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Case Report

Chronic myelomonocytic leukemia: A case report

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ABSTRACT

Chronic myelomonocytic leukemia is a clonal stem cell disorder characterized by persistent monocytosis along with myelodysplasia and/or myeloproliferation. According to the World Health Organization 2016 4th edition, Chronic myelomonocytic leukemia is categorized as a myeloproliferative/myelodysplastic disorder and its diagnosis requires the presence of persistent monocytosis and dysplasia involving one or more myeloid cell lineages. Chronic myelomonocytic leukemiais a rare disease with a heterogeneous clinical presentation. Recent progress in the molecular and cellular pathogenesis of Chronic myelomonocytic leukemia has stirred a renewed interest in this clinically heterogeneous disorder. Herein, we report of case of Chronic myelomonocytic leukemia in a 70-years male patient.

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INTRODUCTION

In the 80s, chronic myelomonocytic leukemia (CMML) was classified by the FAB (French-American-British) system as a subcategory of myelodysplastic syndromes (MDS). However, the presence of characteristics that were common to myeloproliferative diseases was noticed, and in 2001, the World Health Organization (WHO), together with the Hematopathology Society and the European Haematology Association published the Classification of Tumours of Hematopoietic and Lymphoid Tissues which included CMML in the new group of Myeloproliferative/

Myelodysplastic Diseases.[1,2]

The diagnosis of CMML requires the presence of >1 × 10^9/L of monocytes in the peripheral blood. The monocytes may be abnormal in appearance with bizarre nuclei and even cytoplasmic granules.[3] Promonocytes, with more immature nuclear chromatin may be present in the blood, but monoblasts are usually rare to absent. Much controversy surrounds the definition of a promonocyte, and distinguishing a promonocyte from a monoblast or a mature monocyte can be difficult. The peripheral blood may demonstrate cytopenias and dysplastic changes more typical of the myelodysplastic syndromes, or dysplastic changes may be minimal.

Table 1 Diagnostic criteria of Chronic Myelomonocytic Leukaemia according to World Health Organization 2016 (4th edition)

Persistent monocytosis ≥1 × 109/L and monocytes ≥10% of WBC in peripheral blood
No criteria and no previous history of CML, ET, PV and PMF
If eosinophilia, neither PDGFRA, PDGFRB, FGFR1 rearrangements nor PMC1-JAK2 translocation
<20% blasts in peripheral blood and bone marrow aspiration
≥1 of the following criteria:
Dysplasia in ≥1 myeloid lineage
Acquired clonal cytogenetic or molecular abnormality in hematopoietic cells
Monocytosis persistent for at least 3 months, with other causes excluded

CASE REPORT

A 70-year-old male with a history of pain and swelling in the right leg was admitted to the local hospital for debridement. The patient presented to our hospital with the chief complaints of right leg redness and swelling for last 10-14 days with mild hepato-splenomegaly. The patient also had complaints of blackish elevated lesions over the chest, abdomen, back, both hands, and legs with itching and oozing of blood from lesions for 6 months. Routine blood investigation showed Total leukocyte count: 138 x 10^3 /µl, Hemoglobin: 8.3 g/dl, and Platelet count: 297 x 10^3 /µl. The differential count showed blast: 02%, myelocytes: 03%, metamyelocytes: 14%, neutrophils: 39%, lymphocytes: 05%, eosinophils 06% monocytes: 36%, and basophils 00%. Serum creatinine was 3.19 mg/dl with elevated serum uric acid and serum LDH.

Bone marrow examination showed hypercellular marrow for the age with increased myeloid to erythroid ratio. Bone marrow differential count showed- blast: 03%, metamyelocytes:48%, neutrophils:11%, monocytes: 38%, and plasma cells: 03%. Myeloid series was increased in number with increased proliferation of monocytic series with many mature monocytes, promonocytes, and occasional monoblasts (fig.1&2). Megakaryocytes were also increased in number with abnormal maturation. Bone marrow biopsy findings were consistent with aspiration findings and it showed increased proliferation of megakaryocytes (12-14/ Low power field) with abnormal maturation. Reticulin stain on bone marrow biopsy showed grade II fibrosis.

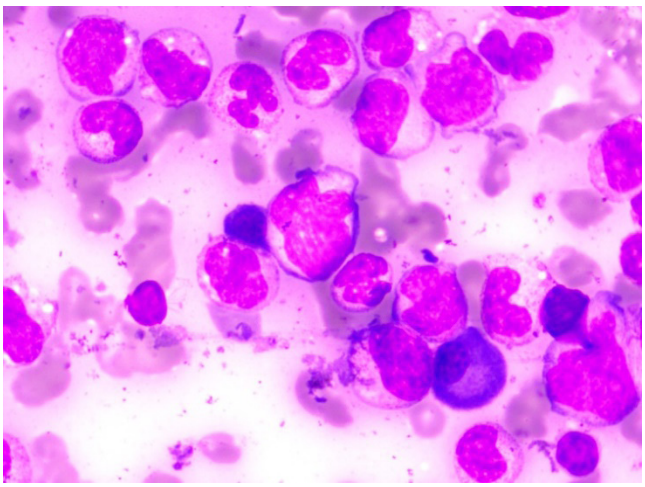

Figure 1: *Bone marrow aspiratoin smear showing increased proliferation of many mature monocytes and promonocytes. (Giemsa stain, X400)*

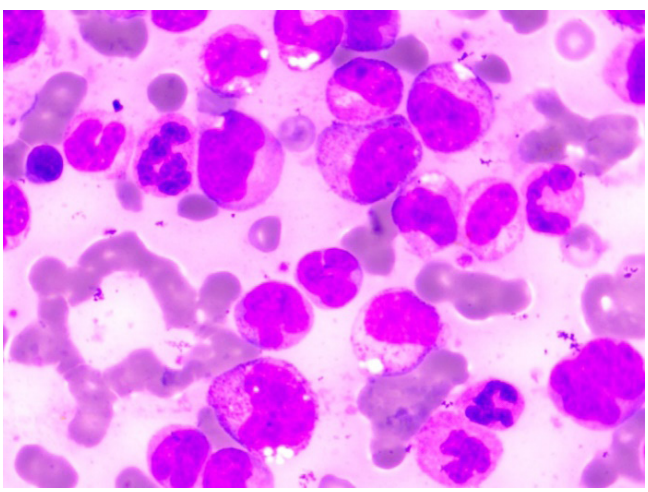

Figure 2: *Increased proliferation of myeloid series (Giemsa stain, X400).*

Immunophenotyping (IPT) was done and it showed about 0.5% myeloblasts gated in CD45 moderate region with low to intermediate side and forward scatter. The gated population expressed moderate CD33, CD13, CD34, CD117, and HLADR. Monocyte cells (~32%) showed abnormal patterns on CD13 vs CD11b, CD14 vs CD11b and HLA DR vs CD14 dot plot, and showed mild expression of CD56. The background granulocytic/non-blasts myeloid cells (~54%) showed reduced side scatter and abnormal pattern of maturation on CD13 vs CD11b, CD13 vs CD16, CD11b vs CD16, CD16 vs CD15 dot plot and showed mild expression of CD56. A plasma cell cluster (~0.5%) seen with bright CD38, CD19, moderate CD45 expression and negative for CD20, CD56. (fig.3)

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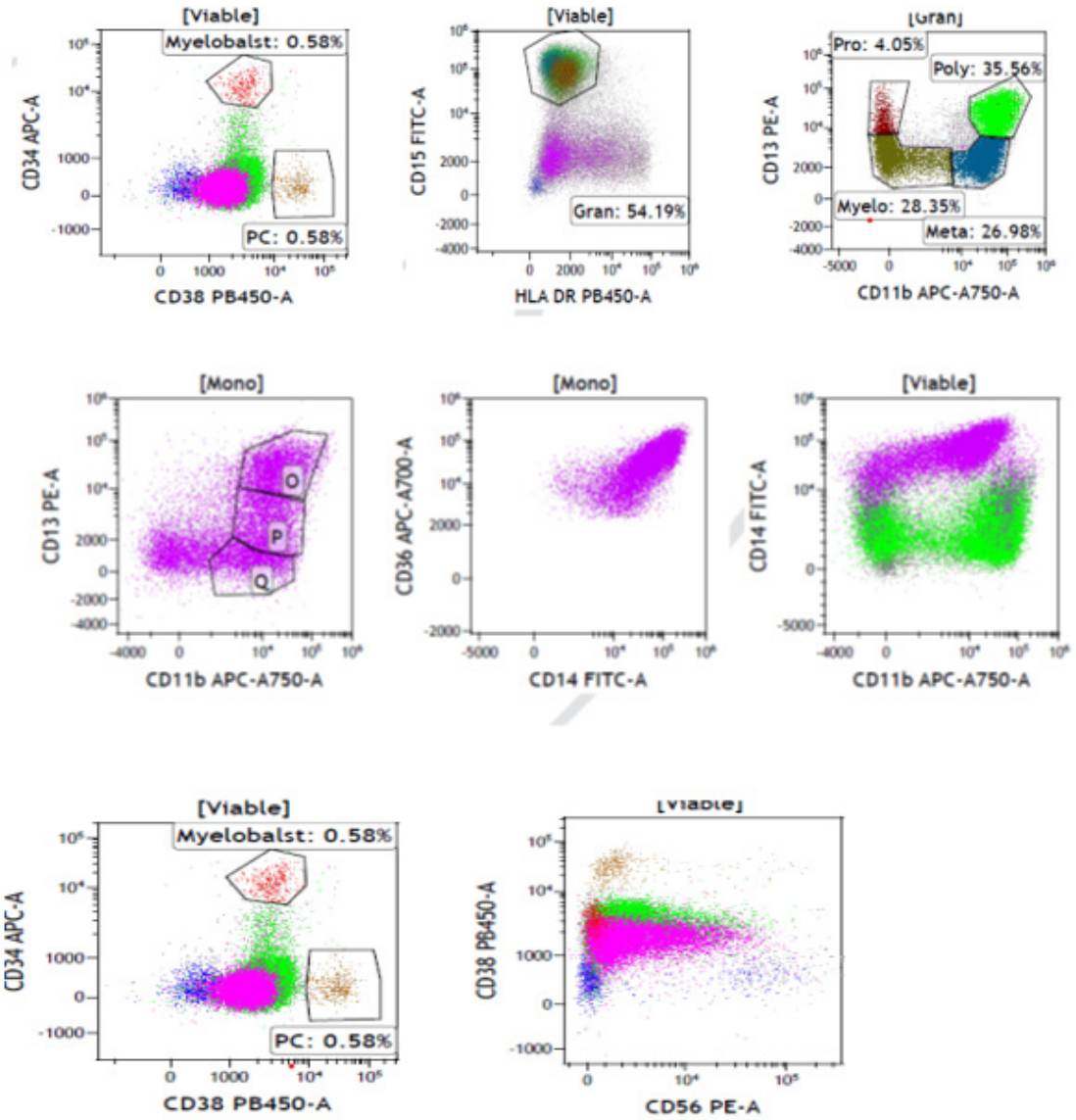

Figure 3: *Immunophenotyping of bone marrow showing 0.5% myeloblast. 54% non-blast myeloid cells show reduced side scatter with abnormal maturation and monocyte (~32%) show abnormal pattern on CD13 vs Cd11b, CD14 vs CD11b, HLA DR vs CD14 dot plot and show mild expression of CD56.*

DISCUSSION

MDS is a group of clonal diseases that have the following clinical presentation: ineffective hematopoiesis in the bone marrow and a highrisk of transformation to acute myeloid leukemia. Before 2008, CMML was classified as a subtype of MDS. As per WHO 2016 4th edition, CMML is categorized under independent, larger disease group (MDS/MPN). CMML includes previous MDS-CMML (more emphasis on dyshematopoiesis) and MPN-CMML (more emphasis on bone marrow proliferative changes).[4]

Current basic and translational research aims at better understanding how the specific clonal architecture of CMML drives its clinical phenotype, identifying therapeutic strategies to eradicate ancestral mutations such as those in the spliceosome, and deriving relevant pre-clinical models to allow unbiased therapeutic screens.[5] Clinical studies are ongoing to derive uniform risk stratification and therapeutic evaluation tools. A coordinated academic effort will be necessary to translate our recent molecular and cellular findings into scientifically informed trials in this rare yet difficult-to-treat disease.

CMML is a rare myeloid neoplasm of the elderly, with an annual incidence of about 4 cases per million in Western countries, a male predominance, and a median age at diagnosis close to 75 years.[6-8] The clinical features of CMML are variable. Cytopenia including macrocytic or normocytic anemia and thrombocytopenia are seen more frequently than neutropenia. Thrombocytopenia can also be of peripheral, auto-immune origin. Myeloproliferative

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features are dominated by splenomegaly but can include skin lesions for which different patterns of infiltration can be seen, requiring systematic skin biopsy, notably to exclude *bona fide* leukemia cutis corresponding to extramedullary transformation to AML.[9]

CONCLUSIONS

CMML may present with heterogeneous clinical manifestation and pose diagnostic challenges, and may commonly be misdiagnosed as Acute myeloid leukemia M5. Bone marrow examination and immunophenotyping are essential for diagnosis.

Conflict of interest: None

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