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An Unusual Case Report - An Adult of Chronic Myeloid Leukemia Presenting as Acute Myeloid Leukemia M7 (Megakaryocytic Blast Crisis)

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Abstract: ***Acute Megakaryoblastic Leukaemia (AML, M7) is a rare type of acute myeloid leukemia (AML) evolving from primitive megakaryoblasts. It accounted for 1.2% of newly diagnosed AML according to Eastern Cooperative Oncology Group (ECOG) trials between 1984 and 1997 [1]. It is an uncommon form of AML accounting for 8 - 10% of all AML cases in adults, and 2 - 3% of cases in children. crisis in CML since it occurs in nearly 20% of Ph positive CML cases [2]. Chronic myeloid leukaemia (CML) presenting primarily as megakaryocytic blast crisis is very rare, with very few case reports published to date [3] In adults, median age 57 years, 59% have prior hematologic disorder or myelodysplastic syndrome [4]. Associated with marrow fibrosis due to megakaryoblast secretion of fibrogenic cytokines, which makes marrow aspiration difficult [5]. Chronic myelogenous leukemia (CML) is a chronic myeloproliferative neoplasm consistently associated with the BCR - ABL1 fusion gene located in the Philadelphia chromosome. The Blast Phase is diagnosed when blasts are ≥20% of the peripheral blood white cell count or of bone marrow nucleated cells or when there is an extramedullary blast proliferation. Megakaryocytic blast crisis as the presenting manifestation of CML is extremely rare [6]. This case report describes a 29 - year - old woman who presented with admitted with complaints of menorrhagia and abdominal distention (Massive splenomegaly). She was diagnosed with the case of AML based on peripheral blood and bone marrow showing features of AML. Chromosomal analysis revealed t (9: 22) (q34; q11.2) in all 40 metaphase analysed and immunophenotyping of peripheral blood with positivity for CD 45, CD41 (84%). CD41 and CD61 are megakaryocyte specific antigens, and CD45 expressed in blast window***

Keywords: acute myeloid leukemia, acute megakaryocytic leukaemia, immunophenotyping, myelosclerosis chronic myeloid leukaemia, blastic crisis.

1. Introduction

Acute megakaryoblastic leukemia (AMKL) is one form of acute myelogenous leukemia (AML). It is classified as M7 according to the FAB system. AMKL is defined as an AML with >20% blasts, of which 50% or more are of the megakaryocyte lineage. AMKL may present in variety of ways. Nonspecific symptoms may be irritability, weakness, and dizziness. Specific symptoms are due to various cell line involvement viz. pallor, fever, mucocutaneous bleeding. Hepatosplenomegaly is a common finding, but lymphadenopathy uncommon

Neurological manifestations are headache, projectile vomiting, papilledema, cranial nerve palsies, chloromas due infiltration of tumor cells. Our patient presented with severe anemia, thrombocytopenia, and hepatosplenomegaly.

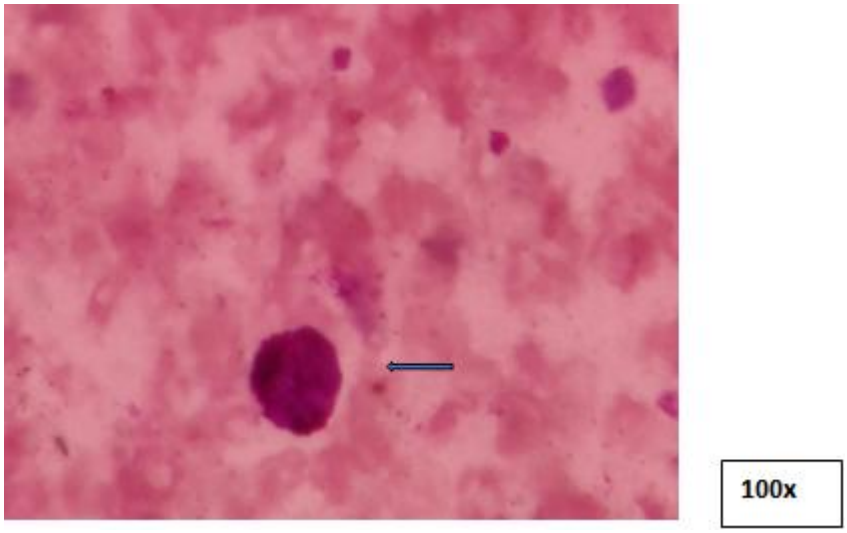
In the French - American - British (FAB) Classification, sub - type classification of AML is based on morphology and cytochemical staining with immunophenotypic data in some instances. Types M0, M1, M2, and M3 are predominantly granulocytic and differ in the stage of maturation. The M4 class is both granulocytic and monocytic, with at least 20% of cells being monocytic. M5 is predominantly monocytic with at least 50% being monocytic. M6 shows primarily differentiation with dysplastic features and megaloblastic changes. The AML classified as acute megakaryocytic leukemia is M7 and is characterized by the presence of megakaryocytic antigens demonstrated by flow cytometry, immunohistochemistry or the presence of platelet peroxides [7]. The disease can be identified by antibodies to glycoprotein Ib (CD42), glycoprotein IIb/IIIa (CD41a) andglycoprotein IIIa (CD61), and is often associated with extensive myelofibrosis. This case of a 29 - year old lady is reported because of the rarity of the disease.

On the other hand, there are cases with larger cells resembling ALL - L2 blasts with moderate amounts of rather basophilic cytoplasm which in some instances contain azurophilic granules. Cytoplasmic blebs and protrusions are the most prominent feature of many cases. The nuclei of these cells are round with more finely reticulated chromatin and with prominent nucleoli. The megakaryoblastic nature of these cells can be suggested by morphology. However, according to our experience there are cases of c - ALL with the very same morphologic picture. Consequently, immunologic phenotyping of these cases is necessary in any instance. Cytochemistry is of limited diagnostic value in megakaryoblastic leukemias. Usually it is used to exclude the more common types of leukemia [8].

2. Case Presentation

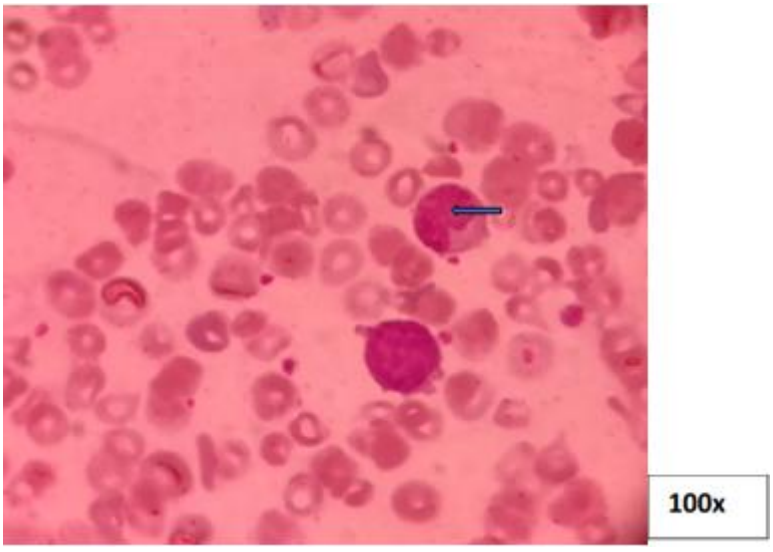
A 29 - year female, from West Bengal, presented at VYDEHI INSTITUTE OF MEDICAL SCIENCE, BENGALURU with history of fever (on and off episode), abdominal distension and abdominal pain which was on and off since 3 years of duration. She was treated outside by ayurvedic medicine for one year, however the symptoms yet persisted and later she went to private hospital in West bengal there she was diagnosed with anemia and splenomegaly. She was also transfused with 5 units of blood for symptomatic anemia. The symptoms, however, started

again 6 month prior to presentation at our medicine department. On examination, Patient was concious and oriented, Vitals stable, Pallor present, Level III and IV Cervical lymphnode enlargement seen, bilateral chest clear, per abdomen examination: Massive splenomegaly up to pelvisBP - 100/60 mmhg, Spo2: 98%, Pulse: 110 beat/min. A complete blood count (CBC) done by an automated haematology analyzer showed a packed cell volume (PCV) of 10.8 white blood cell (WBC) count of 9 × 10^9 /L (Neutrophil - 24.2%, lymphocyte - 27.8%,. Leukocytes are normal in number with myeloblasts (15%), megakaryoblast (5 %) micromegakaryocytes (20%). Basophils - 5 % () and platelet of 225 × 10^9/L.

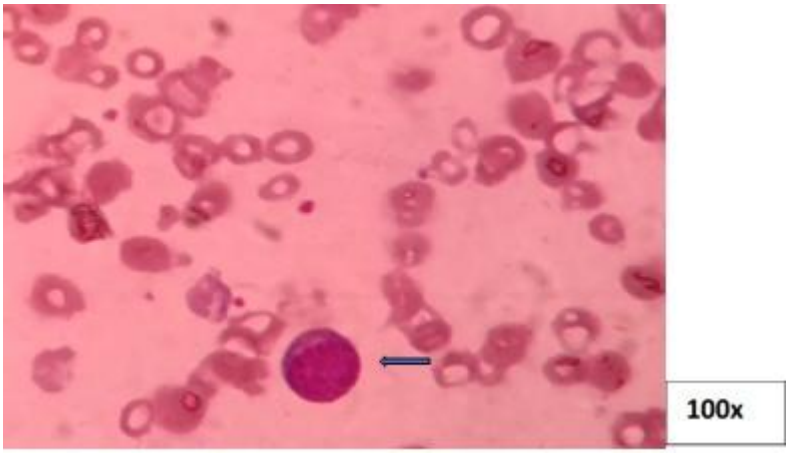


A complete blood count (CBC) done by an automated haematology analyzer showed Basophils () (Figure 1).

Peripheral blood smear examination showed Erythrocytes are microcytichypochromic. Anisopoikilocytosis seen with tear dropcells, elliptocytes, polychromatophilic cells, fragmented cells. Nucleated RBC's 20 per 100 WBCs seen. White blood cells showed normal in number withmyeloblasts (15%) Megakaryoblast (5%) Micromegakaryocytes (15%). Plateletsadequate in number. Thefinal hemtalogical diagnosis given was - **Acute leukemia with leukoerythroblastic blood picture**.



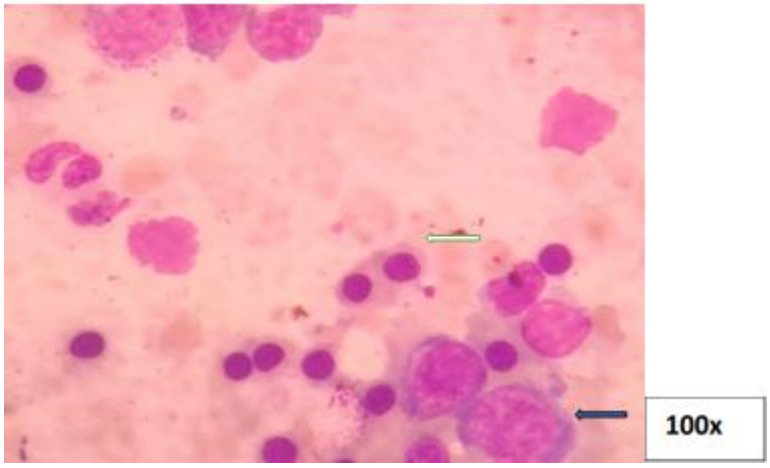
Review of peripheral blood film showed microcytic hypochromic red blood cells () including few nucleated red blood cells and immature mononuclear cells with cytoplasmic blebs () (Figure 2).



Review of peripheral blood film showed blast () Exhibiting high N: C ratio, open chromatin and 1 - 2 nucleoli (Figure 3)

Bone marrow smears were stained with wright Giemsa and analysed according to routine clinical laboratory procedures. Bone marrow aspiration Marrow is hemodiluted and showed Increased in number showing both megaloblastic () and micronormoblastic () maturation. Figure: 4. Many dysplastic features like binucleation andinternuclear bridging noted. Myeloid precursors noted with presence of blasts (20%) Exhibiting high N: C ratio, open chromatin and 1 - 2 nucleoli. Few neutrophilswith dysplastic features noted. Occasional megakaryocytes noted with megakaryoblasts Accounting to 5% no haemoparasites/ no atypical cells/ no granulomas. Hemodiluted and hypocellular marrow **Features were suggestive of Acute leukaemia**.

Dysplastic features noted in all the three lineages.



The bone marrow imprint showing increase in number showing both megaloblastic () and micronormoblastic () maturation.

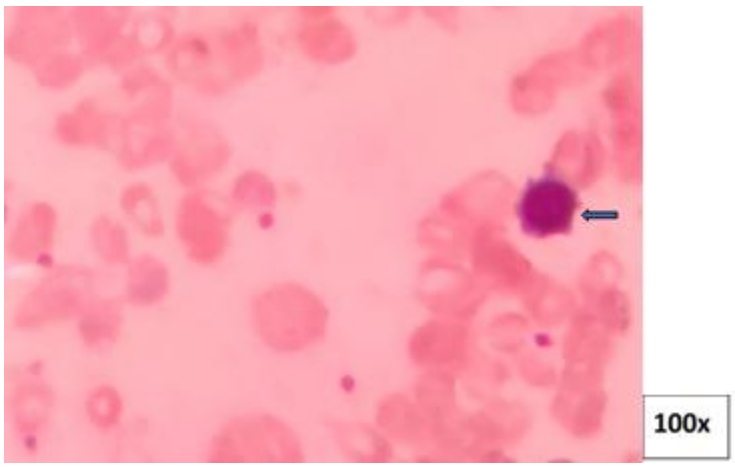


Figure 4

The bone marrow imprint showing micromegakaryocytes () figure: 5

The overall blood picture quantified to AML, most likely Acute MegakaryoblasticLeukaemia (AML, M7), which was confirmed by immunophenotyping of peripheral blood with positivity for CD 45, CD41 (84%). CD41 and

CD61 are megakaryocyte specific antigens, and CD45 expressed in blast window. Chromosome analysis report Analysis revealed t (9: 22) (q34; q11.2) in all 40 metaphase analysed. figure: 6

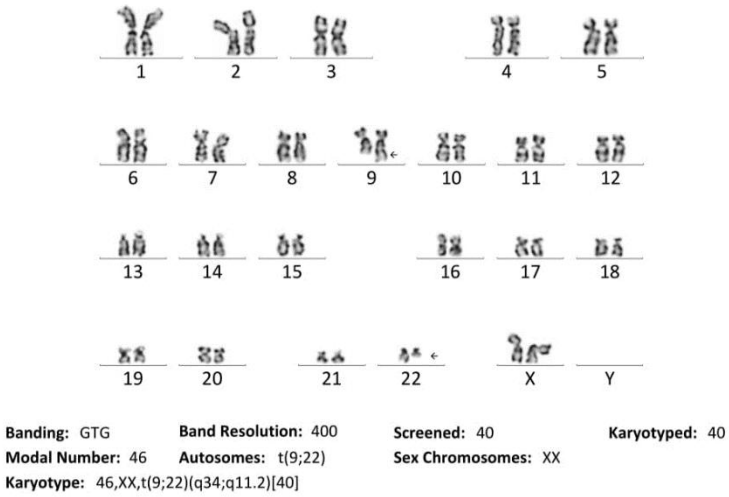


Figure 6

3. Discussion

AML is an uncommon form of AML accounting for 8 - 10% of all AML cases in adults, and 2 - 3% of cases in children. crisis in CML since it occurs in nearly 20% of Ph positive CML cases. The diagnosis of blast transformation of CML is made by a blast count of >20% in peripheral blood and/or bone marrow, presence of extramedullary blast proliferation or presence of large aggregates of blasts in the marrow. The diagnosis of acute myeloid leukaemia (AML M7) can be considered when peripheral blood shows blasts with cytoplasmic blebs and platelet abnormalities, and bone marrow shows abnormal megakaryocytes associated with marrow fibrosis.

Patients usually present with weakness, pallor, fever. The findings of massive splenomegaly, basophilia, and thrombocytosis point toward CML. Our patient had massive splenomegaly and basophilia but a normal platelet count. Confirmation of megakaryocytic lineage is by demonstration of megakaryocyte - platelet lineage - specific markers, namely CD41and chromosomal analysis revealed t (9: 22) (q34; q11.2) in all 40 metaphase analyzed.

Prognosis

The prognosis is significantly poor in both *de novo* AML M7 and CML with megakaryocytic blast crisis. AML M7 by itself is an adverse prognostic factor for disease - free survival. However, the treatment of CML patients in blast crisis with a combination of Cytarabine - based induction regimen and the tyrosine kinase inhibitor Imatinib has a significantly better outcome than when treated with induction therapy alone. Also, the initial use of Imatinib helps to revert from blast phase to chronic phase, which can improve the outcome following stem cell transplantation. [6].

4. Conclusion

AML M7 is a rare manifestation, patients with acute megakaryoblastic leukemia validated by review of morphologic and immunophenotyping data is the largest comprehensive series with cytogenetic data to assess their frequencies and confirmations.

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