PP 22_Case report

LYSOZYME-INDUCED NEPHROPATHY IN CMML: A RARE BUT SIGNIFICANT COMPLICATION REQUIRING EARLY RECOGNITION AND INTERVENTION

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Background: CMML is a clonal hematopoietic disorder with features of myelodysplasia and myeloproliferation, characterized by monocytosis. Monocytes secrete lysozyme, a cationic protein filtered by the glomerulus and reabsorbed in proximal tubules. Excess lysozyme accumulation causes tubular injury, leading to Lysozyme-Induced Nephropathy (LyN). **Case 1:** A 72-year-old male with CMML that transformed into AML with a TP53 mutation. Laboratory results showed WBC 9×10^9/L, Hb 80 g/Platelets 139×10^9/L, and creatinine 162 μmoL/L. Additional findings included Na 129 mmoL/L, Cl 97 mmoL/L, Mg 0.51 mmoL/L, PO4 1.50 mmoLL, and 24-hour urine protein of 1.20 g/L. LyN was suspected and confirmed with a lysozyme level of 117 mcg/mL (2.7–9.4). He was treated with Azacitidine and Venetoclax, achieving CR and normal renal function. **Case 2:** A 60-year-old male with CMML initially presented with a creatinine level of 139 μmoL/L, Na 130 mmoL/L, K 2.6 mmoL/L, normal Magnesium, and a lysozyme level of 153 mcg/mL. His creatinine normalized with prednisone. He progressed to AML after six cycles of Azacitidine and later received four cycles of Venetoclax, achieving CR. Unfortunately, he passed away 18-months post-diagnosis due to pneumonia and pulmonary hemorrhage. **Case 3:** A 57-year-old female with CMML transformed into AML underwent MSD SCT but relapsed after five months. She initially achieved CR with Aza-Ven, followed by DLI, but relapsed again after four years. She was unresponsive to Aza-Ven but improved with palliative cytarabine. Initially, she had AKI due to TLS, which improved with chemotherapy. During her last relapse, she had creatinine of 154 μmoL/L, lysozyme levels 124 mcg/mL and electrolyte imbalances. Her renal function significantly improved after cytarabine injections. **Discussion/Conclusion:** Most frequent renal complications in CMML are LyN (56%) and renal infiltration by the CMML with incidence of AKI (34.9%) and CKD (7.6%). LyN is a rare and poorly understood complication of CMML. Filtered lysozyme accumulates in the renal cortex, causing severe hypokalemia via kaliuresis or direct tubular injury, potentially leading to kidney failure. In our patient CMML treatment, hydration and steroids restored kidney function. LyN in CMML necessitates early recognition and intervention to improve renal outcomes. Further research is needed to optimize treatment strategies.

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PP 23_Case report

LANDSCAPE OF SOMATIC MUTATIONS OF MYELOPROLIFERATIVE NEOPLASMS IN PAKISTANI PATIENTS

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Objective: This study aimed to screen Myeloproliferative Neoplasm (MPN) patients for four known genetic mutations following their clinical and bone marrow examinations to establish a diagnosis before treatment. **Methods:** This descriptive cross-sectional study was conducted at the Armed forces bone marrow transplant center, Rawalpindi, between January 2018 and January 2021. A total of 159 MPN patients who fulfilled inclusion criteria were enrolled. All patients underwent bone marrow biopsy after providing informed consent, history recording, and examination. Peripheral blood samples were screened for somatic mutations in JAK2 V617F, JAK2 exon 12, CALR, and cMPL genes. The JAK2 V617F and cMPL mutations were analyzed using conventional PCR, and the PCR products were analyzed on polyacrylamide gel electrophoresis. JAK2 Exon 12 and CALR mutations were analyzed using the fragment analysis technique. Positive and negative controls were run with each sample. The final results were analyzed using Gene Mapper 5 Software (Applied Biosystems). The gene scan data was interpreted by analyzing the electropherograms and the genotyping data sheet. The data were analyzed using the Statistical Package for Social Sciences (SPSS) version 25.0. **Results:** A total of 159 MPN patients fulfilled the inclusion criteria, with 104 (65.4%) males and 55 (34.6%) females. The median age of patients was 54-years (IQR: 38–64). Among Philadelphia negative (Ph-ive) MPN patients, 69 (43.4%) were diagnosed with Primary Myelofibrosis (PMF), 60 (37.7%) as Polycythemia Vera (PV), and 30 (18.9%) as Essential Thrombocytosis (ET). The frequency of the JAK2 V617F mutation in PV, ET, and PMF patients was 85%, 51.4%, and 34.5%, respectively. CALR mutation was observed only in 1 PMF and 5 (17.2%) ET patients. Additionally, cMPL mutation was not found among our patients. However, 14 (8.8%) patients were triple negative (negative for the JAK2 V617F, CALR, and cMPL mutations). **Conclusions:** PMF was the most frequent (43.4%) condition among Ph-ive MPN patients, followed by PV 60 (37.7%) and ET 30 (18.9%). The frequency of JAK2 V617F mutation in PV, ET, and PMF patients was 85%, 51.4%, and 34.5%, respectively. CALR mutation was observed only in 5 (17.2%) ET and 1 PMF patient. These five mutations are among the diagnostic criteria established by the World Health Organization, which enable a quick and reliable diagnosis of MPN. **Conclusion:** This study highlights the demographics, diagnosis, and mutations in four genes of MPN patients from a low-income country. PMF was the most frequent (43.4%) among Ph-ive MPN patients, followed by PV 60 (37.7%) and ET 30 (18.9%). The frequency of the JAK2 V617F mutation in PV, ET, and PMF patients was 85%, 51.4%, and 34.5%, respectively. CALR mutation was observed in only 1 PMF and 5 (17.2%) ET patients. These five mutations are among the diagnostic criteria established by WHO for a quick

and reliable diagnosis of MPN. Few lines can be included regarding the need of further studies with larger cohort from multi centers Use of high throughput sequencing techniques for identifying mutations located anywhere else in these genes Shouldn't it be 4?

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PP 24_Case report

A CASE OF THROMBOCYTOSIS AND HEMOTHORAX IN A PATIENT WITH ITP FOLLOWING ROMIPLOSTIM USE

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Introduction: Immune Thrombocytopenia (ITP) is an autoimmune disease characterized by isolated thrombocytopenia and normal to large platelets in the peripheral blood smear. It is an autoimmune disorder that leads to peripheral platelet destruction and decreased platelet production. Romiplostim, a peptide-antibody fusion product, is a thrombopoietin receptor agonist indicated for use in patients with ITP. Romiplostim is indicated for patients with ITP who have had an inadequate response to first-line therapy. Side effects of the drug include increased bone marrow reticulin, reversal of severe thrombocytopenia, thrombocytosis and increased immunoblast proliferation. In this case report, we present a patient with ITP refractory to first-line therapies who was admitted to the intensive care unit for thrombocytosis and haemothorax after a single dose of Romiplostim. **Case:** A 34-year-old female patient, who had been followed in the hematology clinic for ITP for approximately 5-years, was admitted to the clinic because of deep thrombocytopenia and deep anaemia due to menometrorrhagia. On admission, the platelet count was 2000 ($10^3/\mu L$) and the hemoglobin level was 5.4 g/dL, and she was taking eltrombopag 75 mg at the time of admission. He was tachycardic and hypotensive and was given erythrocyte suspension. Clinical and radiological examination revealed no bleeding foci other than menstrual and oral mucosal bleeding. The patient was treated with steroids, IVIG and rituximab during the follow-up period in the clinic. Despite the treatments given, bleeding control could not be achieved and a single dose of 2 mcg/kg Romiplostim was administered to the patient in the 2^{nd} week of hospitalization. The patient's platelet count began to rise rapidly on the 3^{rd} day after treatment and was measured at 1,650,000 ($10^3/\mu L$) on the 5^{th} day. At the same time, the patient developed dyspnea and a chest scan was performed, which revealed a hemothorax. The patient was admitted to intensive care. Drainage was performed with a chest tube. Acquired von Willebrand Factor (vWF) deficiency due to thrombocytosis was considered as the cause of the hemorrhage. The vWF level in the blood was found to be low. The thrombocytosis was controlled by platelet apheresis. After clinical improvement, platelet levels were normalized, and the patient was discharged. **Conclusion:** Romiplostim is a generally well tolerated agent. Current evidence suggests that it increases platelet counts, reduces bleeding, reduces the need for rescue therapy, reduces the amount of corticosteroids required, improves quality of life and, in isolated cases, is associated with remission of ITP. However, it should be used with caution as serious side effects include increased bone marrow reticulin, reversal of severe thrombocytopenia, thrombocytosis and increased immunoblastic proliferation

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Adult Hematology Abstract Categories

Multiple Myeloma

PP 25_Case report

IMPACT OF LENALIDOMIDE MAINTENANCE DOSAGE ON SURVIVAL OUTCOMES IN MULTIPLE MYELOMA

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Objective: This study aimed to assess the impact of lenalidomide maintenance dosing on clinical outcomes and the development of lenalidomide refractoriness in Multiple Myeloma (MM) patients who received maintenance therapy following Autologous Stem Cell Transplantation (ASCT) at our institution. **Methodology:** A retrospective analysis was conducted on 82 MM patients who underwent lenalidomide maintenance therapy on a 21/28-day cycle post-ASCT. Low-dose maintenance was defined as a dose below the maximum allowable level, determined by the patient's Glomerular Filtration Rate (GFR) and hematologic parameters at initiation. The Maximum Tolerable Dose (MTD) was defined as the highest dose a patient could tolerate based on these criteria. **Results:** In the overall cohort, median PFS was 56.0-months (95% CI: 40.15–71.85) and median OS was not reached. However, 88.3% of patients were alive at 60-months and 68.2% at 120-months. A response of ≥ VGPR was observed in 91% of patients receiving low-dose maintenance therapy, compared to 73.3% in those receiving treatment at the maximum tolerated dose ($p = 0.005$). While the median PFS was 56.0-months (95% CI 47.06–64.93) in those receiving low-dose maintenance; the median PFS was 33-months (95% CI 23.36–42.63) in those receiving maintenance at the MTD ($p = 0.166$). Dose reductions during maintenance therapy due to adverse effects were reported in 17 patients (20.7%). Of these, 11 patients (16.9%) were initially on low-dose maintenance, while 6 patients (40%) were on the MTD ($p = 0.42$). The median duration of maintenance therapy was 21 months (6–34) for patients on low-dose maintenance and 11 months (4–24) for those on the MTD ($p = 0.114$). Second-line treatment was administered to 40 patients (48.7%) who experienced progression. The median PFS2 was 25.36-months (95% CI 9.24–41.48), and the median OS2 was 73.23-months (95% CI 42.50–103.95). Median PFS2 was 25.43-months (95% CI 0.20–50.66) and the survival rate was 70% at 60-months in those receiving lenalidomide-based second line therapy, while median PFS2 was 25.36-months (95% CI 6.30–44.42) and the survival rate was 53.8% at 60-months in those receiving lenalidomide free