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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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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