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Case Report

Acute Panmyelosis with Myelofibrosis: A Rare Entity

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ABSTRACT

Acute Panmyelosis with myelofibrosis is an exceedingly rare disorder characterized by a fibrotic bone marrow with an increased number of immature trilineage hematopoietic elements, and conspicuously dysplastic megakaryocytes with foci of blasts scattered throughout the marrow. The bone marrow aspirates are usually "dry." The bone marrow biopsies are essential for the diagnosis and show four consistent features.

Keywords: APMF - Acute panmyelosis with myelofibrosis, AML-Acute Myeloid leukaemia, WHO-World Health Organisation, CIMF – Chronic idiopathic myelofibrosis, MDS –Myelodysplastic syndrome, AMKL- Acute megakaryocytic leukaemia

INTRODUCTION

Acute panmyelosis with myelofibrosis (APMF) is an ill-defined disorder .Its true nature is not completely understood. Some believe that it is a variant of AML, and consider it to be equivalent to AMKL. Yet others believe that it is an acute variant of MDS- a group of disorders in which myelofibrosis can also be observed.

Presently it is classified according to World Health Organisation under acute myeloid leukaemias, not otherwise categorised. In this case report we will discuss a case of acute panmyelosis with myelofibrosis having characteristic clinical & haematological profile & dry bone marrow aspiration with diagnosis made on bone marrow biopsy.

CASE REPORT

40 yrs male was admitted to Dayanand medical college & Hospital, Ludhiana with chief complaints of generalized weakness and decreased appetite since 2 wks .On examination pallor was present. No palpable organomegaly or lymphadenopathy was evident Investigations showed pancytopenia in haemogram with Total Leucocyte Count 2.8 X 10^{9} /l, haemoglobin 3.8 gm/l and platelet count 69X 10^{9}/l with 34 % blasts (Fig ii)on differential leucocyte count. Peripheral blood film had predominantly normocytic

normochromic red cell picture (Fig i).Myeloid series of cells exhibited pseudo Pelger – Huet anomaly (Fig i). Giant platelets & megakaryocytic fragments were also present. No organomegaly was detected on ultrasonography. Bone marrow aspiration was tried from both posterior superior iliac spine and sternum but only blood was obtained and no bone marrow could be aspirated despite repeated attempts. Bone marrow biopsy was taken from posterior superior iliac spine under all aseptic conditions and contact smears were also prepared. Bone marrow biopsy contact smears did not yield any bone marrow elements. Biopsy sections showed increased marrow fibrosis with presence of atypical megakaryocytes. These megakaryocytes had hypolobated nuclei with dispersed chromatin. Few other cellular elements seen asblasts, cells of erythroid & myeloid series were also present loosely dispersed in between fibroblasts (Fig iii). Reticulin stain on Bone marrow biopsy showing increased reticulin fibres in the intertrabecular space.

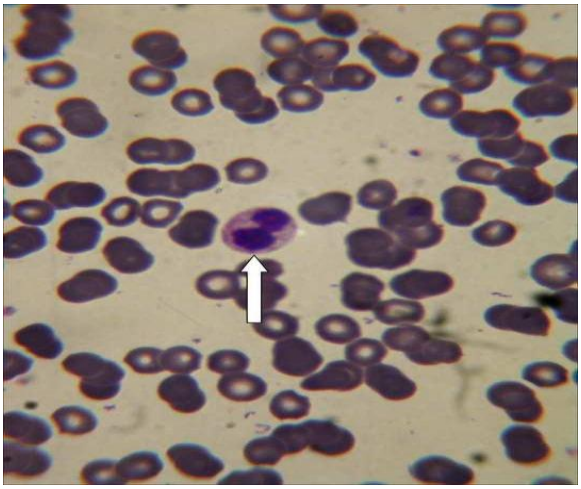

Fig i-Peripheral blood film showing normocytic normochromic red cell picture and a neutrophil (arrow) with pseudo Pelger-Huet

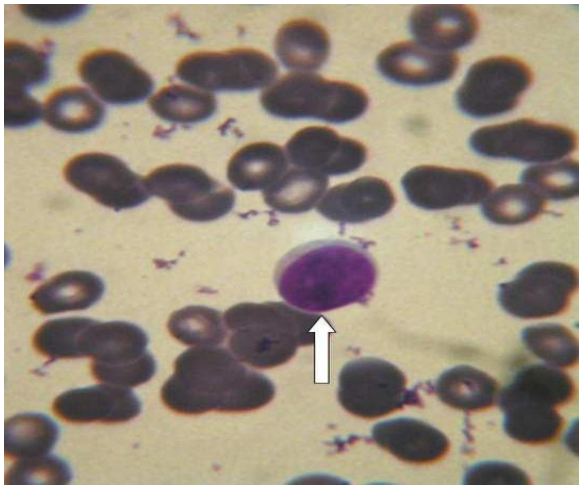

Fig ii-Peripheral blood film showing a blast (arrow).

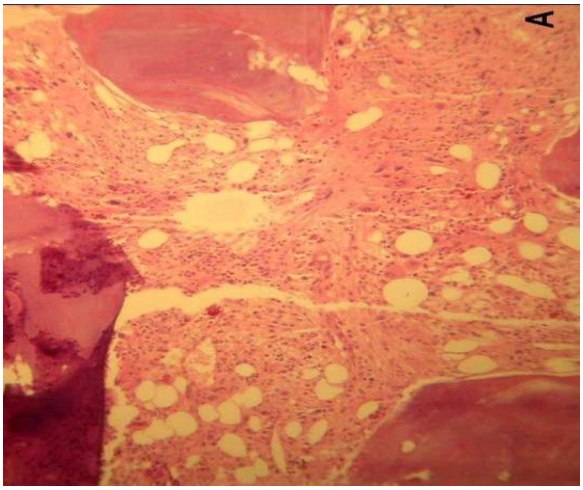

Fig iii: Bone marrow biopsy showing increased fibrosis with prominence of megakaryocytes including hypolobated forms . The other haematopoietic elements are also seen.

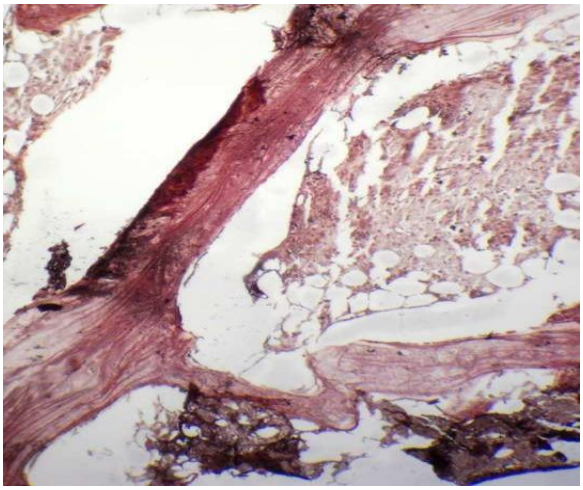

Fig iv: Reticulin stain on Bone marrow biopsy showing increased reticuline fibres in the intrabecular space.

The immunological evaluation showed CD 13, CD33 positivity & CD 41 & 42were negative. On the basis of clinical features, systemic examination, peripheral blood film and bone marrow findings collectively, a final diagnosis of Acute Panmyelosis with myelofibrosis was made.

DISCUSSION

Acute panmyelosis with myelofibrosis is a rare entity which is an acute myeloid disorder with unfavourable prognosis in which there is trilineage differentiation associated with bone marrow fibrosis. [(1)] The critical point is to recognize that it is an acute process that has sufficient numbers of blasts to be considered AML. It is often associated with dysplasia and immaturity in multiple cell lines, with myelosclerosis, acute myelofibrosis, acute myelodysplasia with myelofibrosis, and malignant myelosclerosis. [(1-3)] are synonymous with APMF. The WHO criteria for the diagnosis of APMF include:panmyelosis, significant marrow fibrosis, pancytopenia, normal erythrocyte morphology, lack of splenomegaly, and a rapidly fatal course. [(4)] The primary differential diagnosis of APMF is with Acute Megakaryocytic Leukaemia (AMKL) .Other differential being chronic idiopathic myelofibrosis & Myelodysplastic syndrome with fibrosis. Morphologically, APMF & AMKL are known to show overlapping characteristics. Most of the past evidence, however, was based on cytologic analysis of blasts and abnormal megakaryocytic forms, as seen in smears or touch preparations, an approach that does not allow for a clear distinction between the two conditions. Besides providing a superior way to analyze megakaryocytic cells morphology and blast cell distribution, bone marrow biopsy overcomes difficulties connected to the absence or scarcity of marrow aspirate material in these myelofibrotic conditions [(5)] Most cases of APMF are characterized by a fibrotic bone marrow with an increased number of immature trilineage hematopoietic elements, and conspicuously dysplastic megakaryocytes predominantly of small size showing variable degrees of atypia including the presence of hypolobulated or nonlobulated nuclei. Foci of blasts are found scattered throughout the marrow. The overall frequency of blasts in APMF marrows is uncertain; however, its precise determination is not considered a diagnostic requirement,according to the WHO system. The peripheral blood in APMF usually shows pancytopenia with absent or only rare circulating blasts and lacks the anisocytosis and poikilocytosis. Splenomegaly is minimal or absent. The course is rapidly fatal, often terminating with an overtly leukemic myeloid phase, or rarely with a lymphoblastic malignancy. In the terminal stage, splenomegaly may be observed, which usually results from leukemic infiltration of the red pulp. [(6-8)] The disease usually occurs in adults, but rare cases have been described in children. [(4)]

Acute megakaryoblastic leukemia (AMKL) is a rare form of AML and accounts for 3–5% of all myeloid leukemias. AMKL is diagnosed according to criteria of the WHO system. [(5)] The main requirement is a minimum of 20% blasts, the majority of which showing megakaryocytic differentiation. i.e. there is proliferation of predominantly one cell type seen as megakaryoblasts. (WHO) and a marked degree of reticulin fibrosis.

The distinction between APMF and CIMF is usually much less problematic. The characteristic peripheral blood changes (i.e anisopoikilocytosis and leukoerythroblastosis), and the presence of significant splenomegaly help in diagnosis. In CIMF, the peculiar bone marrow biopsy

findings seen as peculiar characteristics of the megakaryocytes, which include anisocytosis with a predominance of large size forms arranged into tight cellular clusters, the abnormal chromatin clumping with hyperchromatic nuclei and clumped (cloud shape) nuclear lobulation allow for a distinction with APMF. [9] The distinction between APMF and aggressive subtypes of MDS with fibrosis (MDS-F) such as refractory anemia with excess of blasts type 2- with fibrosis, in particular, may be difficult. One of the reason concerns the degree of myelofibrosis which, in both conditions, shows significant overlap. However, important clinical differences exist between the two conditions, particularly the abrupt onset for APMF and its shorter survival rate in comparison with MDS-F.[(10)] It seems therefore prudent to retain the diagnostic terms separately, and to consider APMF a variant of AML as defined by the WHO system. Lastly, as briefly mentioned, it is particularly important to rule out the history of exposure to leukemogenic therapeutic agents (e.g. post alkylating agents) or environmental toxins before diagnosing APMF. These secondary cases should be more properly termed MDS- or AML-therapy-related, and not APMF.

CONCLUSION

APMF though is an ill defined disorder but in the new WHO classification of AML it is included under AML, Not otherwise categorized. Its main differential diagnosis is Acute megakaryoblastic leukaemia that shows proliferation of one cell type in contrast to APMF in which there is trilineage proliferation. Nowadays immunohistochemistry is also used to differentiate the two.

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