Aleukemic Variant of Mast Cell Leukemia- A Rare Phenomenon

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Abstract- Mast cell leukemia is a rare variant of mastocytosis, accounting for less than 1% of all mast cell disease and pose one of the greater challenges in the management of these patients, with a grave prognosis. Diagnosis of this neoplasm rests on the detection of abnormal mast cells in marrow and subsequent spill over to the peripheral blood. We report a case of aleukemic variant of mast cell leukemia in a pediatric patient, presenting with fever and chest pain for 10 days. The peripheral smear showed a picture of pancytopenia with abnormal/ atypical lymphoid cells. Bone marrow aspirate showed dense aggregates of atypical, hypogranular and partially degranulated mast cells expressing toluidine blue and CD117 positivity.

Index Terms- Mast cell, mastocytosis, aleukemic variant of Mast cell leukemia.

I. INTRODUCTION

WHO has updated the diagnostic criteria and classification of the mastocytosis; characterized by neoplastic proliferation of mast cells in one or more organs.[1] Mast cell leukemia is one such rare neoplasms which is identified by leukemic spread of mast cells, with frequent and multiple organ involvements such as liver, peritoneum, spleen, bone and bone marrow.[2] A detailed examination of the peripheral smear, bone marrow aspirate and biopsy is the utmost requirement for the diagnosis of mast cell leukemia as the threshold of > 20% mast cells in the bone marrow along with the features of aggressive systemic mastocytosis is the criteria. An "aleukemic" variant of mast cell leukemia is frequent. This diagnosis is made, if the number of circulating mast cells are less than 10%.[1]It has been referred to in the literature that in contrast to adults with systemic mastocytosis, definitive marrow involvement in children is less common.[3]We present a unique dilemma in a pediatric age group.

II. CASE REPORT

A15 year old male patient was brought to the hospital with history of fever and right- sided pricking type of chest pain for 10 days**.** Fever was not associated with chills, but patient had cough with no hurried breathing or wheeze. Developmental milestones were appropriate for age. On physical examination, the heart rate, blood pressure and respiratory rate were within normal limits. Respiratory system examination showed a reduced air entry with stony dullness on percussion over the right hemithorax but no adventitious sounds were heard on auscultation. Per abdomen examination revealed an enlarged liver and splenomegaly 4 cms below right costal margin and 5 cms in splenic axis respectively.

III. INVESTIGATIONS

The coulter hemogram revealed pancytopenia (anemia, leukopenia and thrombocytopenia) with the following parameters: Hemoglobin- 7.1 g/dl, total WBC count- 2800 /µL, platelets- 58000/µL.The peripheral smear confirmed the above findings, additionally showing occasional spherocytosis and 5 nucleated RBCs/100WBCs. The differential count showed mild left shift with 20% of atypical/abnormal lymphoid cells. Liver function test and renal function test were within normal limits. The patient did not have any skin lesion. With the above smear findings, an impression of leukoerythroblastic picture with an advice to perform bone marrow study was given.

Patient was also subjected for the contrast enhanced computed tomography (CECT) thorax, which revealed a well - defined large, lobulated and heterogenous hypodense lesion in the right hemithorax and anterior mediastinum showing heterogenous enhancement, cystic areas and few hyperdense areas.

Bone marrow aspirate showed cellular marrow particles with suppressed myelopoiesis and megakaryopoiesis with increased erythropoiesis. Dense aggregates and scattered atypical spindly mast cells(Figure 1) with hypogranular and degranulated forms were seen. The differential count of these mast cells accounted to be 34%.

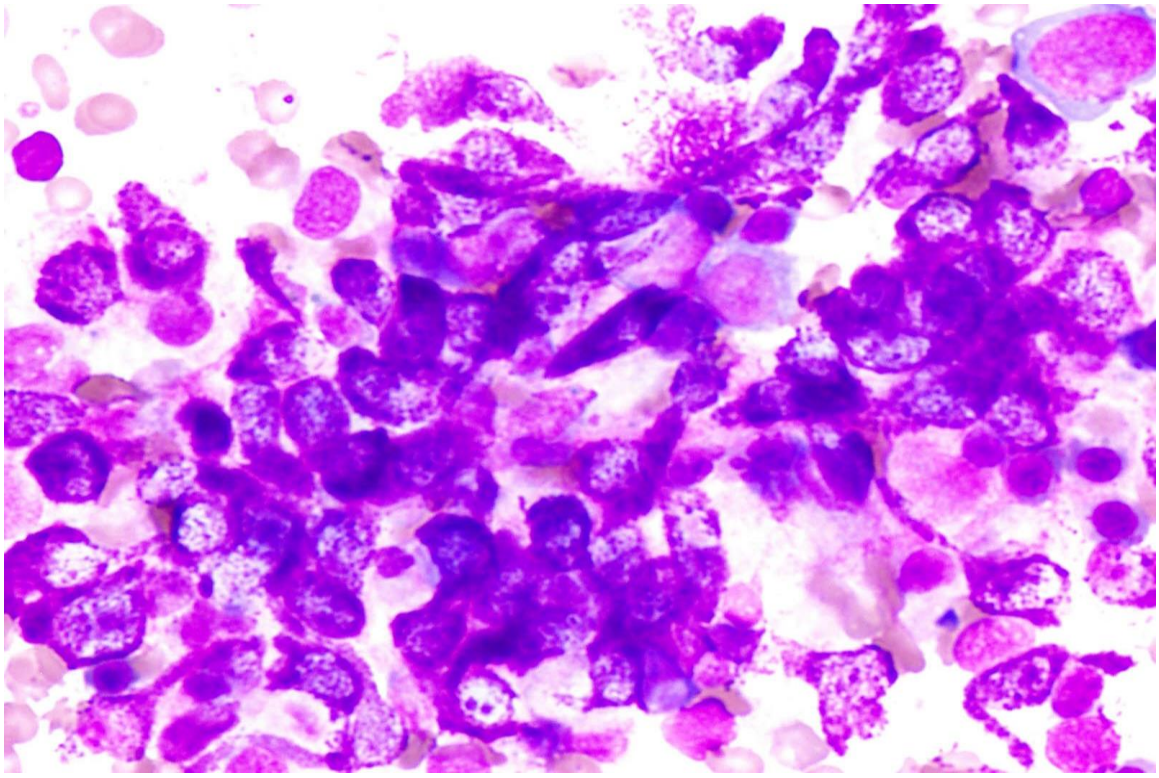

Figure 1: Dense aggregates and scattered atypical spindly mast cells with hypogranular and degranulated forms. (Leishman;x200)

Immunohistochemistry done on the bone marrow biopsy was positive for CD68 and CD117. Cytochemistry showed positivity with toluidine blue; showing metachromatic granules in the mast cells (Figure 2).

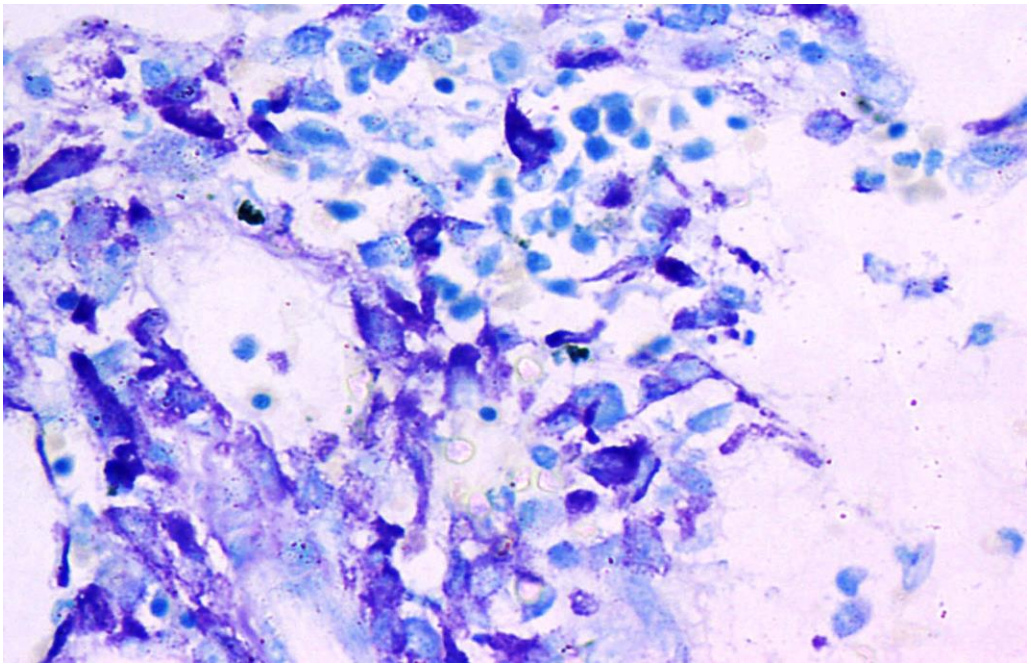

Figure2: Bone marrow biopsy sections showing aggregates of mast cells with metachromatic blue granules. (Toluidine Blue; x200).

In light of above morphological features and the available clinical data, the diagnosis of "aleukemic"variant of mast cell leukemia with C- Finding was given after referring various sources of literature. A request was made to biopsy the mediastinal mass to rule out anextracutaneous mastocytosis.

IV. DISCUSSION

Systemic mastocytosis is characterized by the proliferation of atypical mast cells in tissues, principally in the bone marrow (BM) and skin.[4] According to the World Health Organization (WHO)[1], systemic mastocytosis is grouped into 4 major clinical variants: 1) indolent systemic mastocytosis; 2) systemic mastocytosis with an associated clonal, hematologic, non-mast cell lineage disease; 3) aggressive systemic mastocytosis; and 4) mast cell leukemia based on distinct clinico-pathological features. Mast cell leukemia is regarded as rare form of aggressive systemic mastocytosis; accounting for less than 1% in prevalence. Georgin-Lavialle and co-workers described two distinct forms of presentation: *de novo* or secondary to previous mastocytosis and shares more clinicopathological aspects with systemic mastocytosis than with acute myeloid leukemia.[2] A lack of skin lesions has been described in cases of aggressive systemic mastocytosis and mast cell leukemia. However, bone marrow mastocytosis (BMM), a subvariant of indolent systemic mastocytosis was recognized by the 2008 WHO classification.[1] But when a diagnosis in absence of typical skin involvement is to be rendered, it presents a challenge for clinicians and pathologists alike. Some other common clinical conditions, such as unexplained anaphylaxis, osteoporosis of unknown etiology, etc pose as differential diagnoses. Moreover, indolent systemic mastocytosis without skin lesions has been frequently reported in patients with systemic allergic reaction to hymenoptera venom and raised basal tryptase.[5]

In a study by Sophie Georgin-Lavialle et al.[2],the median age of diagnosis of mast cell leukemia was 51.5 years with a female predominance(sex ratio (F/M) of 1.5). On physical examination, hepatomegaly and splenomegaly were the most frequent clinical signs. Gastrointestinal manifestations frequently included gastroduodenal ulcers (29%)which were often complicated by gastrointestinal hemorrhage (64%)[2]. Gastroduodenal ulcers seem to be more frequently associated with the *KIT* D816V (12.5%) mutation than with other KIT mutations. Our case was a young male patient of 15 years of age.

According to a study by Robert I. Parker[6,7], almost 50% of pediatric patients with mast cell disease, have normal cellularity on bone marrow aspirate smears and more than 50% of them showed predominantly perivascular lesion on the bone marrow biopsy. The present case also showed marked increase in the cellularity with perivascular and paratrabecular clusters of mast cells on biopsy which were positive for various markers of mast cell.

In contrast to ISM (Indolent systemic mastocytosis), patients with ASM (Aggressive systemic mastocytosis) often presents without maculopapular skin lesion, whereas patients with MCL(mast cell leukemia) have characterstic rapidly progressive C- Finding.[8] Irrespective of the clinical course, no curable therapy for ASM and MCL has become available till date. Rather, the primary goal for treatment is the amelioration of symptoms and pharmacologic control of growth of neoplastic cells.

The role of cytogenetics in cases of ASM as well as MCL is very limited because of the paucity of analysis in this field. However, the proposal of role of trisomy 8 and 9 was brought forward by Lishner et al[9], and a case report by Callera F,[10] who showed positive detection of trisomies 9 and 8 by FISH (fluorescent in situ hybridization) in patients with systemic mastocytosis. On the contrary,Swolin B et al.[11]did not find these trisomies with FISH in patients with mastocytosis. So, there is need of more clinical research into the clinical consequences resulting from the occurrence of chromosomal abnormalities in patients with mast cell disease.

The present pediatric patient in this case report was not subjected to various tests and the biopsy from the lesion in the mediastinum as was referred to the specialized treatment centre for further management in view of the limited prognosis in these cases.

In summary, this case described herein illustrate the presentation of mast cell disease without any skin lesion with a mass in the mediastinum, hepatosplenomegaly with normal liver function test. Bone marrow showing marked infiltration of perivascular and paratrabecular region with neoplastic mast cell.A recognition of this rare entity is mandatory in order to avoid diagnostic dilemmas.

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