CASE REPORT

The patient, a 45-years-old gentleman, was evaluated at nephrology institute in February 2009 for end-stage renal disease due to diabetic nephropathy requiring hemodialysis. He had a history of uncontrolled diabetes for 7 years, diabetic retinopathy and hypertension for 2 years. He subsequently underwent a spousal renal transplant uneventfully on April 17, 2009. He received interleukin-2 receptors blocker (Inj Daclizumab) as induction agent and cyclosporine, azathioprine, and prednisolone for maintenance therapy. Post-transplantation he had good graft function. He remained in good health until 2016 when the patient started developing intermittent low-grade fever. Hemogram done in August 2016 was suggestive of mild leukocytosis and monocytosis. In January 2017, the patient developed febrile neutropenia; immunosuppression was stopped and treated with antibiotics and growth factors. Immunosuppressive medications were restored on recovery of the leukopenia. In November 2017, the patient developed the acute coronary syndrome, requiring percutaneous transluminal coronary angioplasty with drug eluting stent and antiplatelet medications aspirin and clopidogrel were started. Since November 2017 patient developed worsening bicytopenia (anemia and thrombocytopenia) with monocytosis and was referred for hematological evaluation.

On physical examination, the patient had pallor, ecchymotic patches over the skin and mild hepatosplenomegaly.

Blood investigations were as follows: White blood cell was 9.6 × 10^9/L, hemoglobin of 4.6 mmol/L, and platelet level of 168 × 10^9 6 mmol/L. The differential on the complete blood count revealed a monocytic hyperproliferation at 25% with (5%) promonocytes, (20%) lymphocytes, (5%) blast cells, and (45%) segmented neutrophils. Peripheral smear examination was suggestive of anisopoikilocytosis, macroovalocytosis, dysmyelopoiesis, dysmyelopoiesis, and reduced thrombocytes.

BM aspiration was hypercellular with overall cellularity of 50–55%, with M:E ratio of 2.2:1, differential counts were suggestive of monocytes 15%, promonocytes 12%, blast 07%. Dyserythropoiesis and dysmyelopoiesis are shown in Figure 1. BM biopsy revealed infiltration by atypical cells which were large, having vesicular nuclei with prominent nucleoli in many of them with moderate to abundant cytoplasm [Figure 2].

BM flow cytometry was as follows: About 21.3% monocytic cells with partial dim CD56 expression, 7.6% myeloid blasts, 0.1% mature b-lymphoid cells, and 5.2% mature t-lymphoid cells with rest of the cells being maturing myelocytes.

Fluorescence *in situ* hybridization (FISH): Monosomy 7 was observed in 90% cells [Figure 3]. Monosomy 5, chromosome

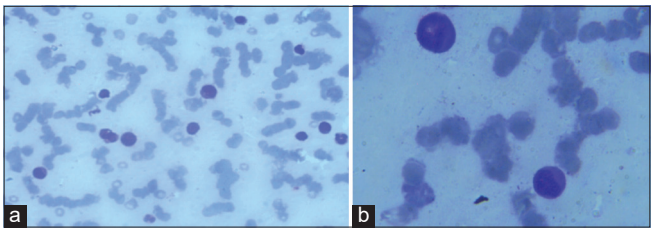

Figure 1: (a) Bone marrow aspiration ×400 (b) bone marrow aspiration ×1000.

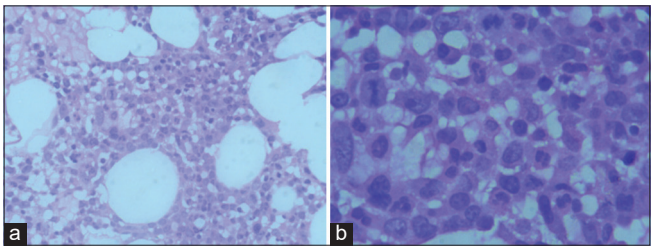

Figure 2: (a) Bone marrow biopsy ×400 (b) bone marrow biopsy ×1000.

8 abnormality, Del 20, *BCR/ABL1*, *FIP1L1-PDGFRA,* and *ETV6/PDGFRB* translocations were negative.

CMML was diagnosed based on the peripheral monocyte proliferation >1 × 10^9/L documented for 3 months, <20% blasts, and BM pathological findings consistent with both myeloproliferative and dysplastic features. The absence of Philadelphia chromosome and of a PDGFRA rearrangement on FISH along with clonal cytogenetic abnormality of Monosomy 7 in the bone marrow confirms the diagnosis of CMML.

The patient was treated with azacitidine and supportive care. He received two cycles of azacitidine. The clinical course was complicated with febrile neutropenia, transfusion dependence, labile hyperglycemia, and worsening of renal function. After the second cycle of chemotherapy, patient developed lower respiratory tract infection and succumbed to acute respiratory distress syndrome.

DISCUSSION

CMML is a rare disease. As per the WHO classification, CMML is classified under the category of myelodysplastic/MPD (MDS/MPD).[5] MDS/MPDs, including CMML, can occur de novo or as a result of exposure to therapy. tMDS/AML have been reported after exposure to alkylating agents, topoisomerase II inhibitors and radiation therapy.[6] These chemotherapy agents and radiation therapy are conventionally used to treat a variety of primary malignancies such as Hodgkin's lymphoma, non-Hodgkin's lymphoma, acute leukemia, sarcoma, breast, ovarian, and testicular cancers. The median time to develop tMDS/AML is 3–5 years. However, the incidence of secondary malignancies

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