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Case Report

MONOCYTOSIS IN AUTOMATION- CAN WE NEGLECT?

***S. Naveen Kumar[1], D. Febe Renjitha Suman[1], Sri Gayathri[1] and Suresh Sudalaiandi[2]**
[1]Department of Pathology, Sri Ramachandra Medical College and Research Institute, Sri Ramachandra University, Chennai
[2]Department of Oncology, Sri Ramachandra Medical College and Research Institute, Sri Ramachandra University, Chennai
**Author for Correspondence*

ABSTRACT
41 year old lady with hepatosplenomegaly presented to our hospital. Complete blood count revealed monocytosis. Further investigations by bone marrow aspirate, biopsy and immunophenotyping with the help of flow cytometry, a very rare diagnosis of chronic myelomonocytic leukaemia was made. The diagnostic work up stresses the importance of smear review criteria and white blood cell histogram to arrive at a proper diagnosis.

Keywords: *Monocytosis, Chronic Myelomonocytic Leukemia*

INTRODUCTION
Chronic myelomonocytic leukemia (CMML) is a very rare condition with an annual incidence of 0.37/100000 population (Rollison *et al.,* 2008). CMML once grouped under myelodysplastic syndrome (MDS) had been reclassified under myeloproliferative neoplasms/myelodysplastic syndrome (MPN/MDS) (Arber *et al.,* 2016; Vardiman *et al.,* 2008). As the condition is rare, it is often forgotten as a differential diagnosis for monocytosis. Monocytosis is reflected in Beckman Coulter haematology analyzers in various conditions. The false positive monocytosis is reflected in reactive lymphocytosis, plasmodium infections and in the presence of precursors of neutrophils. The smear review criteria necessitates a peripheral smear to be looked upon by pathologist when there is flagging. A case of CMML is presented here for its rarity and to create awareness about this condition in monocytosis flagging.

CASES
A 41 year old lady who was well before two months developed fever and vomiting on and off, and palpitation. She was treated in an allopathic hospital a month back and the symptoms recurred for which she stepped into our medicine unit. On examination she was pale and had angular chelitis. She had mild hepatomegaly and moderate splenomegaly. No other significant clinical signs were noted.
Complete blood count done in Beckman Coulter LH 780 haematology analyzer showed red blood cell (RBC) count of 1.67×10^{12}/L, haemoglobin of 5.3g/dL, haematocrit of 15.9%, total white blood cell (WBC) count of 11.6×10^{9}/L and a platelet count of 106×10^{9}/L. Differential count revealed monocytes comprising 67.9% with an absolute count of 7.8×10^{9}/L. There was a flagging of monocytosis (Review alert high, monoblasts and neutrophil blasts). The WBC histogram showed a peak in the monocyte area. In addition lactate dehydrogenase level was 597U/L. Peripheral smear showed normocytic normochromic RBCs, monocytosis with 2% blasts and thrombocytopenia.
In view of the high monocyte count, bone marrow aspirate was done which showed a cellular marrow with increase in monocytoid cells (blasts 8%, monocytes 60%) as shown in Figure 1 and dyspoiesis in myeloid cells. Flow cytometry showed moderate positivity in CD 36, CD 64, CD 14, CD 11c and aberrant low expression of CD 33 in the CD 45 gated cell population as shown in Figure 2. The cells showed variable positivity for HLA-DR and weak positivity for CD123. CD 13 and cytoplasmic myeloperoxidase (MPO) were negative. Florescent in-situ hybridisation for bcr-abl was not detected. Bone marrow biopsy revealed a cellular marrow with myeloid hyperplasia and monocytic cell infiltration. Reticulin was increased. Immunohistochemistry (IHC) on the biopsy showed 70% CD 68 positivity and 30% MPO positivity among the CD 45 positive cells as shown in Figure 3.

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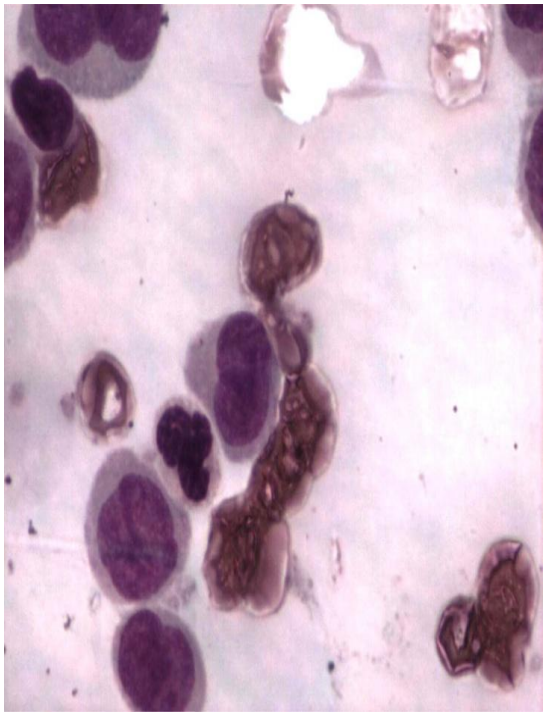

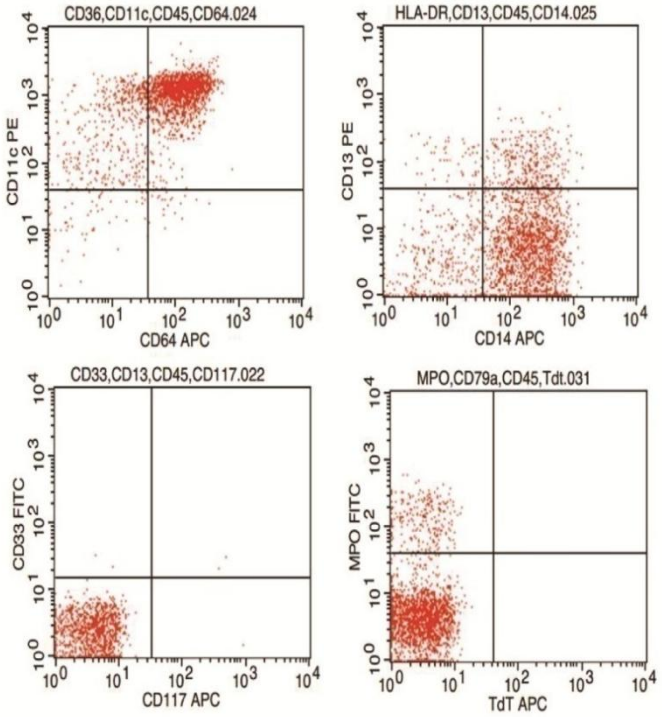

Figure 1: Bone Marrow Aspirate, Leishman Stain, x400

Figure 2: Flow Cytometry

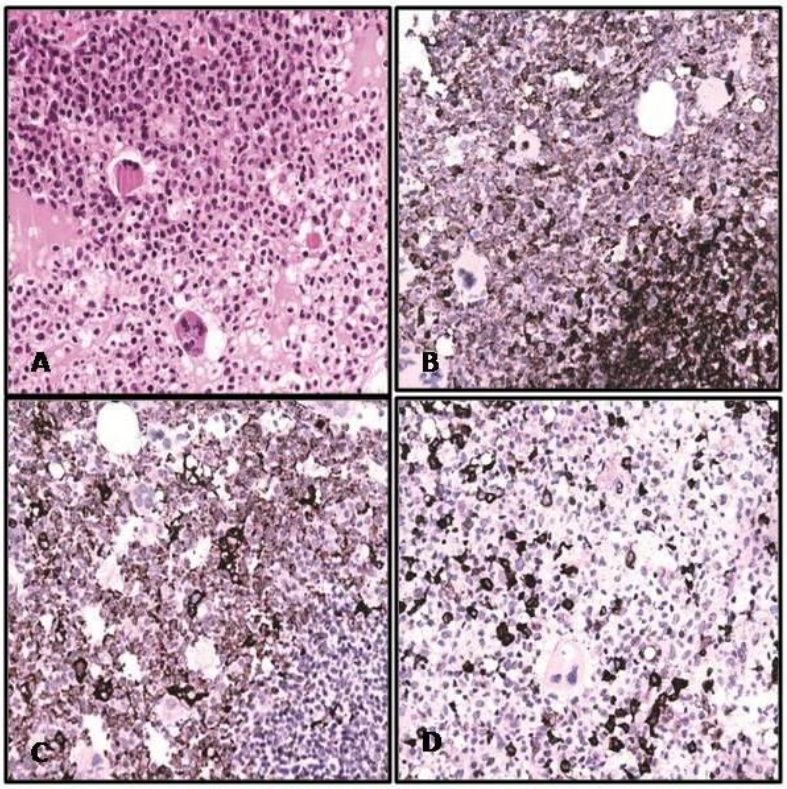

Figure 3: Bone Marrow Biopsy-x200-A.H&E, B to D-IHC, B-CD 45, C-CD68, D-MPO

DISCUSSION

Acute monocytic leukemia was ruled out since blasts were less than 20% of non erythroid cells (Bain *et al.*, 2010). A typical chronic myeloid leukemia was ruled out since the circulating WBC precursors were less than 15 % (Vardiman *et al.*, 2008). The infectious causes of monocytosis were ruled out because of the absence of clinical symptoms, aberrant low expression of CD 33 and negative serology for infections (Sojitra *et al.*, 2013). Reactive large lymphocytes, presence of malarial parasites and sometimes myelocytes are flagged as monocytosis in Beckman coulter 780 haematology analyzers. However, the WBC histogram provides a valuable opinion on the flagging rather than the scattergram as in this case. The final diagnosis of CMML was made based on the criteria of monocyte count more than 1×10^9/L, absent bcr-abl fusion gene, presence of less than 5% and 10% blasts including promonocytes in the peripheral blood and bone marrow respectively and dysplastic changes in myeloid lineage (Orazi *et al.*, 2008).

CMML, a rare MPN/MDS neoplasm has to be cautiously diagnosed following the WHO criteria, in adult patients presenting with hepato-splenomegaly and monocytosis. Educating technical staff and junior pathologist to recognize flags and adhere to smear review criteria helps in detecting these rare conditions. A case of CMML is presented here for its rarity and to create awareness about this condition in monocytosis flagging.

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