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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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