradural extramedullary mass with a craniocaudal extension of 6 cm and an AP diameter of 1 cm that was isointense to the spinal cord on T1-weighted sequences and slightly hyperintense on T2-weighted series, and showed diffuse homogenous contrast enhancement after intravenous contrast agent injection was determined between the vertebral levels T6 and T8. In the surgical operation, the mass showed partial invasion of the vertebral bone and the surrounding muscle. The mass invading the dura was resected and laminectomy was performed at T6-T9. On histopathological examination of the mass, there was diffuse malignant

infiltration by large atypical lymphoid cells with prominent nucleoli and a coarse chromatin structure. On immunohistochemical examination, neoplastic cells showed; CD20 (+, diffuse), CD3 (–), MPO (–), Tdt (–), CD1a (–), S100 (–), ALK (–), CD68 (–), CK (–), actin (–), vimentin (–) staining, and the Ki67 proliferation index was 70%. The pathology department reported the mass to be consistent with a diffuse large B cell lymphoma (centroblastic type). Cervical-thoracic-abdominopelvic CT was performed to determine the extent of the disease, and no masses, organomegaly, or enlarged lymph nodes were detected. Bone marrow aspiration and biopsy did not show bone marrow involvement. The patient received chemotherapy consisted of R-CHOP and was administered with six cycles. After chemotherapy, radiotherapy was given at a total dose of 40 Gy as 2 Gy per fraction. The strength of the bilateral lower extremity muscle groups showed daily improvement and the patient was able to walk normally with two courses of chemotherapy, after approximately six weeks. The patient remains in remission without clinical or radiological relapse under follow up after nearly 3 years.

Conclusion: The differential diagnosis of patients who present with a spinal mass should be made carefully. It must be considered that, although rarely, DLBCLs can present as massive disease-causing spinal compression, and that clinically significant improvement can be achieved by timely and effective treatment. In patients who present with spinal compression, early decompression, particularly by means of surgery, is of great importance. Considering that spinal DLBCL is a malignant disease, appropriate treatment approaches play a vital role in achieving neurological recovery, longer survival times, and better life quality.

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PP 24

Comparison of 68ga-psma and 18f-fdg pet/ct uptake in different lymphoma

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Objective: Few reports have documented the uptake of radiolabeled Prostate-Specific Membrane Antigen (PSMA) in lymphomas.[1,2] It is not known how PSMA uptake varies among various histological subtypes and how it correlates with 18F-FDG uptake in lymphomas. This study aimed to compare 68Ga-PSMA and 18F-FDG in different lymphoma subtypes.

Methodology: Nine randomly selected patients with biopsy-proven lymphoma with a median age 43 (32–70) years, 5 female – were submitted to whole-body 18F-FDG and 68Ga – PSMA PET/CT (time interval: 1–6 days between procedures). Lymphoma subtypes included: nodular-sclerosis Hodgkin's lymphoma (HL; 2 patients); diffuse large B-cell lymphoma (DLBCL; 1); marginal-zone lymphoma (2); MALT lymphoma (ML; 1); follicular lymphoma (FL; 1); lymphoplasmacytic lymphoma (1); and B-cell non-Hodgkin's lymphoma, unspecified (BCNHL-U; 1). Eight patients were under initial staging and 1 (HL) with disease relapse after treatment. Two experienced nuclear physicians analyzed the images by consensus. The intensity of tracer uptake was visually classified as marked, moderate or mild. The affected sites (lymph node chains, spleen, diffuse bone marrow involvement and non-lymphatic focal lesions) were counted in both sets of images and their respective maximum SUV (SUVmax) were measured.

Results: PSMA PET/CT was positive in all patients except for one with ML. FDG PET/CT was positive in all patients. At visual analyses, FDG uptake was higher than PSMA uptake in all patients, except for one patient with BCNHL-U (both tracers with similar low-intensity uptake). The intensity of FDG and PSMA uptake was respectively classified as marked in 3/9 and 0/8 patients, moderate in 4/9 and 1/8 and mild in 2/9 and 7/8. One patient (FL) presented a "mismatch" uptake pattern with different parts of an extensive lesion presenting predominant uptake of PSMA or FDG. Brain infiltration in one patient (DLBCL) was more easily identified on PSMA than on FDG images. FDG detected a total of 58/58 and PSMA 43/58 affected sites in all patients with a median SUVmax of respectively 5.4 (2.0–31.1) and 2.8 (1.3–5.4), $p < 0.0001$. The median SUVs of the 43 lesions with uptake of both tracers was respectively 5.5 (2.0–28.9) and 2.8 (1.3–5.4) for FDG and PSMA, $p < 0.0001$.

Conclusion: Distinct lymphoma subtypes present PSMA uptake, with less intensity than FDG uptake. Although PSMA uptake is usually mild, several lymphoma subtypes might cause false-positive results in PSMA PET/CT performed to assess prostate cancer.

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PP 25

Prognostic value of pre-treatment neutrophil-lymphocyte and platelet-lymphocyte ratio in diffuse large B-cell lymphoma: a single-center experience

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Objective: The neutrophil-lymphocyte ratio (NLR) and platelet-lymphocyte ratio (PLR) as inflammatory biomarkers have emerged as prognostic factors for patients with cancer.

We aimed to explore the association between the NLR/PLR and prognosis in diffuse large B-cell lymphoma (DLBCL).

Methodology: The study was carried out retrospectively. A systematic search of the hospital database regarding DLBCL patients was performed between April 2004 and March 2019. Completely accessible data were included in the study.

Results: Overall, 122 patients included in the study. There were 64 males and 58 females. At the time of diagnosis, the mean age was 51.3 ± 14.3 years, whereas 26 (21.3%) were under 40 years, 26 (21.3%) between 40–49 years, 35 (28.7%) between 50-59 years, and 35 (28.7%) were over 60 years old. Approximately 50% were at an advanced stage. At the time of diagnosis, the mean NLR was 3.8 with an absolute neutrophil count of 4852.4/μL (0.600–16.000/μL), and the absolute lymphocyte count of 1757.9/μL (0.100–15.000/μL). The mean PLR was 213.6, with a mean platelet count of 250,000/μL (range 260,000–715,000/μL). ROC analysis gave the cut-off point for PLR as >152.86, and NLR >3.05. All patients (90.2%) received R-CHOP based therapy. The median follow-up time was 69 months (range 3–244). During the follow-up period, 8.2% of patients died. Patients with high NLR levels showed more frequent B symptoms ($p = 0.034$). Patients with high PLR levels had a statistically significant lower overall survival (OS) and progression-free survival (PFS) ($p = 0.012$ and $p = 0.004$, respectively). In patients with high NLR levels, the OS rate proved to be shorter, but this finding has not achieved a statistical significance. However, PFS was statistically significantly shorter ($p = 0.022$). In the multivariate analysis of PLR and clinical factors in terms of non-progressive survival, age, IPI score, and high PLR level are independent risk factors for non-progressive survival ($p = 0.013$, $p = 0.039$ and $p = 0.031$, respectively). In multivariate analysis of NLR and clinical factors, age and IPI score are independent risk factors for non-progressive survival ($p = 0.026$ and $p = 0.046$, respectively).

Conclusion: This study demonstrated that elevated pretreatment PLR was significantly associated with poor prognosis in DLBCL patients. PLR could be helpful as a potential prognostic biomarker to guide clinical decision-making and select individualized treatment strategies for DLBCL patients.

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PP 26

Two diseases in a single lymph node: nodular lymphocyte predominant hodgkin lymphoma and kaposi's sarcoma

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Objective: Kaposi's Sarcoma (KS) is the most common low-grade mesenchymal angioproliferative disease seen in patients infected with the human immunodeficiency virus (HIV). Lymph node involvement is rare in classical KS, but it is common in endemic and epidemic (AIDS-related) KS. Kaposi's sarcoma-associated herpesvirus (KSHV), also known as human herpesvirus type 8(HHV8), was first described in HIV-associated KS. Nodular lymphocyte predominant Hodgkin Lymphoma (NLPHL)is a rare lymphoma with an incidence of 0.1 to 0.2/100,000/y. Significant histological feature is the presence of CD20 (+) CD15 (–) CD30 (–) variants in a nodular infiltration lymphocyte pattern of Reed-Sternberg cells. The coexistence of Hodgkin's disease (HD) and KS is a rare condition.

Case report: A 41-year-old male patient presented to the hematology outpatient clinic with painless swelling in the left armpit. There were no B symptoms at the patient's presentation. He had a history of RAI due to hyperthyroidism in 2004 and using 100 mcg of Levothyroxine. He also had a history of 7 packs/year of cigarette (exsmoker) and alcohol use as a social drinker. On physical examination, a well-demarcated, flip, painless lymphadenomegaly (LAM) was detected in the left axillary region, and hepatosplenomegaly (HSM) was not spresent. The laboratory results were as follows: wbc: 8300 UL; 15.1 g/dL, lymphoyte: 1450 mm^3, plt: 197,000 UL, albumin: 4.5 g/L, calcium: 10.9 mg/dL, ldh: 156 U/L, uric acid: 6.5 mg/dL. The serological tests were negative, other biochemical parameters were normal. The peripheral smear of the patient was evaluated as normal morphology. An cxcisional lymph node biopsy was taken from the left axilla. The pathology result was interpreted as nodular lymphocyte predominant Hodgkin's lymphoma (NLP) classical type and Kaposi's sarcoma with diffuse HHV-8 positivity. Bone marrow biopsy revealed no Kaposi's or Hodgkin's lymphoma infiltration. PET-CT imaging was performed for lymphoma staging. Lymphoproliferative disease involvement was observed at the left axilla level 2, 3 in bilateral, cervial, left infraclavicular, retropectoral area and along the medial line of the spleen. It was evaluated as stage II S. No additional lesion was detected in the patient evaluated by dermatology for Kaposi's sarcoma. Gastroscopy and colonoscopy were performed for gastrointestinal tract involvement and evaluated with biopsy. Helicobacter Pylori was observed in gastroscopy and eradication treatment was given. No pathological finding was seen in colonoscopy. By evaluating as early-stage NLP Hodgkin's Lymphoma, the patient was initiated on radiotherapy.

Methodology: Except for the need for an impaired immune system for the development of KS, it is thought that the relationship of KS with HD may be related to common pathogenic mechanisms instead of a direct causal relationship.

Results: Recently, HD and KS development has been associated with EBV and HHV-8, respectively. Although there are cases of KS and classical HD coexistence in the same lymph node, the coexistence of KS and NLPHL subtype in the same lymph node is quite rare.

Conclusion: Although KS is most commonly associated with immunodeficiency due to HIV infection or other causes of immunosuppression, it was not associated with any immunodeficiency status in our case. Due to the fact that KS and NLPHL were present in the same lymph node as two separate primers and were not immunosuppressed, we presented our

case below. It was also unusual for KS to have primary lymph node involvement without cutaneous involvement.

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PP 27

Extranodal marginal zone lymphoma of the ocular adnexa

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Objective: Ocular manifestations of non-Hodgkin lymphoma are rare, and the diagnosis can be delayed because of nonspecific symptoms and a tendency to mimic the appearance of other ocular diseases. Suspicious presentations will require confirmation of the lymphoma through surgical biopsy. The aim of this study was to present an ocular non-Hodgkin marginal zone lymphoma without systemic involvement, which was successfully managed with external beam radiation.

Case report: A 77-year-old female developed redness and swelling in the right eye which was initially treated as a nodular episcleritis and applied to our outpatient clinic. When the situation did not resolve, a subsequent biopsy diagnosed a low-grade non-Hodgkin marginal zone lymphoma. Systemic involvement was not detected in the images performed. Magnetic resonance imaging did not demonstrate any uveal or orbital extension and no intraocular involvement was noted. The lesion was treated with 30 Gy external beam radiation for a total of 10 days, resulting in significant tumor regression. Six month after the radiotherapy, the tumor has not recurred, and there has been no systemic involvement.

Conclusion: It is not unusual for ocular adnexa lymphomas to masquerade as another clinical entity, sometimes making the initial diagnosis challenging. A biopsy to rule out malignancy should be considered. We wanted to present this case because it is a rare case.

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PP 28

Alk (–) anaplastic large cell lymphoma diagnosed by tongue root biopsy: case report

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Objective: Anaplastic large cell lymphoma(ALCL) which was described in 1985, is rare subtype among non-hodgkin lymphomas with rate of 2%. ALCL is located' mature T and NK neoplasms' group in 2016 WHO' mature lymphoid, histiocytic and dendritic neoplasms' classification. Besides ALCL subdivided into anaplastic lymphoma kinase (ALK) negative (–), ALK positive (+), primary cutaneous, group of associated with breast implant. CD30 and ALK are key molecules at pathology, diagnosis, treatment of ALCL. ALK (+) ALCL has a better prognosis than ALK (–) ALCL. Peripheral and mediastinal-abdominal lymphadenopathies (LAP), appears in more than half of patients. Approximately 60% of patients have extranodal involvement. The most common extranodal involvement sites are; skin, bone, liver, lung, spleen, bone marrow and soft tissue. Rare involvement occurs in the central nervous system and gastrointestinal tract. We wanted to our patient with ALK (–) ALCL diagnosed with tongue root biopsy in order to contribute to the literature.

Case report: It was learned that a-60-year old female patient applied to the otolaryngology department with the complaint of swelling in the neck, and in her detailed examination, tonsillectomy and tongue root biopsy was performed due to suspicious mass. The patient direct to us on the reporting of tongue root biopsy pathology as ALK(–) ALCL. PET-CT was taken for staging. As a result of PET-CT: left submandibular 15 mm × 8 mm LAP (SUVmax: 4.15), right submandibular 14 mm × 10 mm LAP (SUVmax: 6.32), left jugular 27 mm × 37 LAP (SUVmax: 15.91), left deep servical 11 mm × 8 mm (SUVmax: 10.35), left supraclavicular 13 mm × 10 mm (SUVmax: 15.08) was detected and there was no involvement in bone marrow biopsy. The patient was considered stage ll ALK (–) ALCL. A total of 6 cure of CHOEP (cyclophosphamide 100 mg/day, vincristine 2 mg/day, adriamycin 85 mg/day,etoposide 150 mg/day and methlylprednisole 100 mg/day) were planned. In the evaluation after 6 cure chemotherapy:the patient with complete remmision was followed up.

Conclusion: Although ALCL is rare, it is a disease that needs to be diagnosed and treated quickly due to its clinical course. Although skin, bone, liver, lung, spleen, bone marrow and soft tissue involvement are common, it should be kept in mind that it can be seen rare cases such as central nervous system, gastrointestinal system and tongue root as that our case. Protocols containing anthracycline such as CHOP/CHOEP (cyclophosphamide, doxorubucin, vincristine, prednisone/cyclophosphamide, doxorubucin, vincristine, etoposide, prednisone) form the basis of treatment. Non-CHOP induction strategies:ifosfamide, carboplatin, etoposide (ICE), autologous stem cell transplant/allogeneic stem cell transplant after ICE plus intrathecal methotrexate. Despite this protocols and new treatment agents (pralatrexate, ibrutinib, etc.) early diagnosis is very important at ALCL.

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PP 29

Polatuzumab based chemoimmunotherapy showing complete response in a patient of r/r diffuse large b-cell lymphoma

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Objective: Diffuse large B-cell lymphoma (DLBCL) is the most common subtype of non-Hodgkin lymphoma and it is curable in approximately half of cases with current therapy. However, some of the patients require 3 or more line of therapy. Optimal management for patients who experience two or more relapses of DLBCL is unknown. New treatment options are needed and are being investigated. One of them, polatuzumab vedotin (PV) is a monoclonal antibody that targets CD-79B. We would like to talk about a relapse refractory (R/R)-DLBCL patient who had received 4 previous line of therapy with a follow-up time of about 15 years and showed complete response to PV based chemoimmunotherapy.

Case report: The patient, 47 years old male was diagnosed with stage-IE DBBHL after orchiectomy in 2006 and received 6 cycles of R-CHOP chemoimmunotherapy. After the patient followed up for 8 years in complete remission, isolated central nervous system relapse confirmed by biopsy in 2014. A protocol including 3 cycles of high-dose methotrexate and cytosine arabinoside was applied to the patient. Since the patient failed mobilization with chemotherapy + granulocyte colony stimulating factor (G-CSF) and plerixafor + G-CSF, the treatment of the patient was completed with cranial radiotherapy. The patient followed in remission then developed a second relapse with an abdominal bulky mass that invaded the bladder, ureter and rectum in 2018. Relapse was demonstrated by a biopsy. Although more than 50% response was observed after 3 cycles of gemcitabine-oxaliplatin plus rituximab, there was a loss of response after 6 cycles. Radiation therapy was applied in 2019 and then ibrutinib was used. After radiation therapy and 3 months of ibrutinib treatment, the patient continued to be treated with ibrutinib with a response rate of more than 50%. In the 7th month of treatment a disease progression developed, and the patient was included in the Polatuzumab vedotin (1.8 mg/kg) + Bendamustin (90 mg/m^2) + Rituximab (375 mg/m^2) (Pola-BR) early access program in August 2019. After 3 cycles of PV based chemoimmunotherapy with complete response, the treatment of the patient was completed to 6 cycles in January 2020. Then, lenalidomide was started for maintenance therapy. The patient is still asymptomatic and being followed in remission.

Results: The general recommendation in relapse patients is autologous stem cell transplant (ASCT) after rescue chemotherapy. For patients with second or later relapse, relapse after ASCT and chemoresistant disease, prognosis is poor. The treatment options at this stage include if appropriate, allogeneic stem cell transplantation, monoclonal antibodies such as obinituzumab and PV, oral agents such as ibrutinib and lenalidomide, and CAR-T cell treatments. In June 2019, the FDA granted accelerated approval to polatuzumab vedotin with BR for the treatment of adults with RR-DBBHL who received a minimum of two rows of treatment. A trial that randomly assigned 80 transplant-ineligible patients to bendamustine plus rituximab (BR) versus BR plus PV reported that PV based treatment arm achieved superior outcomes. In our case with recurrent intraabdominal bulky disease, despite the 4th order treatment, dramatic response was obtained with Pola-BR.

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MYELOMA

PP 30

Isatuximab plus carfilzomib and dexamethasone vs. carfilzomib and dexamethasone in relapsed/refractory multiple myeloma (ikema): interim analysis of a phase 3, randomized, open-label study

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Objective: To demonstrate benefit of adding Isatuximab (Isa) to (Kd) vs. Kd in relapsed/refractory multiple myeloma (RRMM).

Methodology: In this Phase-3 study (NCT03275285), patients with RRMM and 1–3 prior lines of therapy were randomized 3:2 and stratified by number of prior lines and R-ISS to receive Isa-Kd or Kd. Isa-Kd arm received Isa (10 mg/kg IV) weekly for 4 weeks, then every 2 weeks. Both arms received K (20 mg/m^2 days 1–2, 56 mg/m^2 thereafter) twice-weekly for 3 of 4 weeks, and d (20 mg) twice-weekly. Treatment continued until disease progression or unacceptable adverse events (AE). Primary objective: increase in PFS of Isa- Kd vs. Kd, determined by an Independent Response Committee (IRC). Comparison between arms conducted through log-rank testing. Key secondary objectives: overall response rate (ORR), rate of very good partial response (VGPR) or better, complete response (CR) rate, MRD negativity-rate (10^5 by NGS), and

overall survival (OS). Key secondary endpoints tested with a closed test procedure. Safety data included treatment emergent adverse events (TEAE), hematological, and biochemistry results for all patients. Interim efficacy analysis is planned once 65% of total expected PFS events are observed.

Results: 302 patients (Isa-Kd: 179, Kd: 123) were randomized. Median age 64 (33–90) years; R-ISS I, II, III was 25.8%, 59.6%, 7.9% respectively; 44%, 33% and 23% had 1, 2 and ≥3 prior lines respectively; 90% and 78% had prior proteasome inhibitor and IMiD respectively; 24% had high-risk cytogenetics. At a median follow-up of 20.7 months and with 103 PFS events per IRC, median PFS was not reached for Isa-Kd vs. 19.15 months Kd; HR 0.531 (99% CI 0.318–0.889), one-sided $p = 0.0007$. Thus, the pre-specified efficacy boundary ($p = 0.005$) was crossed. PFS benefit was consistent across subgroups. ORR (≥PR) was 86.6% Isa-Kd vs. 82.9% Kd, one-sided $p = 0.1930$. ≥VGPR rate was 72.6% Isa-Kd vs. 56.1% Kd, $p = 0.0011$. CR rate was 39.7% Isa-Kd vs. 27.6% Kd. MRD negativity-rate (10–5) in ITT was 29.6% (53/179) Isa-Kd vs. 13.0% (16/123) Kd, descriptive $p = 0.0004$. OS was immature (events 17.3% Isa-Kd vs. 20.3% Kd). 52.0% Isa-Kd vs. 30.9% Kd pts remain on treatment. Main reasons for treatment discontinuation were disease progression (29.1% Isa-Kd vs. 39.8% Kd) and AEs (8.4% Isa-Kd vs. 13.8% Kd). Grade ≥3 TEAEs were observed in 76.8% Isa-Kd vs. 67.2% Kd. Treatment-emergent SAEs (59.3% vs. 57.4%) and fatal TEAEs were similar in Isa-Kd and Kd (3.4% vs. 3.3%,) and Infusion reactions were reported in 45.8% (0.6% grade 3–4) Isa- Kd and 3.3% (0% grade 3–4) Kd. Grade ≥3 respiratory infections (grouping): 32.2% Isa-Kd vs. 23.8% Kd. Grade ≥3 cardiac failure (grouping): 4.0% Isa-Kd vs. 4.1% Kd. As per lab results, grade 3–4 thrombocytopenia and neutropenia were reported in 29.9% Isa-Kd vs. 23.8% Kd and 19.2% Isa-Kd vs. 7.4% Kd, respectively.

Conclusion: Addition of Isa to Kd provided superior, statistically-significant improvement in PFS with clinically meaningful improvement in depth of response. Isa-Kd was well tolerated with manageable safety and favourable benefit-risk profile, and represents a possible new standard of care treatment in patients with relapsed MM. Data first presented at EHA 2020 virtual meeting, June 11–21st. Study sponsored by Sanofi.

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PP 31

Relapse of multiple myeloma presenting as extramedullary plasmacytoma surrounding the aorta: a rare case report

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Objective: Extramedullary plasmacytoma (EMP) defines soft tissue tumors that are characterized by plasma cell infiltration and develop secondary to hematogenous spread, in an anatomical site distant from the bone marrow (usually liver, skin, central nervous system, pleura, kidneys, lymph nodes, and pancreas) (3,4). The prevalence of EMP in MM patients is approximately 6–8% at diagnosis and approaches 10–30% during the course of the disease. Here, we present a case of relapsed MM concomitant with a large EMP surrounding the aorta, which is an extremely rare pattern of involvement.

Case report: A 66-year-old male patient presented to our clinic with back pain and weakness in the legs. The patient had been diagnosed with IgG kappa multiple myeloma six years ago. In the initial diagnosis, he had been evaluated as an ISS stage-II, transplant eligible based on clinical and laboratory findings. He had received monthly zoledronic acid, two courses of VAD and two courses of VD regimens. Subsequent to complete response, he had undergone aHSCT with high-dose melphalan for the purpose of consolidation. The patient had achieved complete remission under follow-up after aHSCT. The disease had relapsed approximately 4 years after the first aHSCT, and the patient had undergone another aHSCT with high-dose chemotherapy after a VCD chemotherapy regimen, and had been in complete remission under follow-up. He presented with the complaints stated above 18 months after the second transplantation. On physical examination, bilateral lower extremities showed weakness and impaired sensation. Spinal vertebrae were examined with MRI in consideration of the history of MM. On MRI examination, there were diffuse lytic lesions involving all spinal segments and the sternum, and a soft tissue lesion that involved the aorta-vascular structures in the retrocrural space at the level of T7-L1 and extended to the spinal canal and involved the spinal cord at the level of T8-10. An imaging-guided trucut biopsy was taken from the mass and the diagnosis was confirmed as plasma cell myeloma based on histopathological and immunohistochemical findings. Although the patient underwent 2 courses of Len-Dex, and subsequently, 2 courses of VRD, there was no reduction in the size of the plasmacytoma, and the patient was considered non-responsive. As a more aggressive regimen, a combination of VDT-PACE was administered. A very good partial response was obtained after two courses. The patient was not suitable for allogeneic HSCT because of poor performance status. The patient and his relatives were consulted, and it was decided to continue the treatment with chemotherapy agents.

Conclusion: In conclusion, EMPs, although infrequently, are encountered during the course of multiple myeloma and its relapse. EMPs can be found in very rare localizations. Symptoms vary depending on the anatomical localization of the masses or the dysfunctions that result from the direct mass effect or organ involvement. In this regard, radiological, laboratory, and histopathological evaluation of massive lesions during follow-up is important. Particularly, MRI can be effective as an imaging method in the diagnosis and close follow-up of patients with symptoms associated with extramedullary plasmacytomas.

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PP 32

A rare subtype of poems syndrome: IGG4 subtype

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Objective: There is very limited data concerning the relationship between POEMS syndrome and IgG4-related disease.

Case report: A 40 year-old male patient presented with a 3 month history of progressive weakness and numbness in his lower extremities, impotence, diarrhea and weight loss. Complete blood count was as follows: WBC: 7.3×10^9/L, Hgb: 16.5 g/L, platelet 543×10^9/L. Liver enzymes, renal function, electrolytes and routine urine examination were normal. Ig G level was 14.5 g/dL (normal: 7–16 g/L). Serum immunofixation electrophoresis showed IgG λ monoclonality. Endocrine laborotory tests showed hipergonadotropic hipogonadism. Echocardiography showed pericardial effusion. Abdominal USG showed hepatomegaly and splenomegaly measuring 200 mm and 174 mm on longitudunal axis, respectively. On contrast enhanced MRİ, a 6 cm × 3.5 cm mass showing bone destruction was detected in the left sacral ala extending into the pelvis. PET CT scan demonstrated high FDG uptake (SUVmax: 10.5) for the sacral mass lesion. Based on these findings, a diagnosis of POEMS Syndrome was considered. Funduscopic examination showed no papiloedema. Vascular endothelial growth factor (VEGF) was very high (>700 pg/mL, normal: <96 pg/mL). Trucut biopsy of the mass lesion consisted of a nonneoplastic fibrous tissue and a dense infiltrate of mature plasmacytes with dense eosinophilic cytoplasm and eccentrically placed nuclei. Also, perivascular accumulation of sclerotic collagen like substance was noted. On immunohistochemical staining, neoplastic cells showed diffuse positivity for Ig G and Ig G4. Neoplastic cells were CD138(+), κ(−), λ(+), CD38(+), CD30 (−), ALK(−), CD20(−), CD10(−), CD23(−), CD45(−), CD56(−), CD57(−). Bone marrow biopsy showed a 3% monoclonal λ(+) plasma cell infiltration. Diagnosis of POEMS syndrome was confirmed. Taking into consideration high IgG4 expression in the neoplastic mass, IgG4 levels in serum was checked and found to be high 6.34 g/L (normal <1.35 g/L).

Methodology: POEMS syndrome and IgG4 related diseases show similarities including organomegaly and systemic organ damage. Polyneuropathy and bone lesions associated with IgG4 related diseases has not been reported. PET/CT detects bone lesions and lymph nodes in patients with suspected POEMS syndrome. In IgG4 related disease on the other hand, PET/CT identifies multiple lymph node enlargements/organomegaly with normal metabolic activity.

Results: Our patient had an osteosclerotic mass lesion demostrated by PET/CT and histopathological examination. Our patient had high serum IgG4 level and showed IgG4 plasmacyte tissue infiltration, yet her plasmacytes were shown to be monoclonal by bone marrow immunohistochemical staining and serum immunofixation electrophoresis. Therefore, final diagnosis was POEMS syndrome but not IgG4 related disease.

Conclusion: We propose this patient has a subtype of POEMS syndrome because he showed high serum IgG4 levels and a monoclonal IgG4 plasmacyte tissue infiltration. Monoclonal hyperglobinemia is not a feature of IgG4 related disease. It is not clear whether IgG4-positive plasma cell tissue infiltration and elevated serum IgG4 concentrations are origins or outcomes of IgG4 related diseases. To our knowledge, this is the second presumed case of POEMS syndrome-IgG4 subtype. Further research and collecting more cases are essential. We suggest every suspected POEMS patient should be tested for their serum IgG4 concentration.

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PP 33

Monoclonal gammopathy of undertemined significance and solitary plasmacytoma: progression factors in population of gomel region in belarus

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Objective: To define progression factors of MGUS and SP in population of Gomel region in Belarus.

Case report: Solitary plasmacytoma (SP) and monoclonal gammopathy of undetermined significance (MGUS) are characterized by the presence of less than 10% of tumor cells in the bone marrow and the absence of CRAB criteria. Both diseases have a high risk of progression to multiple myeloma due to certain factors.

Methodology: The study included 106 patients: MGUS ($n = 90$) and SP ($n = 16$) of Gomel region (Belarus) in 2017–2019. The average age was 60.5 years; female patients prevailed All patients underwent aspiration biopsy with IPT and FISH, trepanobiopsy of the ilium wing with immunohistochemical examination of the bone marrow. (Bone marrow aspirates IPT and FISH, and biopsies were obtained for cytological and histopathological evaluation of PC infiltration, including immunohistochemical). The determination of the ratio of light chains of immunoglobulins (kappa/lambda) in blood serum was carried out. Results were assessed after 3 years of observation. The signs of progression include the appearance of any one of the CRAB-criteria.

Results: There were no statistically significant differences between groups of patients with MGUS and SP according to signs (presence of tumor plasma cells, CD95+, CD200+, CD27+,

CD56+, IHC of CD138+ plasma cells, presence of M-protein in bone marrow) (Fisher p ranged from 0.292 to 0.73). An aberrant phenotype or the presence of clonal plasma cells <10% in SP patients was detected in 31%. According to the secretion of immunoglobulins: with MGUS, IgG secretion (53.3%) was most common, with SP, we observed non-secretion variant (37.5%), IgG secretion (31.5%). During the observation period, disease progression into MM was recorded in 18.8% in SP and in 16% MGUS patients. Disease progression in SP patients was associated with the presence of cytogenetic changes (the presence of del13) in combination with IHC of CD138+ >10%, an abnormal ratio of κ/λ chains. High expression of CD27+ was observed. In one patient with SP (iliac plasmacytoma), the disease transformed into MM within six months in the presence of risk factors: clonal plasma cells in the bone marrow −3.1%, CD56+ 93.1%, CD95+ 3.8% by IPT, del13, IHC CD138+ 20%. With MGUS, disease progression was associated with the presence of a combination of CD138+ >10% (76.5% vs. 23.6%; $p < 0.0001$), CD95+ <20% (44.0% vs. 71.4%; $p < 0,083$), CD56+ >20% according to IPT (27.3% vs. 78.0%; $p < 0.0001$), loss of CD27+ expression (66.7%), abnormal ratio κ/λ of chains $p < 0.001$.

Conclusion: Our study showed that a combination of such indicators as the presence of cytogenetic changes (in particular, the presence of del13), CD138+ cells >10% according to IHC, CD56+ >20%, CD95+ <20% according to IPT in combination with an abnormal ratio of κ/λ chains can have prognostic value in transformation into MM in both MGUS patients and SP patients.

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PP 34

Poems syndrome: a "multifaceted" entity of plasma cell disorder

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Objective: The objective of this study is to reveal patients with misdiagnosed POEMS syndrome in the group of patients with polyneuropathy and to stratify the right form of the plasma cell disease. POEMS syndrome (polyneuropathy, organomegaly, endocrinopathy, M-protein, skin changes) is a rare paraneoplastic disorder caused by plasma cell proliferative disease. The exact incidence of POEMS syndrome is unknown as diagnosis of POEMS syndrome is prolonged and complicated due to variety and non-specific symptoms. In accordance to some sources the incidence of POEMS syndrome is 0.3 per 100,000, however the disease rate may be higher due to missed diagnosis. POEMS syndrome is a plasma cell disorder and the medications used for the treatment are similar to multiple myeloma treatment regimens. However this is a distinct entity with disease process nuances, that's why the selection of the right medication could be crucial for the wellness and survival of patient with POEMS syndrome.

Case report: The first case of POEMS syndrome is diagnosed in Armenia in 2019. The rate of plasma cell disorders that is mainly presented with multiple myeloma is 1.3 per 100,000 in Armenia. In the last decade there is a tendency of increasing of multiple myeloma cases in Armenia. This fact is associated with the improvement of diagnostic methods. The first reported patient with POEMS syndrome is a young men suffering of severe pain in the legs. He was diagnosed with chronic demyelinating polyneuropathy and treated with plasmapheresis and immunoglobulin for 6 months. No efficacy was observed. The progressive neuropathy and new symptoms such as edema, shortness of breath caused patients' disability and his admission to intensive care department. The CT scan, USD examination, bone marrow biopsy, echocardiography, serum protein electrophoresis, CBC, blood chemistry were performed. The examination results were not consistent with multiple myeloma disease, monoclonal gammapathy of undetermined significance (MGUS) and chronic inflammatory demyelinating polyneuropathy (CIDP). The deviations that were revealed during analysis were compared with POEMS syndrome diagnostic criteria and made the diagnosis of POEMS syndrome.

Methodology: 13 patients not responding to the standard treatment protocols for polyneuropathy and 4 patients not corresponding with classic multiple myeloma criteria were included in this study. The spectrum of standard examinations included bone marrow biopsy, immune fixation electrophoresis, CT scan, echocardiography, CBC, Blood chemistry, Interleukin 6 and Interleukin 12 levels detection.

Results: The results were promising. In 3 patients treated for polyneuropathy, not responding to treatment and taking morphine due to severe pain the blood electrophoresis revealed low quantity of monoclonal immunoglobulin (M-spike) with Lamda component detected by immune fixation and the CT show sclerotic lesions in the bones. 2 patients with uncommon myeloma symptoms such as specific pulmonary impairment show high level of Interleukin 6 and Interleukin 12, that can cause the pulmonary hypertension.

Conclusion: The new examinations must to be involved in the list of obligatory analysis for neurology disease. The spectrum of analyses (diagnostic criteria) adopted for plasma cell disorder have to be extended including echocardiography and analyses of interleukin 6 and interleukin 12 for the right diagnosis and target therapy.

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PP 35

Pomalidomide-dexamethasone in the management of heavily pretreated multiple myeloma

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Objective: Pomalidomide is a new generation IMID, with a very good compliance, thanks to oral administration, which can be used also in heavily pretreated patients, in a domestic setting.

Case report: In this retrospective observational trial, it has been evaluated efficacy and tolerance of pomalidomide plus dexamethasone (PD) as salvage regimen in heavily pretreated patients with relapsed and refractory MM (rrMM), whose prognosis is particularly severe.

Methodology: 57 patients (31 M/26 F), with rrMM, median age at diagnosis 69 years (r. 52–86), and median age at start of treatment 76 years (r.56–90) treated with several lines of treatments (median 7, r. 2–11), every refractory to all the drugs previously received (also Bortezomib, Thalidomide and Lenalidomide), received Pomalidomide-Dexamethasone (Pomalidomide 4 mg for 21 days, Dexamethasone 40 mg days 1, 8, 15, 22, pegfilgrastim day +8) every 28 days, until progression. ISS was equally distributed, and cytogenetic at relapse was evaluable in 14 patients. All the patients had previously been treated with schedule containing bortezomib and IMIDs. 63% (36/57) had undergone at least to a single ASCT. All patients were relapsed and refractory to last therapies received before PD.

Results: Pomalidomide was well tolerated, with grade 3–4 transfusion-dependent anemia in 58% (33/57) of patients, 44% (23/57) grade 3–4 neutropenia (pegfilgrastim in primary prophylaxis was given, no hospitalization was required, no septic shocks were observed), 40% (23/57) grade 3–4 thrombocytopenia without hemorrhagic events and transfusion-dependence. No severe extra-hematologic toxicity was observed. According to IMWG, ORR1 (≥PR) was 47.3% (27/57: 5 CR, 11 VGPR, 7 PR, 4 MR), but, considering that we are evaluating a cohort of heavily pretreated patients, with poor prognosis, another parameter should be considered, ORR2 (≥SD), considering stable disease as a successful result in progressive MM. ORR2 was 77.1% (17 SD). These can be considered as impressive result in this subset of patients. Oral treatment gives a really good compliance, in frail and unfit patients, and response, when present, is always really fast (median time to response: 2 months (r.1–6)), median OS from diagnosis was 94 months (range 21–234), median OS from start of pomalidomide was 9 months (range 1–25). Nine patients have surprisingly achieved a notable response (3 VGPR, 4 PR, 2 MR) after failure of novel agents (i.e. Carfilzomib, Daratumumab and Pomalidomide).

Conclusion: Pomalidomide-dexamethasone has shown significant efficacy and a very good compliance, thanks to oral administration, in a particularly severe setting of heavily pretreated patients, relapsed and refractory to all available therapeutic resources, also after failure of novel agents.

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PP 36

Carfilzomib-lenalidomide-dexamethasone in the management of lenalidomide-refractory multiple myeloma

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Objective: Carfilzomib is an epoxyketone proteasome inhibitor of second generation, proved to be effective and safe in relapsed and refractory Multiple Myeloma (rrMM), in combination with dexamethasone or lenalidomide and dexamethasone.

Case report: In this retrospective observational trial, it has been evaluated efficacy and safety of carfilzomib, in combination with lenalidomide-dexamethasone (KRD) as salvage regimen in patients with rrMM, refractory to lenalidomide, where lenalidomide-based regimens have no proven efficacy.

Methodology: 41 patients (23 M/18 F), with rrMM, median age at diagnosis 63.7 years (r. 43–82), median age at start of treatment 67 years (r. 48–84) previously treated with several lines of treatments (median 3, r. 2–11), underwent to KRD regimen (ASPIRE trial schedule) for a median treatment cycles of 8 (r 2–18). ISS was equally distributed, and all patients had previously been treated with bortezomib and IMIDs, and were refractory to this agents. 61% (19/31) of them had undergone at least to a single ASCT.

Results: According to IMWG criteria, after a median follow-up of 9 months (r. 2–18), ORR was 68.2% (28/41: 9 CR, 12 VGPR, 7 PR) with 5 progressive diseases (PD) and 8 patients in stable disease (SD): this can be considered as an impressive result in this subset of rrMM patients, refractory to lenalidomide. In particular, for 11 patients, KRD was, after having achieved at least a PR, a bridge to second/third autologous SCT. Median time to response was 1.3 months (r.1–4), median OS from diagnosis was 62 months (r. 9–170), median OS from start of Carfilzomib was 11 months (r. 2–18). Carfilzomib was well tolerated, with grade 2 anemia in 39%(16/41) of patients, successfully managed by ESAs, without necessity of blood transfusions; 29% (12/41) grade 3–4 neutropenia (pegfilgrastim in primary prophylaxis was given, no ospedalization was required, no septic shocks were observed); 34% (14/41) grade 2, 21% (9/41) grade 3 and 12% (5/41) grade 4 thrombocytopenia,

without hemorrhagic events and transfusion-dependency. Moreover, it was observed pneumonia in 39% (16/41) of patients, treated by common antibiotic drugs and always solved. A cardiac monitoring was performed for all patients: hypertension (grade 2–3) in 34% (14/41) of patients; fatigue in 39% (16/31) of patients.

Conclusion: Carfilzomib-Lenalidomide-Dexamethasone has shown significant efficacy in a particularly severe setting of patients, relapsed and refractory to all available therapeutic resources, also lenalidomide, and it could be considered as a bridge to a second autologous or allogenic SCT.

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PP 37

The relationship of hepcidin, soluble transferrine receptor, growth differentiation factor-15 and anemia in multiple myeloma

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Objective: Multiple myeloma is a malignant disease of clonal plasma cells and anemia takes part in most of the patients. Although it is similar to the anemia of chronic disease with many parameters, the exact mechanism has not been clarified. Hepcidin, Growth differentiation factor-15 (GDF-15), soluble transferrin receptor (sTfR) have been investigated in many forms of anemia, especially in chronic diseases and cancers. However, there are few studies investigating their role in anemia in myeloma. In this project, we aimed to determine the relationship between hepcidin, sTfR and GDF-15 levels in multiple myeloma patients and their clinical features such as anemia parameters and disease stage.

Methodology: This study was approved by Duzce University Faculty of Medicine Non-Invasive Ethics Committee with the decision dated 20.01.2015 and numbered 2015/110 and supported by Düzce University Department of Scientific Research Projects with Project number 2015.04.03.336. Multiple myeloma patients who were diagnosed at our hematology clinic were evaluated for the study. Among these newly diagnosed patients, those who received erythrocyte or whole blood transfusion, iron, B12 or folic acid treatment within the last month were excluded and total 28 patients were enrolled. A control group of 28 people was formed from the volunteers without any disease and fasting blood samples were taken from all participants. After reaching the targeted number of patients and control groups, serum hepcidin, sTfR and GDF-15 levels were obtained from these preserved samples by ELISA method.

Results: Although myeloma patients had significantly lower Hb and Hct levels compared to the control group (median Hb 9.95 vs. 13.40 g/dL and median Hct 30.35% vs. 40.00%, $p < 0.001$), none of the GDF-15, hepcidin and sTfR levels showed a significant difference between the myeloma and control groups. Among multiple myeloma patients, we found that the anemic subgroup had significantly lower hepcidin levels than the non-anemic subgroup ($p = 0.043$) but GDF-15 or sTfR levels were not different ($p > 0.05$). When the correlations were examined, GDF-15, hepcidin and sTfR levels showed correlation with each other, while GDF15 was positively correlated with creatinine and sTfR levels were positively correlated with many parameters such as LDH, CRP, ferritin, albumin, creatinine, Hb and ISS stage. None of the levels of GDF-15, hepcidin and sTfR had a significant effect on survival.

Conclusion: Our findings suggested that mediators of chronic inflammation may play an important role in myeloma anemia but there is not always a clear interaction as in chronic disease anemia, there may be mechanisms that include partial response deficiencies and accommodate variable responses according to the characteristics of the patient groups.

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OTHER DISEASES

PP 38

Serum & salivary ferritin levels in iron deficiency anemia is there is a difference?

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Objective: Iron deficiency anemia (IDA) is one of the most important nutritional deficiencies in Egypt. The assessment of serum ferritin has been the gold standard method in the detection of this disease But, this involves the drawing of venous blood, which is invasive and is sometimes physically and psychologically traumatic to the patients, and sometimes it is difficult to withdraw blood from hidden veins. This study is done to estimate and correlate the serum ferritin levels & saliva of patients with IDA. Thus, assessing the effectiveness of saliva as an alternative non-invasive diagnostic tool. This study is done to estimate, compare and correlate the Ferritin level in serum & saliva of iron deficiency anemia patients, to determine whether saliva can be used as a predictive marker to monitor the iron levels in iron deficiency anemia.

Methodology: 60 patients with iron deficiency anemia and 20 healthy subjects as control were chosen for the study. Quantitative estimation of serum and salivary ferritin was performed by solid-phase ELISA, hemoglobin levels were also estimated to confirm the anemic status of the patient.

Results: Increased salivary ferritin level in patients with iron deficiency anemia and negative significant correlation between the salivary ferritin, salivary/serum ferritin ratio, and serum hemoglobin and a significant negative correlation between serum and salivary ferritin.

Conclusion: Salivary ferritin is a noninvasive method for the detection of IDA with a good predictive impact.

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PP 39

Hepcidin level changes in type 2 diabetes

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Objective: Background: Diabetes mellitus is a group of metabolic diseases characterized by hyperglycemia resulting from defects in insulin secretion or insulin action, or both. Diabetes and its complications have become a major public health problem in the world and its prevention has become a public health priority. Hepcidin, a 25-amino-acid antimicrobial peptide, is the central regulator of iron homeostasis. Under normal circumstances, hepcidin expression and subsequent release into plasma prevents further absorption of iron from the duodenal enterocytes by preventing the efflux of iron by ferroportin channels, hence reduced amounts of iron delivery via transferrin to hepatocytes. In response to iron loading, hepcidin expression increased to prevent the further uptake of iron. Conversely, during iron deficiency, hepcidin expression decreased. Aim of the Study: Was to assess the possible changes of serum hepcidin that may occur in patients with type 2 diabetes. Objectives: Was to evaluate changes of serum hepcidin level in type 2 diabetes, assess possible relationships of serum hepcidin, iron status, hepcidin: Ferritin ratio and HOMA-IR in type 2 diabetes patients.

Methodology: This study consisted of randomized eighty subjects divided into four groups: Group 1: Included 20 patients with impaired glucose tolerance (pre-diabetes), Group 2: Included 20 patients with controlled diabetes, Group 3: 20 patients with uncontrolled diabetes, Group 4: Included 20 healthy volunteers.

Results: : Hepcidin: Ferritin ratio was statistically high in impaired glucose tolerance and low in uncontrolled diabetes with (p-value <0.001*) and normal in controlled diabetes and healthy volunteers. A significant negative correlation between hepcidin: ferritin ratio and HOMA-IR in impaired glucose tolerance with (p-value = 0.009*) was found.

Conclusion: Serum hepcidin affected by multiple factors so cannot be used for screening of type 2 diabetes. But hepcidin: Ferritin ratio could be a novel marker for early screening of patients with type 2 diabetes.

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PP 40

Chemotherapy delivering port-a-cath migration into the heart: a case report

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Objective: Chronically diseased patients who require long-term therapy through central venous access, a totally implanted central venous port systems are used. Such beneficial devises have life-threatening complications.

Case report: We report a 45-year-old Libyan female diagnosed with poorly differentiated gastric adenocarcinoma, underwent total gastrictomy with eso-jujenal anastomosis with port-a-cath placement to deliver chemotherapy. At the fourth cycle of chemotherapy, unfavourable event occurred; the catheter dislodged and migrated to the right cardiac chambers, which was successful removed by local anaesthesia with loop-snare technique via the right femoral vein.

Methodology: We report a 45-year-old Libyan female diagnosed with poorly differentiated gastric adenocarcinoma, underwent total gastrictomy with eso-jujenal anastomosis with port-a-cath placement to deliver chemotherapy. At the fourth cycle of chemotherapy, unfavourable event occurred; the catheter dislodged and migrated to the right cardiac chambers. The patient refused to reimplant Port-a-cath because of psychological trauma she has experienced, and to complement the chemotherapy cycles peripheral line was the option, which has health, social, and economical consequences.

Results: The port-a-cath was successful removed by local anaesthesia with loop-snare technique via the right femoral vein and the patient preference to complement the chemotherapy cycles through peripheral line after psychological trauma she experianced of the dislodgment and empolization of the port-a-cath.

Conclusion: Port-a-cath is beneficial devise has serious complications. To avoid dislodgment, displacement, and empolization developing of the port-a-cath is needed.

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PP 41

Reactive lymphocytes in blood film of a covid-19 iraqi patient: a case report

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Objective: Coronavirus disease 2019 (COVID-19) is a novel highly infectious disease with variable laboratory parameters changes. The disease is highly contagious and any delay in the diagnosis leads to an increased possibility of its spread. This study explores the use of blood film as a cheap, rapid and feasible laboratory test in the disease diagnosis. In low medical resources countries, this can be a crucial diagnostic method.

Case report: A 51-year-old Iraqi male had investigations done by Istishari Medical – private – Laboratory. He was diagnosed with COVID-19, of a moderate severity. The CBC showed normal hemoglobin of 15.71 g/dL (packed cell volume, PCV of 49.4%), WCC of 7.4×10^9/L, neutrophils of 5.3×10^9/L (71.7%), lymphocytes of 1.0×10^9 (14.1%), monocytes and platelets count 125×10^9/L. Serum ferritin of 664.0 μg/L (NR: 30.0–400.0), CRP of 59.0 mg/L (NR: <5.0) and D-Dimer of 0.27 mg/ml (NR: up to 0.5). The biochemical changes for the liver and renal functions expressed mild changes. Stained peripheral blood smear showed presence of many characteristic large atypical lymphocytes, constituting about 43% of the all lymphocytes (14.5% of the WCC). The most common subtype seen in the patient's blood film displayed a distinctive abundant pale blue cytoplasm, sometimes confined to its irregular margins which

indented by 'hug' the surrounding RBC. The nucleus exhibits loosely condensed chromatin with inconspicuous nucleoli. Less frequently, lymphoplasmacytoid lymphocyte was noticed in the stained blood smear. These cells showed ample pale blue unevenly stained cytoplasm with paranuclear of which contains eccentric nucleus with condensed chromatin.

Methodology: In this study, a peripheral blood smear of a COVID-19 patient was examined for the presence of abnormal leukocytes morphological changes.

Results: The blood film showed presence of atypical lymphocytes constituting about 43% of all lymphocytes (14.5% of the white cell count). This case report of COVID-19 patient represents an unusual feature of coronavirus family infections other than severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2).

Conclusion: This study shows that the presence of reactive lymphocytes in the patient's blood film can be a pivotal finding in the diagnosis of COVID-19. Additionally, it emphasized the importance of blood film examination as an essential hematological test for COVID-19.

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PP 42

A study of hematological disease prevalence in covid-19 pandemic: a single center experience

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Objective: In the present study we aimed to investigate the prevalence of hematological conditions and patient characteristics among a patient population diagnosed with the COVID-19 infection at our hospital during the COVID-19 pandemic.

Methodology: Our study enrolled patients older than 18 years of age who were diagnosed with COVID-19 infection by physical examination and various studies and managed as inpatients at our hospital designated as a pandemic hospital within a two-month period between 15 March 2020 and 15 May 2020. The patients' age and sex distributions, contact status, comorbidities, primary hematological disorder, polymerase chain reaction (PCR) smear tests, computerized tomographic findings, need for intensive care, treatments regimens, total length of clinic stay, and rates of discharge and mortality were retrospectively reviewed.

Results: We reviewed the medical records of a total of 1928 patients who were admitted to pandemic clinics with the diagnosis of PCR-positive COVID-19 or suspected COVID-19 during the prespecified two-month period. Among these patients, 963 (49.9%) were male, and 965 (50.1%) were female. Their mean age was 51.3 ± 21.4 (min–max: 18–99) years. Eleven (0.57%) patients had a hematological condition and were thus consulted with the hematology department. They consisted of 3 females and 8 males with a mean age of 64.7 ± 18.7 (min–max: 22–89) years. A review of their diagnoses identified 4 patients with chronic lymphocytic leukemia (CLL), 2 patients with acute myeloid leukemia (AML), 1 patient myelodysplastic syndrome (MDS), 1 patient with non-Hodgkin lymphoma (NHL), 1 patient with chronic immune thrombocytopenia (ITP), 1 patient with polycytemia vera (PV), and 1 patient with thalassemia intermedia. While 4 patients had not taken any treatment for a hematological condition prior to the COVID-19 infection, 2 patients had taken azacitidine, 1 patient hydroxyurea, 1 patient chlorambucil, 1 patient R-FC (rituximab- fludarabine, cyclophosphamide), 1 patient R-Benda (rituximab-bendamustine), and 1 patient CHOP (Cyclophosphamide, Vincristine, Doxorubicin, Prednisolone). Three patients had a history of contact with COVID-19. While all patients had pulmonary involvement on a thoracic computerized tomography, three of them had mild involvement. Four patients needed intensive care. Seven (64%) patients had at least one comorbidity such as diabetes, hypertension, or coronary artery disease. All patients were treated with hydroxychloroquine, azithromycin, and enoxoparine. Four patients showing signs of disease progression were administered favipirapir while a patient received IVIG and another one received plasma therapy. The mean length of hospital stay was 12.7 days (min–max 2–27). Three of 11 patients died.

Conclusion: "COVID-19" and the "pandemic" it has caused, every detail of which we have still not understood, is a significant global problem from every aspects. Alongside of particularly the elderly, the patient group with hematological conditions that are immunosuppressed due to conditions themselves or their treatment regimens are at particular risk of infection by the COVID-19 pandemic. Our study have shown that the prevalence of hematological conditions is about 0.5% among patients infected by COVID-19. Patients with hematological conditions taking utmost care of isolation measures, protecting themselves, having strong family support, and being accustomed to the isolation process make a significant contribution to such a low prevalence.

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PP 43

A case of malignant peritoneal mesothelioma as a rare cause of autoimmune haemolytic anaemia

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Objective: Nearly half of the cases of autoimmune haemolytic anaemia (AIHA) are associated with an underlying disorder that leads to immune dysregulation, and malignancies is one of them. Although AIHA is reported in patients with a wide range of haematological malignancies, most frequently in Chronic Lymphocytic Leukameia and Non-Hodgkin Lymphoma, only 1–2% are associated with solid organ malignancy. This case report highlights malignant peritoneal mesothelioma as a rare cause of autoimmune haemolytic anaemia.

Case report: We report a case of a twenty-nine year old female who initially presented to her general practitioner with a six month history of symptoms suggestive of irritable

bowel syndrome. Her blood count identified a significant anaemia (haemoglobin 53 g/L) and thrombocytosis (platelets 1260×10^9/L), and was thus referred to haematology clinic. She was diagnosed with IgG-C3d AIHA. The patient was started on prednisolone 1 mg/kg with a good initial response. To investigate the underlying cause, a whole body CT scan was performed, which identified significant abdominal ascites. Serum CA-125 was raised at 6715U/mL (range 0–35) and paracentesis revealed an LDH of 1203 SU suggesting underlying malignancy, but no malignant cells were found on the ascitic fluid cytology. The patient went on to have a PET scan, which confirmed FDG avid serosal disease, with update in the liver, omentum and peritoneum. Diagnostic laparotomy revealed widespread nodules on all serosal surfaces, and the biopsy confirmed a diagnosis of peritoneal epithelioid malignant mesothelioma. Whilst the patient had her workup with the oncology team, her AIHA became refractory to steroid treatment, and was commenced on Rituximab at 375 mg/m^2 weekly infusions. The patient did not respond to 4 doses of Rituximab, and continued to require regular transfusion support. She eventually started chemotherapy for the mesothelioma, which reduced the briskness of haemolysis, and reduced transfusion requirements; although haemolysis did not completely cease.

Conclusion: To our knowledge, this is the third case of AIHA with malignant peritoneal mesothelioma reported in literature. There is currently no established treatment for AIHA associated with solid organ malignancy. This case highlights the poor response to standard treatments, and only a partial response to the definitive treatment for the underlying malignancy.

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PP 44

Erdheim–Chester disease: a single center experience

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Objective: Erdheim-Chester disease (ECD) is a rare histiocytosis which has typical findings including central diabetes insipidus, restrictive pericarditis, perinephric fibrosis, and sclerotic bone lesions. ECD is primarily a disease of middle-aged adults, with a mean age of 46 years at diagnosis in the United States (range, 20–74 and 56 years in the French cohort (range, 29–86). The exact incidence is unknown due the lack of population-based mandatory reporting to national registries.

Case report: Patient-1 Patient-2 Patient-3 Patient-4 Patient-5 Sex Male Male Female Female Male Age at compilation 32 32 51 65 41 Age at diagnosis 28 29 48 64 37 Follow up from disease onset, mo 59 45 40 12 44 Constitional symptoms – – – – + Skeletal involvement + + + + + Extraskletal involvement + + – + + Cardiac involvement Coronary involvement – – – – – Pericardial involvement + – – – – Right atrial pseudotumor – – – – – Valvulopaty – – – – – Large vessel involvement – – – – – CNS involvement Central DI + – – + – SerebellarSyndrome – – – – – Extra–axial mass – + – – – Hypophyseal involvement – – – – Pulmonary involvement + – – – – Orbital involvement – – – – + Cutaneous involvement (xanthelasma) – – – – + Retroperitoneal involvement – – – – – Adrenal infiltration – – – – – Paranasal sinüs involvement – – – – – Maxillary involvement – – – – – Treatment + + + + + Peg IFN-α/IFN-α + – + + + Radiotherapy – – + – – Corticosteroids – – – – + Other – + – – +

Methodology: Data of five patients were retrospectively analyzed in our center. The mean age of the patients was 41.2 years (28–64 years) at the time of diagnosis. The mean follow-up period was 40 months (12–59 months).

Results: The patients were mostly diagnosed with the bone. The most commonly involved organ was the bone, followed by the central nervous system (CNS), heart, lung, periorbita, and skin, respectively. While bone involvement was observed in all patients, non-skeletal involvement was observed in 4 patients. Diabetes insipidus was detected in 2 patients. Patients received different treatments depending on the type of involvement and extent of the disease. Four patients received treatment with Peg-IFN, and one patient received radiotherapy due to the progression of the disease. Following excision of the mass, no recurrence was observed in one patient, and the patient was under follow-up without treatment. One of the patients was diagnosed with the disease before the first-line treatment with vemurafenib, therefore, a combination of vinblastine and methylprednisolone was used. However, a full response could not be achieved. IFN was used as the second-line treatment, and the patient was under follow-up with stable conditions. No patient passed away during the follow-up.

Conclusion: Of our patients, 60% were male, similar to the general epidemiological data. However, the mean age of our patients, who were American and French, were low. Evaluation of the expression levels of BRAFV600E was performed for three patients, but the results were negative. This may be due to the fact that one patient had overlapping entities with LCH and could not be evaluated with a method as sensitive as ddPCR, which is one of the most recent sequencing techniques. Although skeletal involvement was present in all patients, the absence of extra-axial involvement, such as life-threatening retroperitoneal involvement and adrenal involvement, was remarkable. Although the patients were BRAF V600E mutation negative and this made the conversion to vemurafenib therapy difficult, patients were followed up without progression during the conventional Peg-IFN therapy. Clinical profile and treatment approach algorithms of ECD

patients in Turkey should be created with longer follow-up and multi-center data collection.

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PP 45

Acute brucellosis presenting as leukocytoclastic vasculitis

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Objective: Brucellosis is a zoonotic disease caused by Brucella spp. bacteria that is transmitted to humans through contact with animal products and body fluids of animals. It is a multisystemic disease associated with variable clinical symptoms. Although cutaneous symptoms can rarely be encountered at presentation and during the course of the disease, the occurrence of cutaneous vasculitis is extremely rare. Here, we present a case that presented with purpuric eruptions and was diagnosed with brucellosis-induced leukocytoclastic vasculitis.

Case report: A 62-year-old female presented to our clinic with fatigue, tiredness, and eruptions on the anterior aspects of both legs that had persisted for two weeks. On physical examination, there were diffuse, non-palpable maculopapular eruptions on the anterior surfaces of both tibias. Detailed patient history revealed complaints of myalgia and arthralgia, lumbar pain, fatigue, and eruptions that had persisted for approximately one month. The patient was a farmer and worked in animal husbandry. Laboratory tests were as follows; hemoglobin level, 12.3 g/dL (range, 12–16 g/dL); white blood cell count, 5.92×10^9/L (range, 4–10×10^9/L); platelet count, 115×10^9/L (range, 150–400×10^9/L); lactate dehydrogenase, 240 IU/L (range, 120–246 IU/L); total bilirubin, 0.8 mg/dL (range, 0–1.1 mg/dL); creatinine, 1.23 mg/dL (range, 0.6–1.2 mg/dL); alanine aminotransferase, 12 U/L (range, <31 U/L); erythrocyte sedimentation rate, 86 mm/h (range, 0–15 mm/h); C-reactive protein, 26.3 mg/L (range, <5); prothrombin time (PT), normal; and activated partial thromboplastin time (aPTT), normal. HBsAg was negative, Anti-HCV was negative, Anti-HIV was negative, anti-nuclear antibody (ANA) was negative, rheumatoid factor was 19 IU/ML (range, 0–15), p-ANCA and c-ANCA were negative. Rose Bengal test performed due to clinical suspicion was positive. Brucella standard tube agglutination (STA) test was performed twice and was positive at a titer of 1/1280. A skin biopsy was taken from the purpuric lesions on the anterior aspect of the tibia. On histological examination; vascular structures in the dermis showed diffuse inflammation and neutrophilic and lymphocytic infiltration. On immunofluorescence examination; IgA: (–), IgM: (–), IgG: (–), C3: (–) and the results were consistent with leukocytoclastic vasculitis. Leukocytoclastic vasculitis could not be explained by medication use or infective endocarditis, and cryoglobulin tests were negative. The clinical picture was considered to be induced by acute brucellosis. The patient was started on rifampicin (600 mg/day PO), doxycycline (100 mg PO, q 12 h) as brucellosis treatment. Vasculitic lesions showed significant improvement after two weeks of follow-up. Complete recovery was achieved with 6 weeks of antimicrobial treatment for brucellosis and Brucella SAT titres declined to 1:40 after the treatment.

Conclusion: Brucellosis is associated with a wide variety of cutaneous symptoms. Various cutaneous lesions such as maculopapular lesions, papules, petechia, purpura, and papulonodular lesions can be observed. Cutaneous symptoms encountered at presentation or during the course of the disease, particularly vasculitic eruptions, are extremely rare. Further, these eruptions can sometimes resemble subcutaneous bleeding induced by a hemostatic defect. However, in regions where brucellosis is endemic, such as Turkey, brucellosis should certainly be considered in the differential diagnosis when vasculitis is unexplained and classic brucellosis symptoms are concomitant.

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PP 46

The frequency of anemia in the elderly patient population in Van Province, Turkey. A cross-sectional study

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Objective: Anemia is a common health problem among elderly patients and its prevalence increases with aging. Although it used to be considered as a natural consequence of aging in the past, many current studies indicate that anemia reflects a deterioration of health status and leads to unfavorable consequences if not treated. This study aims to determine the prevalence and morphological distribution of anemia among elderly patients who presented to the hospital during a certain time period.

Methodology: Hemogram parameters of all patients aged 60 or older who attended our hospital for any reason between April 2018 and October 2018 was reviewed. Anemia was defined according to the criteria by the World Health Organization (WHO), as a hemoglobin level lower than 12 g/dL in females and 13 g/dL in males. Cases of anemia were classified based on the mean corpuscular volume (MCV) results of the patients as microcytic, normocytic, or macrocytic. The prevalence and morphological classification of anemia were examined with respect to age and gender.

Results: Of 1192 total patients, 608 (51%) were female. The majority of the patients were in the 60–70-year range, with a rate of 60.3% (718). Mean age was 69.70 ± 7.55 years in females and 69.8 ± 7.15 in males, with no significant difference ($p = 0.680$). Anemia was detected in 340 patients (28.5%) in total. The rate of anemia was 24.8% in females and 32.4% in males, and the prevalence of anemia was significantly different between genders ($p = 0.004$). Mean hemoglobin level was found as 13 ± 1.89 g/dL in females

and as 13.7 ± 2.24 g/dL in males, with a significant difference between genders ($p = 0.001$). Mean MCV was higher in males than in females with a significant difference (84.98 ± 6.32 vs. 87.15 ± 7.28 fl, $p = 0.001$). According to morphological classification; 66 patients (19.4%) had microcytic anemia, 245 (72.1%) had normocytic anemia, and 29 (8.5%) had macrocytic anemia. Distribution of anemia across age groups revealed 169 (23.5%) patients with anemia in the 60–70-years age group, with a significant difference between genders (69 [18.2%] vs. 100 [29.6%], $p = 0.001$). The prevalence of anemia was different between genders in both the 60–70-years and ≥81 years groups; however, these differences were not statistically significant (respectively, 52 [14.6%] vs. 66 [18.5%], $p = 0.426$ and 30 [25.6%] vs. 23 [19.7%], $p = 0.295$).

Conclusion: In daily practice, determining the prevalence of anemia in the elderly patient group and, if possible, its distribution according to etiologic factors, may provide practical knowledge regarding the approach to be adopted towards patients in a certain region. In our study, the prevalence of anemia in patients aged 60 or older, and the distribution of anemia based on morphological classification were determined. The major limitation of this study is that etiologic distribution could not be revealed. However, we think that our study still provides important insight and awareness regarding the elderly anemic patient population in our region. It will contribute to the studies that will be conducted in the same region.

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PLATELET DISEASES

PP 47

Effect of helicobacter pylori infection on the first-line treatment outcomes in patients with immune thrombocytopenic purpura

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Objective: In immune thrombocytopenic purpura (ITP) patients, studies in the literature have generally focused on the effects of the eradication of Helicobacter pylori (H. pylori) infection on increasing the platelet count in ITP patients, and the effect of H. pylori positivity on the response to conventional first-line treatment is not clear. This study aims to determine whether or not the response to the first-line treatment is affected by the states of H. Pylori-positivity and -negativity in ITP patients.

Methodology: The diagnosis of ITP was confirmed according to the Consensus Report on the Investigation and Management of Primary ITP. Untreated adult newly diagnosed or chronic ITP patients were included. H. Pylori-positive and -negative patients were categorized into two groups. Fecal antigen testing was used for the diagnosis of H. pylori infection in all patients. Patients who had received eradication therapy for H. Pylori infection were excluded from the study. The bleeding symptoms were evaluated according to the International Working Group (IWG) bleeding scale. Demographic data of the patients at diagnosis, presence, and severity of bleeding, initial platelet count, administered treatments, treatment response rates, and post-treatment platelet count were inspected.

Results: Of 119 total patients, 66 (55.5%) were female, 32 (26.9%) were H. pylori-positive, 87 (73.1%) were H. pylori-negative. H. pylori-positive and H. pylori-negative groups were not significantly different in terms of age ($p = 0.127$), gender ($p = 0.078$), diagnosis status ($p = 0.094$) and the distribution of bleeding symptoms ($p = 0.712$). The most common treatment was standard-dose steroid in both groups (62.5% vs. 68.9%, $p = 0.524$). Rates of complete response, partial response, no response were comparable for the two groups (respectively, 75% vs. 73.6%, and 18.8% vs. 19.5%, and 6.2% vs. 6.9%), and there was no significant difference between the groups ($p = 0.283$).

Conclusion: The diagnosis of ITP was confirmed according to the Consensus Report on the Investigation and Management of Primary ITP. Untreated adult newly diagnosed or chronic ITP patients were included. H. Pylori-positive and -negative patients were categorized into two groups. Fecal antigen testing was used for the diagnosis of H. pylori infection in all patients. Patients who had received eradication therapy for H. Pylori infection were excluded from the study. The bleeding symptoms were evaluated according to the International Working Group (IWG) bleeding scale. Demographic data of the patients at diagnosis, presence, and severity of bleeding, initial platelet count, administered treatments, treatment response rates, and post-treatment platelet count were inspected.

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PP 48

Safety of caplacizumab in patients without documented severe adamts13 deficiency during the hercules study

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Objective: To describe the safety of caplacizumab in patients enrolled in HERCULES for whom the diagnosis of aTTP was not confirmed based on documented severe ADAMTS13 deficiency.

Methodology: In HERCULES (NCT02553317), ADAMTS13 was measured at study baseline (following initial TPE), weekly following cessation of daily TPE during the treatment period, and twice during the follow-up period. Data from patients for whom the diagnosis of aTTP was not confirmed based on documented ADAMTS13 levels <10% were extracted and analyzed descriptively for efficacy and safety outcomes, with a focus on bleeding events.

Results: Overall, 7 patients in the placebo group (9.6%) and 13 patients in the caplacizumab group (18.1%) had a baseline ADAMTS13 ≥10%; of these, 4 and 9 patients, respectively, had a prior medical history of aTTP and/or ADAMTS13 values <10% at other time points during the study. This left 3 patients in the placebo group and 4 patients in the caplacizumab group for whom the diagnosis of aTTP could not be confirmed based on subsequent ADAMTS13 values or prior medical history, suggesting a diagnosis other than aTTP. Baseline ADAMTS13 levels were >60% for all patients and remained well above 10% throughout the study period. Possible alternative diagnoses included pancreatitis-induced TTP in 2 patients. One patient was reported as having 'thrombotic microangiopathy' and discontinued study drug treatment after 4 days (but continued daily TPE). The fourth patient had a report of 'megaloblastic anemia' and 'general adenopathies' and was withdrawn from the study due to a 'non-TTP diagnosis' after 2 days. The patients who continued daily TPE achieved a platelet count of $>150 \times 10^9$/L. Two patients experienced a moderate bleeding-related serious adverse event (SAE), 1 case of 'gastric ulcer hemorrhage' (considered unlikely related to study drug and recovered without intervention) and 1 case of epistaxis that led to study drug discontinuation (considered possibly related to study drug and recovered without intervention). Other mild bleeding-related non-serious adverse events (AEs) were reported in 1 patient: gingival bleeding (possibly related), ecchymosis (possibly related), and rectal hemorrhage (not/unlikely related). All events recovered spontaneously without intervention. Two other non-bleeding related SAEs were reported in 2 patients, both considered unrelated to study drug: 1 case of bacteremia and 1 case of cardiac tamponade.

Conclusion: The experience of caplacizumab in patients with a suspected non-aTTP diagnosis to date is limited, and so no definite conclusion can be drawn. Bleeding-related AEs were reported in 3 of the 4 patients; however, the type, nature and manageability of these events appear similar to those reported in the other patients in the study. Data first presented at American Society of Hematology annual meeting, December 7–10, 2019. Study sponsored by Sanofi.

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PP 49

Caplacizumab induces fast and durable platelet count responses with improved time to complete remission and recurrence-free survival in patients with acquired thrombotic thrombocytopenic purpura

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Objective: To characterize the durability of platelet count responses in the HERCULES trial.

Methodology: In this post hoc analysis of the HERCULES (NCT02553317) intent-to-treat population (caplacizumab, $n=72$; placebo, $n=73$), we identified patients with a fast platelet count response (i.e., ≤3 days vs. >3 days) and described the exacerbation rate by treatment group. Time to durable platelet count response (defined as time to last daily TPE during the overall treatment period), time to complete remission (defined as platelet count $>150 \times 10^9$/L and lactate dehydrogenase <1.5 × the upper limit of normal for >30 days after cessation of daily TPE), and recurrence-free survival (absence of exacerbation or relapse during the overall study period) were calculated.

Results: More than half of the patients in the HERCULES trial achieved an initial platelet count normalization within 3 days (caplacizumab, 56/72 [78%]; placebo, 43/73 [59%]). In patients with a fast platelet count response (ie, ≤3 days), the exacerbation rate was 3.6% (2/56) with caplacizumab and 44.2% (19/43) with placebo, suggesting that the rapid platelet count response was sustained with caplacizumab, whereas almost half of the fast responders in the placebo group subsequently exacerbated. In patients with time to platelet count response >3 days, the exacerbation rate was 6.7% (1/15) with caplacizumab and 30.0% (9/30) with placebo, confirming the durable response with caplacizumab. The exacerbation rate among placebo patients with platelet response >3 days remained high but was numerically lower compared with fast responders. Of the patients who experienced exacerbations, 90% (2/3 in the caplacizumab group and 26/28 in the placebo group) switched to open-label caplacizumab, which may have favored the outcomes of placebo patients. Despite this bias, the median (95% CI) time to durable response was 4.5 (4.4–4.6) days with caplacizumab and 10.5 (6.5–14.5) days with placebo; accordingly, the median (95% CI) time to complete remission was shorter in the caplacizumab group (40.0 [37.7–41.1] days) compared with placebo (44.2 [42.0–48.2] days). The analysis of overall recurrence-free survival during the entire study period demonstrated an early and sustained benefit for caplacizumab over placebo, mainly driven by significant reduction in exacerbations during the study drug treatment period. The effect was sustained, despite six relapses in the caplacizumab group in the follow-up period in patients with unresolved underlying autoimmune disease activity.

Conclusion: Caplacizumab demonstrated a faster and sustained platelet count response compared with the placebo group, in which many fast responders subsequently had an exacerbation. Fast platelet count responses with caplacizumab were maintained and translated into clinically relevant improvements in time to complete remission and overall recurrence-free survival. Data first presented at EHA 2020 virtual meeting, June 11–21st. Study sponsored by Sanofi.

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STEM CELL TRANSPLANT

PP 50

Transplant in aplastic anemia using combined G-CSF primed blood and bone marrow stem cells – a retrospective analysis

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Objective: Aplastic anemia is characterized by diminished or absent hematopoietic precursors in the bone marrow, most often due to injury to the pluripotent stem cell. In Pakistan, Aplastic Anemia is not uncommon and allogeneic hematopoietic stem cell transplant remains the only curative option in these patients. We aim to determine the transplant outcome of combined, G-CSF primed blood and bone marrow grafts in adult and pediatric patients with aplastic anemia.

Methodology: We retrospectively collected data of all transplant procedures performed from 2004–2019 at Aga Khan University Karachi, Pakistan. Variables analyzed included type of transplants, age, gender, type of stem cells used, conditioning regimens and overall survival for patients undergoing transplant in aplastic anemia.

Results: A total of 351 transplants were performed during the study period. Out of these, 239 were allogeneic transplants whereas 112 were autologous procedures. There were 254 males and 97 females. The main indications for allogeneic stem cell transplant were aplastic anemia (70), acute leukemia (58) and beta thalassemia major(40). Out of 70 patients with aplastic anemia, 52 were males and 18 were females. 38.6% percent of patients were from pediatric age group. The median age ± SD was 17.5 ± 9.4 years (range: 2–43 years). Cyclophosphamide/ATG was used as a conditioning regimen in 67 patients, while ATG/cyclophosphamide/fludarabine was used in 2. Haploidentical transplant was done in 1 patient. Twenty seven percent of patients underwent sex-mismatched procedures. In 52 patients, a combination of GCSF primed blood and bone marrow stem cells were used. The mean CD34 count was 5.2 × 10/kg. GVHD prophylaxis was done with cyclosporine and methotrexate. All patients received standard infection prophylaxis. Engraftment was achieved in 75% of patients. The median day of myeloid engraftment was 15 (range 10–22 days). Chronic GVHD was present in 3 patients while 4 had acute GVHD. The overall survival was 71.2% (median duration of 80 months). The causes of mortality included gram-negative sepsis (5), graft versus host disease (4), graft failure (4), disseminated fungal infection (2), intracranial bleed (2), bleeding diathesis (2) and transplant associated microangiopathy (1).

Conclusion: Combination of blood and bone marrow stem cells results in early engraftment with decreased frequency of GVHD in aplastic anemia. The overall survival was comparable to international literature.

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PP 51

Comparison of single and double autologous stem cell transplantation in multiple myeloma patients

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Objective: Multiple myeloma (MM) is the second most common hematological malignancy and autologous stem cell transplantation (ASCT) is one of the standard treatment of choice for eligible MM patients. The role of double ASCT as a treatment in patients with MM and its superiority over single ASCT are still a matter of discussion. Herein, we aimed to analyze MM patients at our center and compare the clinical outcomes of single and double ASCT patients.

Methodology: This study has been designed retrospectively. The patients who were diagnosed as multiple myeloma and had undergone ASCT in Hacettepe Hematology Department between the years 2003–2020 were evaluated.

Results: Disease assessment after ASCT stable or progressive disease, partial remission, very good partial or complete remission in single and double ASCT groups were 62/44/105 and 8/4/5, respectively, p: 0.22. Among the double transplanted patients, five of them were transplanted within 1 year after the first transplant. The median duration between the first and second transplant was 1322 (414–4242) days in double ASCT patients. OS duration of the single and double transplanted groups were 4011 ± 266 versus 3526 ± 326 days, respectively, p: 0.33. There was no statistically significant difference between OS durations of single and double ASCT patients. Only 4 patients had died from TRM in single ASCT group, whereas no patients had died from TRM in double ASCT group. Progression free survival durations of the single and double transplanted groups were 2344 ± 228 versus 685 ± 120 days, respectively, p: 0.22. There was no statistically significant difference between PFS durations of single and double ASCT patients. The factors that are related with the OS of double ASCT patients were analyzed. In univariate analysis, serum calcium levels and IgA type M protein were found to be related with OS of double ASCT patients (p: 0.09 and p: 0.06, respectively); however this relationship was not found in multivariate analysis. In univariate analysis, serum uric acid levels and beta-2 microglobulin were found to be related with PFS of double ASCT patients (p: 0.04 and p: 0.07, respectively); however this relationship was not found in multivariate analysis.

Conclusion: ASCT remains to be one of the main treatment options in MM. Many studies tried to find the best way of this procedure to maximize the benefit for the patients. Given the survival benefits observed with ASCT, trials have evaluated the use of additional intensive chemotherapy followed by a second ASCT. The recent general opinion among clinicians is that a second ASCT tends to be a feasible and rational treatment choice, particularly in patients with high risk MM. In the present study, it has been demonstrated that there seems to be no benefit with double ASCT in MM patients in terms of disease response rates and PFS and OS durations over single ASCT. Our study points out that the double ASCT treatment option in MM may not be effective as suggested, especially in the era of novel MM drugs. Further prospective larger studies are needed to clarify the role of double ASCT especially in high risk MM.

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PP 52

Are the hemoglobin values different after sex-mismatched allogeneic stem cell transplantation?

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Objective: Allogenic hematopoietic stem cell transplant (HSCT) is used as a curative treatment approach in many hematological diseases. Allogenic HKHN made for nearly 30 years bone marrow microenvironment and stroma after transplantation are known to protect the recipient identity. It is well known that if sex mismatch allogeneic HSCT is performed from multipar women to men, graft-versus-host disease frequency and therefore transplant related mortality is increased. Inborn difference and its change after transplant in hemoglobin (Hb) levels between male and female did not draw attention on a scientific basis. The aim of this study to analyze Hb and red cell distribution width (RDW) changes after mismatch allogeneic HSCT.

Case report: 18–72 years old 62 cases with acute leukemia were included in this study, between 2016–2019. All of them underwent allogeneic HSCT with used conditioning regimens like myeloablative or non-myeloablative or RIC (reduced-intensity conditioning) and were in the first complete remission.

Methodology: The patients were divided into four groups according to the transmitter and gender compliance, as well as demographic features; MM (male to male), MF (male to female), FF (female to female) FM (female to male). Hemoglobin and red cell distribution (RDW) interval differences were evaluated before and after transplantation.

Results: There was no significant difference between groups in terms of age and performance status. The mean Hb level was significantly increased in all patients from 9.16 g/dL to 12.34 g/dL ($p < 0.0001$) after transplantation. The average RDW before transplantation was 16.60% after transplantation was 15.57%. When the mean Hb values at 12 months were compared with post-transplant, it was found to be 12.79 g/dL and 12.99 g/dL in male recipients and female recipients respectively. While mean values of male recipients were 15.78% and 15.02% in the MM group and FM group, it was observed that female recipients were 13.43% and 15.13% in the FF group and in the MF group, respectively. While the male recipient

therefore male stromal structure was terminated with >12 g/dL Hb values at 12 months, the mean value in female recipients was <12 g/dL. Male allogeneic HSCT recipients are more fortunate than women in this respect but in the study, no significant difference was found between women who have male donors and gender-matched sex in hemoglobin elevation.

Conclusion: In our study, no significant difference was found between women who have male donors and gender-matched sex in hemoglobin elevation. Finally, we think that in patients with both male and female donors, it can be concluded that the recipient's hemoglobin value may be higher by choosing a male donor.

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PP 53

Experience of istanbul faculty of medicine bone marrow bank: periodical activity documentation

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Objective: Unrelated stem cell transplant (SCT) is an option for patients who have no available related donor, and a transplant is the best treatment modality for them. We aimed to document our bone marrow bank activity to define the proficiency and unmet requirement.

Methodology: We retrospectively screened the medical records from electronic files. The data from 2016 until 2019 were collected. The statistical analysis of the patients who presented for stem cell transplant, and of the healthy donors for demographic features, stem cell counts, stem cell sources, diagnosis, survival, GVHD, CMV, and HLA matches were performed using the SPSS 21.0.

Results: A total of 640 patient and donor pairs enrolled in the study. Most of the patients were adults ($n = 359$). Patients' mean age was 26.77 ± 21.06 years (range 0–74), and donor's 31.9 ± 9.6 years (range 24–75). The gender distribution was as male to female 377/263 for patients and 333/304 for the donors. The primary (43%) SCT indication was acute leukemia. Preference of stem cell sources was as follows; peripheral blood ($n = 450$; pediatric/adult: 137/313), bone marrow ($n = 161$; pediatric/adult: 130/31), and cord blood ($n = 8$; pediatric/adult: 8/0). In 21 cases, donor leukocytes were provided (pediatric/adult: 6/15). The total HLA tissue group compatibility between the patient and the donor was *10/10 in 47.8% of cases, *9/10 in 51.3% cases, and *8/10, *5/6, *6/8 in 9% of cases. The survival analysis showed no statistical difference between 10/10 and 9/10 HLA matched transplants. The sex match between patient and donor and the stem cell source has no significant effect on GVHD development ($p > 0.005$ and p: 0.226, respectively).

Conclusion: The outcome of SCT is effected mainly by HLA tissue compatibility, age, sex, and blood group match. Istanbul Bone Marrow Bank, with the HLA tissue typing laboratory, works internationally and provides stem cells since 1999 for SCT. With the collaboration of SCT centers, donor and stem cell source selection, and transfer is getting faster. The SCT outcome information is also a modulating factor to improve the quality of work. We, therefore, periodically document our activity and pursue to find a solution for getting better.

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TRANSFUSION MEDICINE AND APHERESIS

PP 54

Therapeutic plasma exchange in gastric signet ring cell carcinoma presenting as microangiopathic hemolytic anemia: a rare case report

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Objective: Cancer-associated microangiopathic hemolytic anemia (MAHA) is a rare but serious condition that is encountered in patients diagnosed with a malignancy. We describe a case of signet-ring cell carcinoma with a very rare presentation, namely a laboratory and clinical picture of MAHA, who demonstrated an effective thrombocyte level in response to therapeutic plasma exchange (TPE) therapy that was administered during the diagnostic period.

Case report: A 42-year-old male patient was referred to our hospital by an external center due to the complaint of recurrent epistaxis in the recent days, leukocytosis, anemia, and thrombocytopenia detected in his complete blood count. Hemogram data included the following; hemoglobin, 8.2 g/dL; white blood cells, 12.9×10^9/L; platelet count, 25×10^9/L; mean corpuscular volume (MCV), 82 fl. Laboratory data included the following: lactate dehydrogenase (LDH), 2826 IU/L; total bilirubin, 4.7 mg/dL; indirect bilirubin, 3.4 mg/dL; and a negative result on the direct antiglobulin test (Coombs). Vitamin-B12, folic acid, serum iron, and total iron-binding capacity levels, transferrin saturation, and thyroid function tests were normal. Peripheral blood smear showed fragmented erythrocytes (schistocyte), findings of erythrodysplasia, polychromasia, poikilocytosis, and in some areas, normoblasts and reticulocytosis. Reticulocyte percentage was nearly 14%. The patient was suspected of having MAHA based on these clinical, laboratory, and peripheral smear morphologic findings. Further tests were conducted in order to determine the etiology, primarily, TTP. A serum sample was collected to determine plasma ADAMTS-13 activity and therapeutic plasma exchange (TPE) was started as a treatment. Bone marrow aspiration (BMA) and biopsy (BMB) performed to examine bone marrow infiltration by hematologic and nonhematologic malignancies did not determine malignant cell infiltration. Serologies for viral infections autoantibodies were negative. A cervical-

thoracic-full abdominal computed tomography (CT) scan was performed in order to detect malignancies. On abdominal CT, 1 to 2 lymphadenopathies of 15 × 12 mm in the peripancreatic and perigastric area and pathological wall thickening (2.5 cm) at the level of the gastric corpus were detected. Gastroduodenoscopy revealed an edematous, partly ulcerated lesion protruding from the mucosa that extended to the angularis from the gastric cardia. Gastric tissue biopsy report indicated poorly differentiated adenocarcinoma (signet-ring cell predominant). The case was accepted as MAHA secondary to gastric carcinoma (ADAMTS-13 activity tested earlier was within normal limits at 84%). While waiting for the results of the biopsy and the other tests, the patient underwent 14 sessions of TPE in total. Following TPE, platelet count increased from 25×10^9/L up to 162×10^9/L, fragmented erythrocyte rate in peripheral smear decreased more than 75% and other laboratory findings of hemolysis (LDH, bilirubin, etc.) significantly decreased. The patient was transferred to the medical oncology clinic for the chemotherapeutic treatment of the primary gastric carcinoma.

Conclusion: Malignancy-associated MAHA is generally linked to a poor prognosis and the optimal treatment is not known. However, there is evidence for the importance of promptly initiating an effective antineoplastic regimen and it is also noteworthy that administering therapeutic plasma exchange (TPE) therapy for the purpose of immunocomplex removal could be beneficial in patients with symptoms of bleeding and thrombosis.

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PP 55

A signet ring cell carcinoma presented as refractory acquired thrombotic thrombocytopenic purpura

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Objective: Microangiopathic hemolytic anemia (MAHA) can be observed as a paraneoplastic syndrome (PS) in certain tumors. MAHA related signet ring cell carcinoma (SRCC) of an unknown origin is very infrequent. Herein we present a SRCC case presented with refractory acquired thrombotic thrombocytopenic purpura (TTP).

Case report: 35 years old men applied to emergency service with fatigue and headache on January 2020. In his anamnesis he had a history of alcoholic pancreatitis. His physical examination was normal except the neurological symptoms which are temporary loss of consciousness and disorientation. His laboratory tests resulted as white blood cell 9020/μL, hemoglobin 3.5 g/dL, platelet 18,000/μL, MCV 110.7 fl, urea 58 mg/dL, creatinine 0.84 mg/dL, AST 68 u/L, ALT 33 u/L, indirect bilirubin 1.88 mg/dL, LDH 2257 u/L, reticulocyte 0.1, haptoglobulin <8 mg/dL, INR 1.42, Prothrombin time 13.2, fibrinogen 184 mg/dL, coombs negative. He had consulted to our clinic with bicytopenia and hemolysis. Schistocytes, micro-spherocytes and thrombocytopenia were observed in his blood smear. Microangiopathic hemolytic anemia was present and he was considered as thrombotic thrombocytopenic purpura. Plasma exchange treatment was initiated however he was refractory to this treatment. He had epistaxis and blurred vision during the follow-up. Superficial hemorrhages on the edges of the optic disc and roth spots were detected. Pain had emerged in his right arm. Doppler ultrasonography revealed the occlusion of cephalic vein with non-recanalized thrombus in the subacute process from the antecubital level at the forearm level. Thorax and abdomen computerized tomography (CT) resulted as liver 220 cm, spleen 14 cm, minimal pleural effusion, thickening of minor curvature in stomach corpus with hepatogastric and paraceliac lymphadenopathy. As a result of CT endoscopic examination was planned. Bone marrow investigation by our clinic resulted as the metastasis of adenocarcinoma. Ulcerations and necrosis was observed by gastric endoscopy procedure. Biopsy was taken during endoscopic intervention which resulted as signet ring cell carcinoma. He was transferred to oncology clinic for his treatment. Unfortunately he died in one month after his transfer.

Conclusion: Only 40% of TTP cases have the complete pentad and in 75% of the cases there is a triad of microangiopathic hemolytic anemia, thrombocytopenia, and neurological findings. In our case there was no acute kidney failure, however all the other features favored TTP, and diagnosis was made without the kidney failure. MAHA may be seen as a PS in some tumors, especially gastric cancers. Tumor related MAHA is generally accompanied by bone marrow (BM) metastases. As a result, BM investigation may be used as the main diagnostic method to find the underlying cancer. Total plasma exchange is usually performed in the treatment of cancer-associated TTP, however fewer than 20% of the cases respond to plasma exchange. Likely, our case did not respond to plasma exchange treatment either. The clinical course of cases with tumor related MAHA is usually poor, and these cases are usually refractory to plasma exchange treatment. In conclusion, physicians should suspect a malignancy and BM involvement when faced with a case of refractory TTP.

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PEDIATRIK HEMATOLOGY
HEMATOLOGY – GENERAL

PP 56

Health-related quality of life for children with leukemia: child and parental perceptions

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Objective: The importance of health-related quality of life (HRQoL) in patients with acute lymphoblastic leukemia (ALL) has increased in recent years. This study aimed to assess HRQoL in children with ALL, affecting factors, and the relationship between parent proxy-report and child self-report HRQoL.

Methodology: The study sample consisted of 2–12 years old children with ALL between November 2016 and May 2017 at the University of Health Sciences Ankara Child Health and Diseases Hematology and Oncology Training and Research Hospital, Department of Pediatric Hematology. Patients and their parents (both mother and father) were enrolled in this cross-sectional study. Turkish version of the Pediatric Quality of Life Inventory (PedsQoLTM) 3.0 Cancer Modules were used to determine HRQoL. Patients' diagnosis, risk group according to the ALL-IC BFM 2009 protocol [standard risk group (SR), intermediate-risk group (IR), high-risk group (HR)], treatment status, the period between the cessation of the chemotherapy to the study and total hospitalization period, was obtained from the patients' medical record. Demographic data regarding the information on parents' age, education level, employment status, monthly income, and chronic medical condition were noted. Cardiovascular diseases, cancer, asthma, diabetes mellitus, thyroid disorders, and psychiatric problems were classified as chronic medical conditions by the Centers for Disease Control.

Results: A total of 59 patients (52,5% male) with a mean age of 7.28 ± 2.67 years at study period and 4.02 ± 2.51 years at diagnosis were enrolled. 57 patients (96.6%) were pre-B ALL and two (3.4%) patients were T-ALL. According to the risk groups; 18 (30.5%) patients had SRG, 25 (42.4%) patients had MRG and 16 (27.1%) patients had HRG. There were not any significant differences between on-treatment and off-treatment groups, age at study period, age at diagnosis, gender. There was no significant relationship between total scores of PedsQL cancer module self-report and the leukemia or sociodemographic features. According to subscales of self-report form; nausea and operational anxiety scores differed significantly by the treatment status; communication score varied considerably by the total hospitalization period; pain and hurt, cognitive problems and perceived physical appearance scores differed significantly by maternal chronic disease status ($p < 0.05$). No significant relationship was found between the total scores of the PedsQoLTM-cancer module parent-proxy report (father) and leukemia or sociodemographic features. The presence of maternal chronic disease was significantly related to the total score of the PedsQLTM-cancer module parent-proxy report (mother) ($p < 0.05$). There was a moderate correlation between total scores of child and mother ($p < 0.05$, $r = 0.419$) but not with the father.

Conclusion: Children on-treatment had significant problems in nausea and procedural anxiety subscales; however, children who hospitalized more had fewer issues in the communication subscale. Also, children whose mother had chronic disease had poorer HRQoL regarding pain and hurt cognitive problems, and treatment anxiety. Given the importance of assessment and monitoring HRQoL in children with ALL, health professionals should be aware of how parents' chronic disease affects HRQoL. Psychosocial support should be provided to children and their parents, especially whose parents have a chronic illness.

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PP 57

Rare infectious agents in children with hematological disease

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Objective: Infections are among the most important causes of mortality and morbidity in immunocompromised children. Although, the microbiological agents are usually opportunistic infections, sometimes rare infectious agents can also cause severe clinical conditions. Here, we present eight different microbial agents that can rarely cause infections in children with febrile neutropenia.

Case report: Case 1 is a 5-year-old girl with acute lymphoblastic leukemia (ALL) had a bloodstream infection during the reinduction therapy. Candida pelliculosa was detected in the blood culture taken from the port catheter. The catheter was removed and the patient was successfully treated with caspofungin. Case 2 is a 1-year-old girl with acute myeloblastic leukemia had a bloodstream infection during the first induction therapy. Cronobacter sakazakii was detected in peripheral blood culture. The patient was treated with cefepime and amikacin without port removal. Case 3 is a 5 month old girl with hemophagocytic lymphohistiocytosis had a pneumonia during the HLH 2004 protocol. Nocardia asteroides was detected in the bronchoalveolar lavage fluid. The patient was treated with trimethoprim-sulfamethoxazole and meropenem, however, she died of sepsis and multiple organ failure. Case 4 is a 2-year-old girl with ALL had a sepsis during the consolidation therapy. Candida tropicalis was detected in the port catheter and peripheral blood culture and renal abscess had developed. The patient was treated with broad spectrum antibiotics however she died sepsis and multiple

organ failure. Case 5 is a 9-year-old male with ALL had a bloodstream and port catheter infection after the first induction therapy. Herbaspirillum huttiense was detected in the blood culture taken from the port catheter. The patient was successfully treated with meropenem without port removal. Case 6 is a 10-year-old girl with ALL had a bloodstream and port catheter infection during the second induction therapy. Ralstonia pickettii was detected in the blood culture taken from the port catheter. The catheter was removed and the patient was successfully treated with piperacillin-tazobactam. Case 7 is a 7 month old male with Juvenile myelomonocytic leukemia had a bloodstream and port catheter infection in the neutropenic period. The patient was constantly inserting the port catheter into her mouth. Staphylococcus salivarius was detected in the blood culture taken from the port catheter. Then, 5 day after, Rothia mucilaginosa was detected in the peripheral blood culture. The patient was successfully treated with meropenem without port removal. Case 8 is a 9-year-old girl with ALL had a infective endocarditis and sepsis during the induction therapy. Magnusiomyces capitatus was detected in the peripheral blood culture. The patient was treated with fluconazole and amphotericin-B, but she died of multi-organ failure.

Conclusion: Many different microorganisms can cause infections in immune-compromised children as a result of primary disease or chemotherapy. Though empiric antibiotic therapy should be initiated early, the treatment should be revised according to the antibiogram and catheter should be removed as needed.

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PP 58

Idiopathic hypereosinophilic syndrome associated pulmonary hypertension in a child

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Objective: Hypereosinophilic syndrom (HES) is defined by showing eosinophilic infiltration in any tissue or organ and increased eosinophils in peripheral blood. Other pathologies that cause eosinophil increase must be excluded. Pulmonary eosinophilic infiltration may have different symptoms and signs, but clinical presentation as PHT has not been shown in children.

Case report: A 6-month-old girl presented with dyspnea and hypoxia. A blood cell count and a morphological evaluation of a peripheral blood smear and confirmed hypereosinophilia (white blood cells 40,600/μL, eosinophils 18,900/μL, hemoglobin 10.3 g/dL, and platelets 425,000/μL). There was not any cellular morphological abnormalities in bone marrow aspiration examination. Pnomonia and parasites, allergic diseases, clonal abnormalities, cancer and vasculitis that might have caused HES were excluded. Echocardiogram showed 38 mmHg for pulmonary arterial pressure (PAP), suggesting pulmonary hypertension (PHT). After exclusion of other causes such as vasculitis, connective tissue diseases, bronchopulmonary displasia, congenital heart diseases, lung diseases, and chronic thromboembolic PHT. The patient was diagnosed with pulmonary arterial hypertension associated with idiopathic HES. Methylprednisolone treatment was started at 2 mg/kg/day. PHT and HES were both improved in the evaluation one month later.

Conclusion: Eosinophilic infiltration causes thickening and remodeling of the pulmonary artery intima and media, thereby causing pulmonary hypertension. Thus, PHT can be seen as HES clinical presentation. With corticosteroid therapy, HES and PHT clinical findings can be controlled.

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PP 59

A rare variant of dyskeratosis congenita: RTEL1 defect

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Objective: Dyskeratosis congenita (DC) is a rare hereditary disorder characterized by bone marrow failure, malignancy predisposition and skin findings. As the disease progresses, patients may develop pulmonary fibrosis, esophageal stenosis, urethral stenosis and liver cirrhosis. Herein, we present a patient who was referred with a diagnosis Diamond Blackfan anemia and was diagnosed to have dyskeratosis congenita on whole exome sequencing (WES).

Case report: A 18 month-old girl who was initially transfused at the age of three-months old and was on mothly transfusion programme, was referred to our center for molecular work-up with a diagnosis of DBA. There was second degree consanguinity between parents. On physical examination, body weight: 8.7 kg (5th percentile) height: 44 cm (<3rd percentile) was measured. Cubitus valgus was seen with camptodactyly. Liver and spleen were not palpable. Complete blood count showed hemoglobin (Hb) 7.9 g/dL, mean corpuscular volume (MCV) 104.1 fl, white blood count 6.9×10^9/L, absolute neutrophil count 1.3×10^9/L, platelet count 682×10^9/L, reticulocytes 2% and peripheral smear showed hypochromia and macrocytosis in erythrocytes. Biochemical parameters, globin electrophoresis, vitamin B12 and folic acid levels were normal. Parvovirus B19 was negative. ADA2 enzyme level was determined as 24 U/L (5–20 U/L). Steroid was started at the age of 18 month-old with a clinical suspicion of DBA. She became transfusion independent after steroid initiation. WES analysis for DBA from the patient revealed RTEL1 gene mutation (c.1368G> T p.1trp456Cys). This mutation was found compatible with DC and no other mutations in DBA related genes were detected, including CNV analyses for large deletions. Steroid was ceased gradually and she did not require further transfusions after complete cessation.

Results: In dyskeratosis congenita cases where the disease does not follow classical presentation, the use of genetic

testing confirms the diagnosis at an early stage and reduces morbidity and mortality due to the disease. WES is helpful to detect such cases.

Conclusion: Various genes such as DKC1, CTC1, RTEL1, TERF1, TINF2, TERC have been found to be responsible for DKC. RTEL1 is a DNA helicase necessary for telomere replication and stability. With the understanding of the molecular basis of the disease, patients with hematological findings at the time of diagnosis and those without skin findings were also identified. In our case, signs of bone marrow failure were observed primarily and no changes in nail dystrophy, leukoplakia and skin pigmentation and neurological findings were detected. In cases where the disease does not follow classical presentation, the use of genetic testing confirms the diagnosis at an early stage and reduces morbidity and mortality due to the disease. WES is helpful to detect such cases.

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PP 60

Acquired aplastic anemia in childhood: single-center experience

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Objective: Acquired aplastic anemia is a rare disease characterized by the irreversible loss of bone marrow function and threatens life when not treated. Bone marrow transplantation (BMT) or immunosuppressive agents (IST) are used in its treatment. In this article, we aimed to evaluate our patients with acquired aplastic anemia in epidemiological, etiological, and treatment outcomes.

Case report: Nine patients who were diagnosed with acquired aplastic anemia over ten years were evaluated.

Methodology: The patients admitted to the Istanbul Medical Faculty Pediatric Hematology-Oncology Outpatient Clinic between 2000 and 2010 were diagnosed with acquired aplastic anemia (those who underwent BMT, IST, or both) were evaluated retrospectively on patient files and computer records.

Results: Nine patients were diagnosed with acquired aplastic anemia over ten years. 4 of them were girls, and 5 were boys. The average age was 10 (1–17 years). There was a history of hepatitis in 3 cases and a history of metamizole use in 1 case. As a treatment, six patients were treated with IST, and five patients were treated with BMT. ATG 40 mg/kg/day 4 days, cyclosporin 10 mg/kg/day (6 months), methylprednisolone 2 mg/kg/day (2 months) and G-CSF 5 μg/kg (2 months) as immunosuppressive therapy. Response to immunosuppressive therapy was received at an average of 3 months. Two of them were fully responsive. One patient was lost due to septic shock before the IST response was evaluated. BMT was performed in 5 cases, three of them were unresponsive to IST. In the follow-up, two cases are in remission, and three are lost due to sepsis. When evaluating our 5 cases with dead, two of them were very severe aplastic anemia, the symptoms of sepsis were present in their first admission, and they died before the treatment started. Two of them died due to the complication of BMT in the very early period. One case was admitted with perforated appendicitis while in remission after BMT and died due to septic shock.

Conclusion: Two primary treatment modalities are used to treat patients with severe aplastic anemia; IST and BMT. The first option is BMT with the matched sibling donor. If there is no suitable sibling, IST is started first, and a fully compatible donor is searched immediately. If there is no response to IST, an allogenic BMT must be applied in the presence of a suitable donor. Our mortality rate is high compared to the literature because of severe disease presentation; most of them were late admission to the hospital due to low socioeconomic level.

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HEMOSTASIS, THROMBOSIS, AND VASCULAR BIOLOGY

PP 61

The course of intracranial bleeding in the patient with immune thrombocytopenia

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Objective: The approach to the treatment of immune thrombocytopenia always remains relevant, despite the fact that the etiology and pathogenesis of the disease is quite clear, and it is clear that the development of the disease is based on the conflict between their own platelets and autoantibodies directed at them. The goal of treatment is to resist the creation of autoantibodies, protect your own platelets and lengthen their life. The proposed standards of treatment with steroids, reticuloendothelial system blockers, anti-lymphocytic antibodies, thrombopoietin, etc.did not find a clear place for a radical change in the course of the disease.

Case report: The article presents a case of a child suffering from chronic ITP who received various medical treatments with periodic remissions for 6 years. At the age of 10, the child had convulsions and neurological disorders due to acute respiratory infection and high temperature. In blood tests: PLT-10×10^9/L. CT scan of the brain showed the presence of intracranial bleeding. The prescribed “pulse therapy” with dexamethasone and platelet transfusions allowed for intracranial surgery (PLT – 234×10^9/L).). However, a few days later, due to the ineffectiveness of “pulse therapy”, and the risk of renewed bleeding, the patient was again transfused platelet mass and prescribed high-dose intravenous immunoglobulin (IVIG), which raised the platelet level to 210×10^9/L. Soon, this therapy was ineffective, and we had to re-transfuse the platelet mass and simultaneously prescribe thrombopoietin (Revoleyd). Against the background of this therapy, the platelet level was stabilized, and the resulting effect was long-lasting.

At the moment, the child's hematological and neurological status is quite satisfactory.

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PP 62

The cause of very severe trombocytosis: iron deficiency anemia

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Objective: Platelet count above 450,000 mm^3 is defined as thrombocytosis. It is called mild thrombocytosis if the platelet count is between 700,000–900,000 mm^3, and severe thrombocytosis between 900,000–1,000,000 mm^3. If the platelet count is over 1,000,000 mm^3, it is considered as very severe thrombocytosis. In this case report; we have showed that iron deficiency can also lead to very severe thrombocytosis by presenting the case of very severe thrombocytosis developing in an adolescent female patient.

Case report: The 12-year-old girl was referred to our hospital for anemia (Hgb: 5.8 g/dL) by an external clinic she applied due to her headache in the morning for the past month. The patient's history and family history were unremarkable. Her physical examination revealed that her general condition was moderate-poor, skin was pale, conjunctiva was extremely pale, peak heart rate: 130–140/min, TA: 90/50 mm/Hg. Lymphadenopathy and hepatosplenomegaly were not detected. In the laboratory tests of the patient, the following findings were detected; the leukocytes count was: 14,900/mm^3, neutrophil count: 11.9/mm^3, Hgb: 4.8 g/dL, Hct: 20%, MCV: 53 fl, RBC: 3.7 milyon/uL, MCH: 12.9 pg (27–31), platelet count 2,629,000/mm^3. Peripheral smear of the patient was analyzed. In eritrocytes, a high degree of hypochromic microcytes were detected and 80% neutrophils, 2% monocytes, 18% lymphocytes, abundant platelets were seen. Serum iron: 6.7 uL/dL (50–120); iron binding capacity: 525 uL/dL (155–355); ferritin: 0 ng/mL; folate: 10.6 ng/mL (0.3–24) and vitamin B12: 437 ng/mL. There was no abnormality in other biochemical examinations. Iron replacement was started at a dose of 6 mg/kg/day considering iron deficiency anemia and related thrombocytosis. Abdominal ultrasonography was evaluated within normal limits according to age. Since the patient had tachycardia, appropriate cross erythrocyte transfusion was performed. Viral serologies and autoantibodies of the patient were evaluated as normal. The control hgb level was 7.9 g/dL and thrombocyte count was 1,875,000/mm^3 after transfusion. In the bone marrow aspiration assessment, the myeloid and erythroid series in the normocellular bone marrow were seen as normal, blasts were not seen, megakaryocytes were increased. The patient had hgb: 10.4 g/dL, platelet: 732,000/mm^3 in the clinical examination performed in the second week. She is under the oral +2 valence iron treatment and had no clinical problem in her follow-up examinations.

Methodology: Information was obtained from the patient file.

Results: In childhood, thrombocytosis usually occurs due to secondary causes and thrombocytosis regresses by controlling the causing disease. Thrombocytosis due to iron deficiency is mostly seen in infancy period.

Conclusion: The cause of thrombocytosis in iron deficiency is not fully understood. The fact that the increase in EPO stimulates TPO receptors (c-mpl) in iron deficiency is known to result in thrombocytosis. However, it is very important that children should be evaluated immediately for infection and iron deficiency before performing further examinations. Keywords: Thrombocytosis; iron deficiency; child.

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LEUKEMIA/LYMPHOMA/HISTIOCYTE DISORDERS

PP 63

Immune markers are closely related to the remission achievement in childhood acute myeloid leukemia

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Objective: Immunophenotyping of the blast population at the diagnosis of acute myeloid leukemia is a routine study that supplements the data obtained by morphological, cytochemical and cytogenetic studies of tumor cells. Currently, risk-stratification of children with acute myeloid leukemia (AML) is based on initial leukocytosis and genetic abnormalities. However, those genetic aberrations which effect the prognosis of childhood AML are found only in about 35% of cases. The search for reliable factors to clarify the stratification of patients into risk groups continues, and along with chromosomal and gene abnormalities, aberrations of the immunophenotype of tumor blasts are of interest. There are conflicting data on the effect of immunological factors on the prognosis of AML. Most of them were obtained by the analysis of AML in adults. It is of interest to analyze the effect of the immunophenotypic "portrait" of blast cells on the course of the disease. The achievement of complete remission (CR) is the main prognostic factor for AML in children.

Methodology: In our study, CR was achieved in 84 of 105 children with AML (80.0%) and achieving complete remission was very significant ($p = 0.000$) prognostic factor in assessing overall survival. We analyzed the influence of gender, age, FAB-variants and immunological markers on the probability of remission achievement. The effects of age, FAB-variants and gender were not significant, though boys achieved complete remission more rarely than girls ($p = 0.11$). We analyzed effect of the following immunological markers: CD7 ($n = 69$), CD117 ($n = 37$), CD34 ($n = 93$), CD13 ($n = 97$), CD33 ($n = 96$), CD20 ($n = 47$), CD19 ($n = 84$), CD9 ($n = 9$), CD38 ($n = 50$), HLA-DR ($n = 83$), CD11b

($n=3$), CD64 ($n=59$), CD14 ($n=20$), CD5 ($n=51$), CD3 ($n=55$), CD56 ($n=52$), CD10 ($n=67$).

Results: Among them presence of CD33, CD19 and CD56 increased the probability of remission achievement ($p=0.005$; 0.025 and 0.049 respectively) while CD14 ($p=0.028$) had a negative effect on it. It is important to note that none of these markers had a significant effect on the overall survival.

Conclusion: In conclusion, search for new prognostic factors for AML in children continues, and aberrantly expressed immunophenotypic markers may become important for clinicians.

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PP 64

The course of toxic hepatitis at the stage of treatment consolidation acute leukemia in children

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Objective: Toxic hepatitis occupies a special place among the complications of chemotherapy in the treatment of patients with acute leukemia. The research work we have presented is devoted to studying the frequency of toxic hepatitis and the choice of treatment tactics for children who are at the stage of consolidating acute leukemia.

Methodology: The study group included 110 children from both sexes who reached complete remission after a course of induction. Patients were 9 months old up to 15 years. The treatment was carried out according to the Moscow-Berlin-2015 program, where the consolidation phase was composed of 3 courses of 8 weeks. The severity of toxic hepatitis was predetermined by its criteria.

Results: According to the data obtained, 81 patients had toxic hepatitis (73.6%). In mild form it was noted in 46 children (56.7%), in moderate severe in 31 (38.4%), and in severe in 4 children (4.9%).

Conclusion: In the mild form of hepatitis from the intravenous use of Essentiale forte and Riboxin against the background of ongoing chemotherapy, a positive effect was obtained. With moderate severity, intravenous administration of Adeomethionine preparations (Heptral/Legend) in combination with Aevit per os turned out to be more effective. In 4 patients, upon transition to a severe form in the last course of consolidation, along with these drugs, ursodeoxycholic acid (Ursobil) + enhanced detoxification therapy was prescribed, which led to a complete recovery. After the treatment of toxic hepatitis, all patients with moderate and severe form, for the purpose of prevention, was prescribed combination therapy with Ursobil + Aevit + Lipoic acid, which gave a long-term positive effect.

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PP 65

Klippel–Trenaunay syndrome associated with chronic myeloid leukemia

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Objective: Klippel–Trenaunay syndrome (KTS) has been associated with capillary, venous, lymphatic and soft tissue malformations, whether it predisposes to malignancy is not clear. We report a case of chronic myeloid leukemia (CML) with KTS. We report this case because of its rarity and need for long term follow-up.

Case report: A 14-year-old boy presented with a painless mass on his left groin which was extending to his knee. Physical examination revealed splenomegaly, limb length discrepancy, left lower extremity hypertrophy and capillary hemangiomas over the posterolateral skin of the left thigh. KTS was suspected and confirmed with heterozygous mutation (c1634A>C/p.Glu545Ala) at the PIK3CA gene. The patient consulted to the hematology due to hemorrhage complication of the surgery. Complete blood counts showed a hemoglobin level of 7.3 g/dL, white blood cell as 164×10^9/L, neutrophil 76.4×10^9/L and thrombocytes 104×10^9/L). The differential was metamyelocytes 20%, bands 4%, neutrophils 70%, eosinophils 4%, lymphocytes 2%, normoblast 4%, except circulating blasts. Bone marrow aspiration showed normocellular myeloid/erythroid ratio of 23:1, granulopoiesis with left shift, increased megakaryocytes seen with normal maturation and blasts were lower than 5%. RT-PCR from peripheral blood was positive for the BCR-ABL p210 transcript. Conventional karyotyping revealed a typical 46 XY, t(9,22)(q34;q11.2) without any additional cytogenetic abnormalities in all (20/20, 100%). Chronic phase CML (CML-CP) was diagnosed, and imatinib was initiated with a 300 mg/m^2 dose daily.

Results: To our knowledge there has been no description of an association between KTS syndrome and CML in the literature. We report this case because of its rarity.

Conclusion: Klippel–Trenaunay syndrome is a rare congenital malformation involving blood and lymph vessels and abnormal growth of soft and bone tissue. The exact cause of KTS is not clear, several genes and pathways have been identified in its pathogenesis. Remarkably, PIK3CA gene mutations have been detected in some cases of KTS. PIK3CA encodes for a subunit of the phosphoinositide 3-kinase enzyme, which is involved in cell proliferation and migration. The angiogenic gene VG5Q has also been implicated in KTS. We report the case of a 14 year-old boy with diagnosed KTS, who presented with a bleeding from the surgical region that was found to be a chronic myeloid leukemia. To our knowledge there has been no description of an association between KTS syndrome and CML. In the literature, there are cases where KTS is associated with Wilms tumor, neurofibromatosis and osteoblastoma, but no hematologic malignancy has been so far.

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PP 66

Multiple relapsed acute lymphoblastic leukemia with t(9;13) in a child

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Objective: Acute lymphoblastic leukemia (ALL) is the most common form of childhood cancer. Patients with ALL are classified into genetic subtypes based on the occurrence of recurrent chromosomal abnormalities detected by karyotyping, fluorescent in situ hybridization (FISH), and/or polymerase chain reaction (PCR) amplification. Both the B-cell precursor and T-ALL comprise multiple subtypes defined by chromosomal alterations. The most known subtypes of ALL are t(12;21), t(1;19), t(9;22), iAMP21, hypo/hyperdiploidy and KMT2A rearrangements.

Case report: A 5-year-old boy was admitted to our hospital with fever and cough. His physical examination was normal, except hepatosplenomegaly. Complete blood count showed hemoglobin of 12.1 g/dL, white blood cell count of 198 $\times$ 10^9/L, and platelet count of 61 $\times$ 10^9/L. His peripheral blood and bone marrow aspiration smear showed L1-type lymphoblasts. He was diagnosed with B-precursor ALL without central nervous system (CNS) involvement, and ALL-IC BFM 2009 protocol was initiated. His bone marrow cytogenetic analysis revealed 46, XY with t (9;13). 33rd-day bone marrow showed >5% blasts, minimal residual disease (MRD) result by flow cytometry was 0.014%. He received a high-risk chemotherapy protocol, and hematopoietic stem cell transplantation (HSCT) was performed with total body irradiation conditioning from a matched unrelated donor. On the 130th day of the HSCT, he was readmitted to the hospital with testicular enlargement. Complete blood count showed a leukocyte count of 111x109/L with lymphoblasts. Orchiectomy was performed for testicular relapse, and REZ-BFM 2016 protocol and then blinatumomab was given. Thereafter, a second HSCT from another matched unrelated donor was performed. However, on the 83rd day of the second HSCT, bone marrow and CNS relapse occurred. He received weekly intrathecal chemotherapy and FLAG-IDA (fludarabine, high dose cytarabine, G-CSF, and idarubicin) protocol that continued with weekly oral methotrexate and daily 6-mercaptopurine and received 18 Gy cranial radiotherapy. Five months later, he admitted to hospital with generalized convulsion and isolated CNS involvement detected. He received intrathecal chemotherapy for six weeks with oral methotrexate and 6-mercaptopurine. However, two months later, he readmitted with headache and combined CNS and bone marrow involvement was detected and ETO-FLAG (fludarabine, high dose cytarabine, G-CSF, and etoposide) regimen was given. He is still followed-up at our clinic with invasive fungal infection and neutropeni.

Methodology: Herein, we present a child had t (9;13) with multi-relapsed ALL.

Results: In English literature, only one adult ALL case has been reported with t (9;13) and poor outcome. Nonrandom abnormalities of chromosome 9p, especially a breakpoint in 9p21-22, may occur in childhood ALL in association with a higher incidence of extramedullary relapse and treatment failure, as in our case.

Conclusion: Treatment of relapsed ALL still is a challenge and experimental trials may be considered for these patients.

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PP 67

Occurence of acute myeloid leukemia after primary hepatic carcinoma in a patient who had liver transplantation

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Objective: Recent advances in disease-free survival rate following organ transplantation have led to an increased incidence of malignancies after transplantation. The most common malignancies after transplantation are solid tumors, including posttransplantation lymphoproliferative diseases, sarcomas and skin carcinomas. Acute leukemias are very rare after transplantation and the incidence of acute leukemia among solid organ recipients is 0.12–2.5%. Herein, we describe a case of AML-M7 after liver transplantation.

Case report: A 10 years-old girl was admitted to our hospital because of abdominal pain and abdominal mass. An abdominal ultrasound examination showed the solid mass lesion in right adrenal region and liver. With the pathology report, the patient was diagnosed with hepatocellular carcinoma. Chemotherapy was started and surgical mass excision was made. After recurrence, liver transplantation was performed from the father. Tacrolimus was started prophylactically. Approximately 5 years after liver transplantation, the patient was referred to hematology with fatigue and leg pain. Family history revealed that mother had breast cancer and her brother died at the age of 2.5 due to hepatoblastoma. She was pancytopenic and bone marrow aspiration and biopsy revealed acute myeloid leukemia with flow cytometry AML FAB M7 was diagnosed. AML BFM 2019 protocol was initiated. Cytogenetic and molecular work-up from bone marrow samples revealed only monosomy 7. Familial cancer susceptibility genes revealed p53 gene mutation and BRCA2 gene mutations. Hematopoietic stem cell transplantation was planned.

Results: Immunosuppressive treatments used after liver transplantation may have impact on secondary cancer development, additionally genetic familial risks in our patient may also have contributed to subsequent leukemia development.

Conclusion: The development of AML after liver transplantation is a relatively rare complication and several such cases of AML have been reported, previously. Immunosuppressive treatments used after liver transplantation may have impact on secondary cancer development, additionally

genetic familial risks in our patient may also have contributed to subsequent leukemia development.

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PP 68

Acute lymphoblastic leukemia with ebv infection and multiple chromosomal abnormalities in a child

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Objective: Acute lymphoblastic leukemia (ALL) is the most common type of cancer in childhood but its etiology is largely unexplained. Epstein Barr Virus (EBV) may play a role in the pathogenesis of ALL by integrating into the genome of precursor B cells, disturbing differentiation and proliferation control.

Case report: Two and a half year old boy admitted with fever. Physical examination findings were unremarkable. Laboratory investigations revealed a low hemoglobin level (9.7 g/dL), a low platelet count (31,000 cells/mm^3), a normal leukocyte count (7130 cells/mm^3) and also an elevated lactate dehydrogenase level (661 U/L). A peripheral blood (PB) examination revealed the presence of leukemic blasts of uncertain origin (51%). A bone marrow (BM) smear showed almost complete infiltration of L1 blasts (94%). Immunophenotyping was consistent with pre-B ALL. Conventional cytogenetic analysis of BM blasts revealed a mosaic karyotype with hypodiploidy (46,XY[7]/45,XY[3]/40-44,XY[2]). FISH analyses showed inversion 16 (20%), trisomy 7(12%). FISH analyses also detected elevated signals suggesting duplications or trisomies at IGH region of 14th chromosome, at ETV6 region of 12th chromosome and at AFF1 region of 4th chromosome. Before chemotherapy EBV DNA was 1563 IU/mL in PB. EBV viral capsid antigen (VCA) immunoglobulin (Ig) M was positive and EBV VCA Ig G was low suggesting a primary acute infection. At the end of induction the patient was in remission and EBV DNA could not be detected neither in BM nor in PB. Karyotype and FISH analyses were both normal. Maintenance treatment is going on without an EBV activation.

Methodology: Herein, we present a child with ALL who has EBV positivity and multiple chromosomal abnormalities.

Results: Since EBV was identified, it has been associated with a variety of diseases of hematological origin such as Burkitt's lymphoma, Hodgkin lymphoma, post-transplant lymphoproliferative disease, hemophagocytic lymphohistiocytosis (HLH) and etc. The same cell type in lymphoma and lymphocytic leukemia lead similar diseases with different clinical manifestations and stages sharing similar biological characteristics. It is reported that lymphocyte chromosome mutations or translocations caused by EBV infection can lead to oncogene activation resulting in the occurrence of lymphoma. In addition, chromosome abnormalities have been observed in EBV-associated HLH and chronic active EBV infection. Ahmed at al. screened 80 pediatric patients with leukemia and 20 healthy controls from Sudan, for the presence of EBV latent membrane protein 1 (LMP1) gene transcripts. Although there was no positivity in the control group, they found high ratios in leukemia group suggesting the role EBV in the etiology of pediatric leukemia. Guan et al. detected EBV DNA copies in BM of both pediatric and adult patients with ALL, AML and they also found higher ratios from healthy controls.

Conclusion: The child we presented herein has pre-B ALL with multiple chromosomal abnormalities detected by karyotype analysis combined with FISH. These anomalies and leukemia itself can be associated with active EBV infection. Studies with large sample sizes to elucidate the possible role of EBV infection in acute leukemias and associated chromosome aberrations are required.

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PP 69

Hypercalcemia due to concomitant use of all trans retinoic acid and voriconazole

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Objective: Objective: All-trans-retinoic acid (ATRA) has been used in the treatment of acute promyelocytic leukemia (APL). Although the well-known side effects include retinoic acid syndrome and Sweet's syndrome, hypercalcemia associated with ATRA has rarely been reported. The metabolism of ATRA occurs through cytochrome p450 enzymes, and the azole antifungals are known to be potent inhibitors of the cytochrome p450 enzyme system. Here, we report a child who had severe hypercalcemia in the treatment of acute promyelocytic leukemia.

Case report: Case: A 8-years old boy presented with epistaxis and petechia. The patients' bone marrow aspiration and flow cytometry results were compatible with APL, and t (15;17) was positive. The treatment of AML BFM 2013 protocol and ATRA were initiated. After induction treatment, voriconazole treatment was started prophylactically. While the patient was receiving voriconazole and ATRA, hypercalcemia (Ca: 12.4 mg/dL) and hypertension (140/90 mm Hg) developed. Endocrine and nephrological evaluations of the patient were normal. After the voriconazole treatment was discontinued, hypercalcemia and hypertension improved and never recurred.

Conclusion: Discussion: Hypercalcemia associated with the treatment with ATRA has been described in the literature. The mechanisms of hypercalcemia due to ATRA include accelerated mineral resorption through increased osteoclastic activity, increased interleukin-6 levels that increase bone resorption, and increased parathyroid hormone-related protein. Hypercalcemia is due to the inhibition of ATRA metabolizing cytochrome p450 enzymes, by voriconazole. To decrease the incidence of this side-effect, the use of any medications that can inhibit the cytochrome P450 enzyme system during ATRA therapy is inappropriate unless mandatory.

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PP 70

Acute lymphoblastic leukemia in the context of constitutional mismatch repair deficiency syndrome: a case report

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Objective: B-cell precursor acute lymphoblastic leukemia (pre-B ALL) is the most common childhood cancer. Although most childhood B-ALL is sporadic, a subset occurs in children with pre-existing conditions that predispose to leukemogenesis.

Case report: Five and a half year old girl admitted with fever. There were multiple cafe au lait spots without axillary freckling, hepatosplenomegaly and cervical lymphadenopathy on physical examination. Family history elicited that her mother and father were first degree cousins and none of them but her little brother had multiple cafe au lait spots. Laboratory investigations revealed a low hemoglobin level (4.9 g/dL), a low platelet count (13,000 cells/mm^3) and a normal leukocyte count (6610 cells/mm^3). A peripheral blood (PB) examination revealed the presence of leukemic blasts of uncertain origin (30%). A bone marrow (BM) smear showed complete infiltration of L1 blasts. Immunophenotyping was consistent with pre-B ALL. Karyotype of BM blasts could not be analysed because of insufficient number of metaphase cells. FISH analyses showed trisomy 8. Accompanied with ALL IC BFM 2009 chemotherapy protocol, diagnostic work up directed to cancer predisposition syndromes proceeded. Next-generation sequencing (NGS) revealed a mutation in one of the CMMRD genes. The mutation was biallelic in PMS2 gene and according to American College of Medical Genetics and Genomics 2015 guidelines, it was an "uncertain clinical significance" mutation. At the end of induction she was in remission and karyotype and FISH analyses of BM were both normal. The patient experienced hepatosplenic candidiasis and lobar pneumonia during chemotherapy but no dose reduction was made. Follow-up for CMMRD and maintenance treatment of ALL is going on.

Methodology: We present a child with constitutional mismatch repair deficiency syndrome (CMMRD) related pre-B ALL.

Results: Although we do not know the exact karyotype of blasts in our case, at least they have trisomy 8. Trisomy of chromosome 8 is frequently reported in myeloid lineage disorders and also detected in lymphoid neoplasms as well as solid tumors, suggesting its role in neoplastic progression in general. Trisomy 8 is associated with poor prognosis in acute and chronic myeloid leukemias but prognostic significance of extra 8th chromosome in lymphoid malignancies is not reported widely. Trisomy 8 could represent an alternative mechanism for increasing c-myc gene dosage to achieve amplification of c-myc oncogene but mechanisms underlying the events need further study.

Conclusion: CMMRD syndrome is a rare disease and related malignancies need individualization of therapy and novel approaches to optimize care. The child presented herein is a unique case who has CMMRD syndrome phenotype with an "uncertain clinical significance" mutation in PMS2 gene and ALL with trisomy 8. To our knowledge, trisomy 8 has not been reported in ALL in the context of CMMRD syndrome.

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RED BLOOD CELL DISORDERS

PP 71

Potential risk of subclinical iron deficiency anemia in misinterpretation of glycosylated hemoglobin a1c (hba1c): a case report

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Objective: Iron deficiency anemia (IDA) which is a global public health problem affecting both developing and developed countries, appears to be more common in diabetic patients compared to non-diabetic population. Gycosylated hemoglobin (HbA1c) which is widely considered as the primary target for glycemic control of diabetic patients, may be altered by certain condition including depletion of iron store with elevation of HbA1C concentrations independent of glycemia. However, reports of the clinical significance of iron deficiency on the glycosylated HbA1c levels have been inconsistent.

Case report: We report a case of 48-year-old diabetic patient with subclinical iron Deficiency, who was in a potential risk of receiving unneeded insulin injection because of false-high values of HbA1c.

Methodology: The false-high values of HbA1c (>7.0%) noticed earlier with the subclinical iron deficiency anemia (hemoglobin 12.7 g/dL, serum iron: 7.94 umol/L, ferritin: 7 ng/mL), then after with frank iron deficiency anemia (hemoglobin 10.1 g/dL, serum iron: 5.68 u, mol/L, ferritin: 5.9 ng/mL).

Results: Interestingly, this high value of HbA1c was subsequently fall (5.8%) simply on correcting the iron deficiency (Ferritin: 10.6 ng/mL) by receiving iron supplementation.

Conclusion: We emphasizes that iron deficiency with or without anemia must be corrected before any diagnostic or therapeutic decision is made based on HbA1c in order to prevent misclassification of diabetes with its hazardous consequences of incorrect treatment.

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PP 72

Hematologic manifestations associated with deficiency of adenosine deaminase 2 and a novel ada2 variant

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Objective: Deficiency of Adenosine-deaminase 2 (DADA2) is an autoinflammatory, autosomal recessive disorder due to mutations in CECR1 gene. DADA2 is phenotypically extending beyond its classical features (fever, early-onset stroke, livedo reticularis and polyarteritis nodosa) to include various hematologic presentations and rarely manifests as pure red cell aplasia (PRCA). We report a novel mutation in CECR1 gene (ADA2), that results in DADA2 and presented with PRCA as a unique manifestation.

Case report: A 5-year-old female who presented with severe pallor, with no family or medical history of concern. Autoimmune hemolytic anemia (AIHA) was suspected due to positive DAT, so the child started intravenous immunoglobulin and steroids but with no response. Bone marrow aspirate/biopsy showed markedly reduced erythropoiesis consistent with PRCA. The child almost required blood transfusion on weekly basis. She has an HLA-matched sibling donor and started hematopoietic stem cell transplant (HSCT) process. Meanwhile, a whole exome sequencing (WES) was requested for final diagnosis.

Methodology: We obtained a sequence analysis of all protein coding genes in the patient's genome, coupled with Whole Exome Deletion/Duplication (CNV) Analysis. Also, we reviewed the literature for hematologic manifestations of DADA2.

Results: Whole Exome Plus identified a homozygous frameshift variant CECR1 c.714_738dup, p. (Ala247Glnfs*16). It duplicates 25 base-pairs and generates a frameshift, leading to a premature stop codon in exon 5 (of 10 total exons), at position 16 in a new reading frame that is predicted to cause a loss of normal protein function. To the best of our knowledge, this variant was not described in the medical literature or reported in disease-related variation databases. Interestingly, our patient did not show any features suggesting DADA2 nor congenital form of aplastic anemia as she presented solely with PRCA. We reviewed a total of 151 patients from 27 published reports for patients with DADA2 in which hematologic manifestations were part of their presentations. One hundred patients, (66%, Female $n=52$), median age 5 years, presented with hematologic manifestations. Different anemias (AIHA, Evans syndrome, PRCA, DBA like features) were the most frequent occurring in 51% of patients, followed by lymphopenia and organomegaly, (32% each). Of concern, PRCA was the main manifestation in 12 patients without typical features of DBA nor vasculitis. Four patients were successful on HSCT, 1 on anti-tumor necrosis factor (TNF), 2 failed on steroids and 2 failed on anti-TNF, while others are either maintained on blood transfusion, steroids, or monthly intravenous immunoglobulins. The treatment for DADA2 previously included steroids, thalidomide and tocilizumab that showed success but associated with severe adverse events. Recently, treatment with anti-TNF-agents is believed to be effective especially in cases of vasculitis due to a subtotal loss of ADA2 function. However, complete loss of function seen in hematologic disorders is not favoring TNF inhibitors. HSCT is the most definitive treatment, particularly, when reversal of cytopenias and immunodeficiency is aimed.

Conclusion: We report a novel ADA2 variant in child presented with PRCA. We emphasis on genetic testing for hematologic disorders that lacks a definitive etiology, as it might result in the best pharmacogenomic-based therapeutic strategies without the need of unnecessary interventions.

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PP 73

Pyruvate kinase deficiency misdiagnosed as congenital dyserythropoietic anemia type i

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Objective: Objective: Pyruvate kinase (PK) deficiency is the most common enzyme abnormality in the glycolytic pathway, which leads to an anemia secondary to decreased ATP synthesis. The disease exhibits autosomal recessive inheritance and is caused by mutations in the PKLR gene. The diagnosis of PK deficiency is based on the presence of clinical signs and symptoms of hemolytic anemia, evidence of extravascular hemolysis on laboratory findings, measurement of the PK activity or antigen levels and detection of mutations in the PKLR gene.

Methodology: Here, we describe two siblings with PK deficiency that was misdiagnosed as congenital dyserythropoietic anemia (CDA) type I.

Results: Cases: The siblings were referred to our hospital for the evaluation of the anemia when they were newborn. On physical examination, they both had an icteric appearance. Their PK, glucose-6-phosphate dehydrogenase and 5' nucleotidase enzyme activities, hemoglobin electrophoresis and osmotic fragility test were normal. Erythroid hyperactivity with many bi-multilobed erythroblasts, which raised the concern of CDA, was seen in bone marrow aspiration. Spongy appearance (Swiss cheese appearance) of heterochromatin in all normoblasts and expansion of the perinuclear areas and the extension of the cytoplasm towards the nucleus in some, were observed with electron microscopy. CDA panel by next generation sequencing showed no mutation. Though their PK enzyme levels were normal, the molecular study of PKLR gene, a homozygote variant c.1623G>C (p.Lys541Asn) in exon 12 was found in our patients.

Conclusion: Discussion: Pyruvate kinase deficiency is a rare cause of hemolytic anemia and given to the rarity and the clinical heterogeneity, the diagnosis of PK deficiency can be difficult, mostly in atypical forms. PK deficiency should be considered in the differential diagnosis of CDA. Instead of the enzyme activity, comprehensive genetic analysis is warranted

more effective diagnosis of patients with suspected CDA and congenital hemolytic anemia.

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SICKLE CELL DISEASE

PP 74

How to treat and manage covid19 in SCD patients

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Objective: Coronavirus disease 2019 (COVID-19) is an infectious disease caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). It was first identified in December 2019 in Wuhan, China, and has resulted in an ongoing pandemic.

Case report: A 24-year-old man with a history of SCD (HbS/β0-thalassemia) on maintenance hydroxyurea therapy presented to our hospital, with a complaint of pain in the extremities and chest over two days. The patient with mild cough and high fever was hospitalized. Blood tests and lung CT were performed. Result of blood test show evidence of systemic hemolysis with a decrease in hemoglobin from 8.9 g/dL to 6.7 g/dL. His white blood cell count was $25.2 \times 10^3/\mu L$, CRP 243.21 mg/L. CT scans of the lungs showed a consolidated area where air bronchograms were observed in and around the medial segment of the middle part of the right lung and the posteriobasal segment of the lower part of both lungs, and an icy glass landscape was observed. Lung damage is 1–5% (grade I). His oxygen saturation SpO2 was normal (98%). The SARS-CoV-2 PCR nasopharyngeal swab testing was sent and returned negative on hospital day one after which the patient was started on antiviral and antibiotic for severe COVID-19 pneumonia. An improvement in blood counts was observed 4 days after starting treatment (WBC $16.93 \times 10^3/\mu L$, CRP 100.31 mg/L). On day ten, after normalization of all symptoms and blood values the patient was discharged home.

Methodology: In this study we selected 1 patient with SCD followed in Thalassemia Center of Azerbaijan.

Results: Given the higher likelihood of ACS it is possible that SCD patients are also at higher risk of such complications from COVID-19, particularly those with a history of pulmonary comorbidities. However, it is unclear if the SARS-CoV-2 pandemic will lead to increased rates of ACS for sickle cell patients. Still, hospitalized sickle cell patients should be monitored closely for development of ACS and if this occurs, exchange transfusion should be promptly initiated.

Conclusion: COVID-19 pneumonia as a cause of acute chest syndrome in an adult sickle cell patient. Patients with sickle cell disease (SCD) who are infected with COVID-19 may have a significant risk of developing acute chest syndrome (ACS), a potentially life-threatening complication. In this case we will present how manage COVID 19 in patient with SCD.

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STEM CELL TRANSPLANTATION

PP 75

High-dose methyl prednisolone in veno-occlusive disease

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Objective: Veno-occlusive disease (VOD) is a serious complication of hematopoietic stem cell transplantation (HSCT). If it is not identified and treated earlier, mortality is high. Combination usage of high-dose methyl prednisolone (MPZ) and defibrotide in VOD treatment have been described in some studies. Here, we present a patient with VOD who responded well to high-dose MPZ.

Case report: 14-month-old girl, diagnosed with thalassemia major, received HSCT from her sibling donor with busulfan and cyclo-phosphamide conditioning. On day +11, the patient experienced painful hepatomegaly and elevated total bilirubin (2.25 mg/dL) with 7% weight gain from baseline and respiratory distress while under defibrotide prophylaxis. VOD was diagnosed according to the modified Seattle criteria. Fluid and salt restriction were performed, spironolactone was started, and defibrotide was continued. Due to lack of significant improvement in the patient condition after 4 days of defibrotide, HDM was started at dose of 250 mg/m^2 per dose every 12 h on day +15.

Methodology: A day after MPZ, the patient's condition started to improve. After six doses of methylprednisolone, the dose was reduced to 2 mg/kg. Then, the dose was reduced by decreasing to half-dose in three-day periods. The defibrotide was discontinued on day +36, and the patient was discharged on day +45. The patient is currently being followed problem-free after 2 years of transplantation with 100% donor chimerism.

Results: VOD treatment response with high-dose MPZ and defibrotide combination can be better than treatment response with defibrotide alone. The easier and cheaper supply of steroids also prevents the treatment delay. In a study, it was shown that receiving high-dose MPZ without defibrotide was also found to be effective in the VOD treatment. The mortality rate in patients with multiple organ failure symptoms in VOD is between 50% and 100%. However, mortality rate can be decreased by early detection of VOD symptoms such as of painful hepatomegaly, weight gain and ascites. This findings may develop before hyperbilirubinemia especially in pediatric patients. Knowing this is important for early diagnosis and treatment of VOD.

Conclusion: As a conclusion; high-dose MPZ was found to be an effective treatment in VOD even at a dose of 250 mg/m^2 per dose every 12 h in aour patient. High-dose MPZ might be an alternative treatment to defibrotide in early phase VOD. Further studies are needed on the efficacy and dosage of MPZ in VOD.

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PP 76

Isolated extramedullary relapse after hematopoietic stem cell transplantation

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Objective: Isolated extramedullary (EM) relapse of acute leukemia is rare. It is more common in patients who undergo hematopoietic stem cell transplantation (HSCT) than patients receive chemotherapy alone. We aimed to describe the demographic and clinical features, and clinical outcomes of children diagnosed with isolated EM relapse after allogeneic HSCT.

Methodology: Between 2012 and 2020, patients aged <18 years and treated with the diagnosis of isolated EM relapse after HSCT at the Department of Pediatric Hematology and Oncology, Health Sciences University Ankara Pediatric Hematology-Oncology Training and Research Hospital were enrolled in our study. The demographic features, clinical manifestations, treatment, and prognosis were analyzed retrospectively.

Results: Eight patients with extramedullary relapse after allogeneic HSCT were evaluated. Two patients were female, and six patients were male. The mean age of the patients was 9.8 years (min–max value: 12/12–168/12years). The type of leukemia was precursor B acute lymphoblastic leukemia (ALL), acute myeloid leukemia (AML), and chronic myeloid leukemia (CML) in four, two, and two patients respectively. One patient had mass in the left iliac fossa, 1 patient had multiple mass in the right femur distal and tibia, 2 patients had mass in the testis,1 patient had mass head of the femur,1 patient had mass left orbit, 1 patient had central nervous system relapse and mass in the right lateral of the nose, medial part of the sacrum, 1 patient had mass in kidney. All patients had a biopsy-proven histopathological diagnosis. The mean relapse time after HSCTwas 17.3 months (min–max duration; 3–48 months). The mean follow-up time was 41.7 months (min–max: 12–120 months). Four patients died during the follow-up period. One patient; developed severe febrile neutropenia, mucositis attacks, and acute pancreatitis with systemic chemotherapy. After 13 months, HSCT was performed from her other compatible sibling due to medullary relapse, and she is still in remission. Other one patient was treated with systemic chemotherapy and imatinib, donor lymphocyte infusion, and local radiotherapy and continued to be followed in remission. Two patients treated with systemic chemotherapy; however, they had recurrent relapses and still on systemic chemotherapy.

Conclusion: Isolated extramedullary relapse is mostly reported during AML, rarely during other myeloproliferative diseases (CML) and more often in male patients. In our study, male patients were predominant that was similar to the literature. Of interest, four patients with precursor B ALL had isolated EM. Although the survival rates were low in these patients, the mean follow-up time was 41.7 months.

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ONCOLOGY
SOLID TUMORS

PP 77

Candida guillermondii onychomycosis involving fingernails in a breast cancer patient under decetaxel chemothrapy

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Objective: Onychomycosis has been shown to have a higher incidence in cancer patient. Nail toxicity is quite common side effect of anticancer agents, Taxotere© is a chemotherapeutic known to cause great incidence of nail change and has a role of subungual suppuration. We present a case of onychomycosis induced by Taxotere chemotherapy and proved by mycological tests.

Case report: We report on a 52 year-old female, with breast cancer admitted in our institution for onycholysis. Because of stage and histology of breast cancer neoadjuvant chemotherapy was initiated, patient received 8 cycles of taxotere and Adriamycin (AT), and she underwent a modified radical mastectomy. Three-month later, patient evidence of onycholysis developed, involving all the fingernails. We observed the following changes in nails of all the digits in both hands: onycholysis, dystrophy, oedema, and exudate.

Methodology: Nail scraping and purulent discharge were collected for culture and direct examination by KOH and chloral lactophenol for mycological examination, fungal identification was based on physical features of the colonies and biochemical tests (Auxacolor©).

Results: Physical features of the colonies and biochemical tests (Auxacolor©)revealed Candida guillermondii as sole etiologic agent of onychomycosis. This case details an onycholysis in cancer breast case successfully managed solely with amorolfine lacquer 5% for a minimal duration of 3 month.

Conclusion: Candidiasis is one of the commonest complications seen in immunosuppressed cancer patients, and Candida guillermondii is frequently isolated in onychomycosis. Early recognition and treatment of yeast onychomycosis with purulent discharge is important especially in immunocompressed patients.

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PP 78

Pretreatment neutrophile lymphocyte ratio (NLR) may have a prognostic role in patients receiving pemetrexed treatment for advanced stage non small cell lung adenocarcinoma

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Objective: We aimed to investigate the prognostic effect of Neutrophil/Lymphocyte ratio (NLR) on overall survival (OS) and progression time (PFS) as an inflammatory marker in patients diagnosed with lung adenocarcinoma who started pemetrexed treatment after primary level platinum-based chemotherapy.

Methodology: Laboratory data before initiation of treatment was retrospectively analyzed in 63 patients who were admitted to our outpatient clinic with a diagnosis of lung adenocarcinoma between 2017 and 2020, and who were deemed appropriate to start pemetrexed treatment. NLR was calculated as "Neutrophil/Lymphocyte". The pre determined cut-off value for NLR was derived from meta-analysis results from the literature. The analysis of the relationship between NLR and survival and progression times was assessed. The normal distribution was evaluated by the Kolmogorov–Smirnov test. Continuous variables were expressed as mean and standard deviation displaying normal distribution, and as median and 95% confidence intervals if not displaying normal distribution. Statistical difference was considered as $p < 0.05$.

Results: The median age of diagnosis of patients included in the study was 60.62 (34–78) years; 63.5% (40) consisted of denovo metastatic patients. 50.8% of the patients consisted of patients who received radiotherapy before (32). Median pemetrexed duration of use was 4.01 months (95% CI 4.89–8.45). 68.3% (43) of the patients who received pemetrexed treatment progressed. Median PFS was 4.22 months (95% CI 3.51–8.35). At the end of the study follow up period, 68.3% (43) of the patients have died. Median OS was 5.49 months (95% CI 5.75–11.56). Clinical benefit rate was not significantly different between two study groups ($p = 0.09$. The death rate of those with NLR above 5 before receiving pemetrexed treatment was significantly higher (p: 0.012) while the median PFS and OS times were significantly shorter compared to patients with NLR lower than 5[PFS (median ± IQR): 2.07 ± 3.02 vs. 5.32 months ± 6.54; $p = 0.018$ and OS (median ± IQR): 2.79 months ± 3.52 vs. 6.29 months ± 8.32; $p < 0.004$; respectively].

Conclusion: In our study, we found that high NLR was an independent poor prognostic factors in patients receiving pemetrexed treatment as second line therapy for advanced stage lung adenocarcinoma. This simple parameter which is an established surrogate marker for systemic inflammatory response can prove to be useful in identifying high-risk patients and making individual treatment decisions.

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PP 79

Systemic inflammatory markers as predictors of response to chemoradiotherapy in rectal cancer

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Objective: Both Neutrophil to Lymphocyte (NLR) and C-reactive protein to albumin (CAR) ratio are surrogate markers of host immune system's reaction against systemic inflammation generated by tumor microenvironment. Recent studies have reported the efficacy of host's reaction to systemic inflammation as a prognostic marker in various cancers. However, its association with tumor response to neoadjuvant chemoradiotheraoy treatment in rectal cancer has not been fully elucidated.

Methodology: Pretreatment NLR and CAR along with other clinical and serological markers were evaluated in 54 patients undergoing chemoradiotheray for rectal cancer from February 2019 to February 2020. The predictive significance of these markers were then determined by both univariate and multivariate logistical analysis. Predetermined cutoff values for NLR and CAR and serum CEA levels were used for response prediction

Results: Pretreatment low NLR (<2, $p < 0.01$), pretreatment low CAR (<0.025, $p = 0.01$) and lower CEA levels were significantly associated with both good pathological response and complete pathological response to chemoradiotherapy in univariate analysis. However, in multivariate Cox analysis although both NLR and CAR levels were found to be independent predictors for complete response to neoadjuvant therapy, NLR seemed to be a better predictor in terms of hazard ratio(HR) than the CAR (HR = 2.870 versus HR = 1.784). Patients with NLR < 2 had significantly better response to chemoradiotherapy and NLR was superior to other serum inflammatory markers for predicting response to neoadjuvant therapy.

Conclusion: Pretreatment NLR and CAR were significant predictors of complete pathological response to neoadjuvant chemoradiotherapy in rectal cancer patients. However, NLR is found to be a better discriminator for complete response to neoadjuvant chemoradşotherapy in patients with rectal cancer.

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