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Acute myeloid leukemia: A rainbow to explore

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Abstract

Acute leukemia refers to the rapid, clonal proliferation in the bone marrow of lymphoid or myeloid progenitor cells known as lymphoblasts and myeloblasts, respectively.[1]

Acute myeloid leukemia is a heterogenous disease characterized by clonal expansion of myeloid progenitors (blasts) in the bone marrow and the peripheral blood.

Previously incurable,it is now curable in approximately 35%-40% of patients younger than the age of 60 years.[2]

AML develops due to inhibition of maturation of myeloid stem cells due to mutations.

AML can arise in patients with an underlying hematological disorder or as a consequence of prior therapy (e.g., exposure to topoisomerase II,alkylating agents or radiation).[3,4]

In the 1970s ,AML was classified according to the French-American-British classification system using mainly morphology and immune-phenotype /cytochemical criteria to define eight major AML subtypes(FAB M0 to M7).[5]

Clinical Features

Clinical manifestations of AML are divided into 2 groups: those due to bone marrow failure, and those due to organ infiltration.

Due to bone marrow failure

a. Anaemia producing pallor, lethargy, dyspnoea.
b. Bleeding manifestations due to thrombocytopenia causing spontaneous bruises, petechiae, bleeding from gums and other bleeding tendencies.
c. Infections are quite common and include those of mouth, throat, skin, respiratory, perianal and other sites.
d. Fever is generally attributed to infections

Due to organ infiltration

a) Pain and tenderness of bones.
b) Splenomegaly of moderate grade may occur.
c) Hepatomegaly is frequently present due to leukaemic infiltration.
d) Gum hypertrophy due to leukaemic infiltration of the gingivae.
e) Chloroma or granulocytic sarcoma is a localised tumour forming mass occurring in the skin or orbit due to local infiltration of the tissues by leukaemic cells.

f) Leukaemic infiltration of the kidney may be present.[6]

Methods

4 Cases of acute myeloid leukemia were identified in the year 2018 from October to December at Narayan medical college and hospital,Jamuhar,Sasaram,Bihar.

Herein,we present a series of 4 cases of acute myeloid leukemia with varied clinical findings.

Case Report

Case 1

A 12 years old male patient presented with intermittent fever,right sided chest pain and breathlessness since 1 month.Physical examination showed pallor and mild splenomegaly.

Laboratory investigations revealed heamoglobin of 7.2g/dl,total leukocyte count of 25,000/cumm with differential count being polymorphs-52%,lymphocytes-45%,eosinophil-3% and platelets-40,000/cumm,MCV-70fl,MCH-27pg,MCHC-30g/dl.

Red blood cells-normocytic normochromic and white blood cells showed leukocytosis, however, no blast cells were seen.

Montoux test was negative.3 consecutive sputum smear for acid fast bacilli were negative.

Chest X-ray revealed moderate pleural effusion on right side with no mediastinal lymphadenopathy.

- Pleural fluid examination showed uniformly dispersed blast cells with mesothelial cells.
- Bone marrow aspirate showed hypercellular marrow with presence of blasts-80% and monocytoid cells-20%.
- Cytochemically,monocytes were positive for non-specific esterase.
- On flow cytometry,the cells were positive for the myeloid antigens CD13 and CD33 and the monocytic antigens CD14,CD64, and CD36.

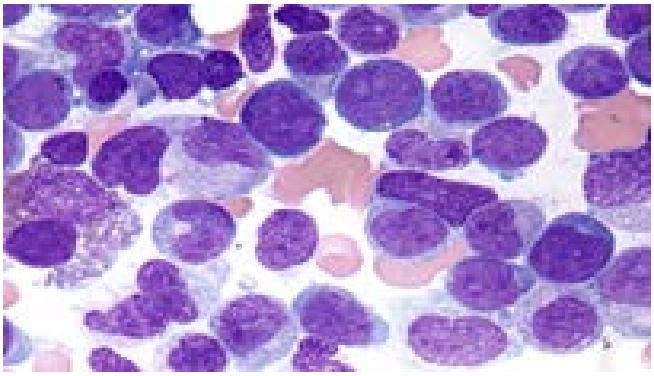

Fig.1 : Bone marrow smear showing mixture of myeloblasts and monoblasts

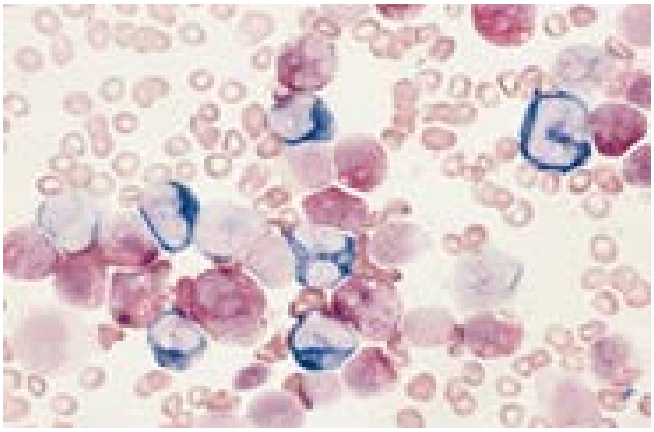

Fig.2: Cytochemistry showing monocyte in red brown colour stained with nonspecific esterase and neutrophils in blue colour with chloroacetate esterase

- A diagnosis of AML-M4(acute myelomonocytic leukemia) was suggested.

Case 2

- A 21 year old male patient presented with soft tissue swelling at lateral side of left cheek for last 9 months.
- On physical examination,a solid mass was palpable on lateral side of left cheek,4cm in diameter and was mild tender.
- Fine needle aspiration was advised which showed smear with high cellularity of blast cells.
- Complete blood count revealed anaemia(heamoglobin of 6gm/dl),leucocytosis with total leukocyte count of 1.5lacs/cumm and thrombocytpenia(platelet-80,000/cumm).

- On peripheral blood smear examination 30% cells were blasts with polymorphs-40%,promyelocyte-5%,myelocyte-15%,metamyelocyte-10%

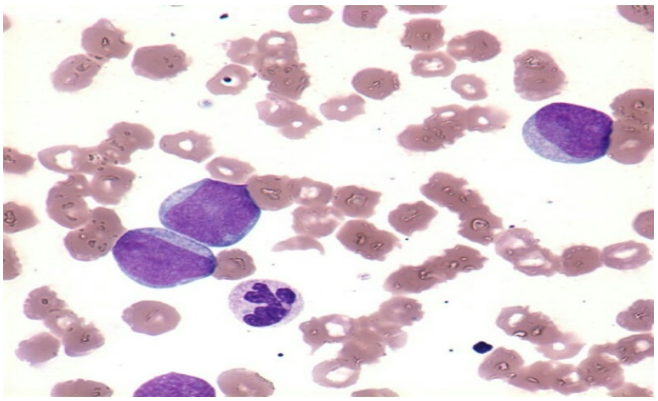

Fig. 3: PBS Showing Blasts

- Bone marrow aspirate showed hypercellular marrow with blast-40%,promyelocyte-20%,myelocyte-10%,metamyelocyte-10%,neutrophil-20%.
- **Cytochemistry**-The blasts were largely Myeloperoxidase positive.
- By flow cytometric analysis, cells were positive for CD 33, CD15 & MPO and CD117 was not expressed.

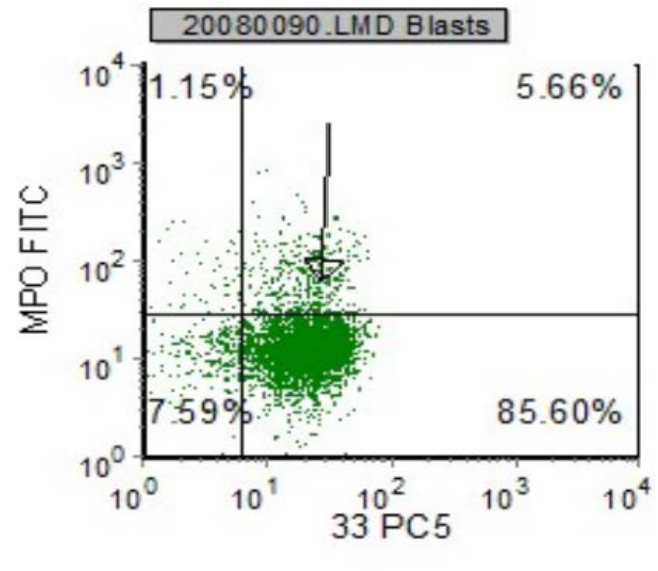

Fig.4

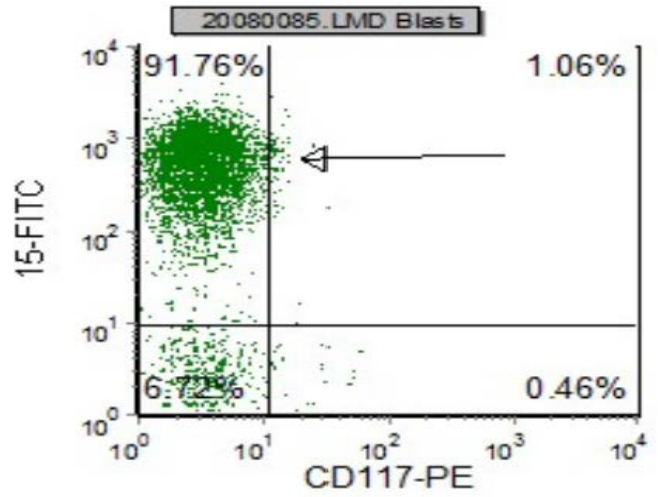

Fig.5

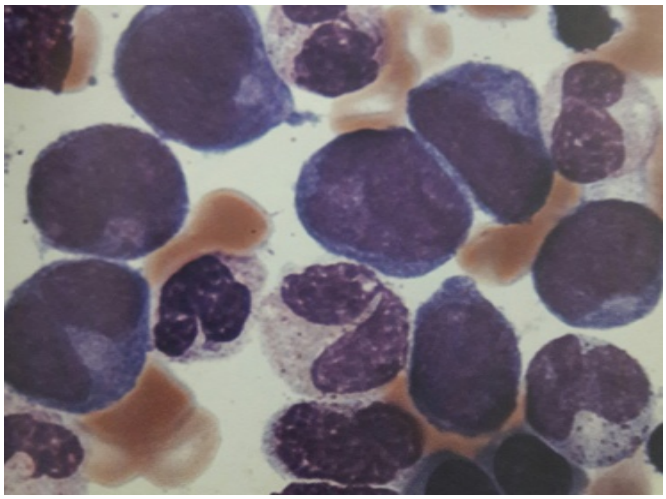

Fig. 6: Bone marrow smear showing myeloblasts and admixed more mature granulocytic forms.

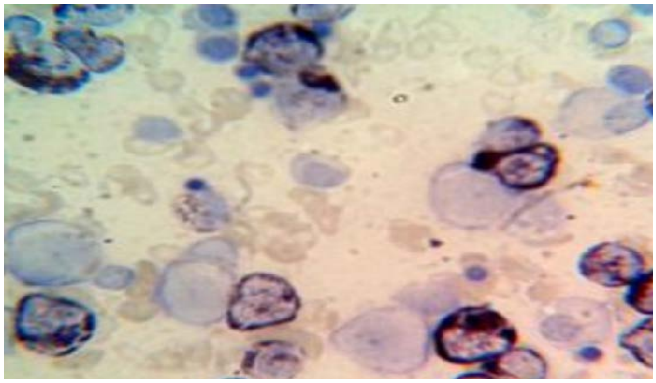

Fig .7: Myeloblasts showing positivity to myeloperoxidase

- Bone marrow biopsy-hypercellular marrow with predominantly large population of myeloblasts with

prominent nucleoli.These blasts were MPO positive.

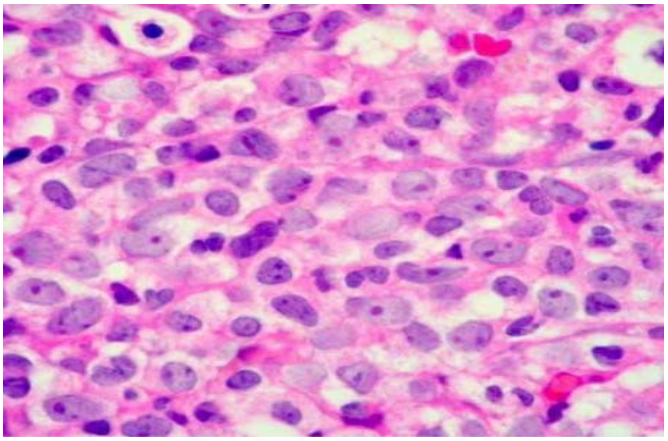

Fig .8: Bone marrow biopsy showing large population of myeloblasts.

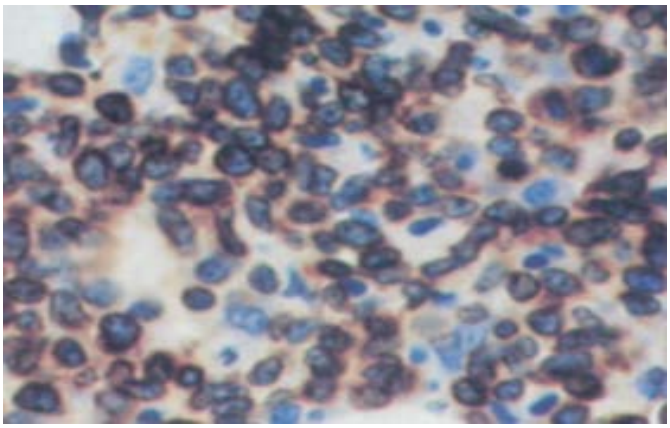

Fig. 9: MPO Positive blasts

- Tru-cut biopsy was performed from the mass and there were atypical,large neoplastic cells with round,fine hyperchromatic nuclei.MPO was positive in neoplastic cells.These findings were consistent with myeloid sarcoma.
- By cytogenetic analysis inv(16) was positive.
- A diagnosis of Acute myeloid leukemia with maturation (AML M2) with myeloid sarcoma was suggested.

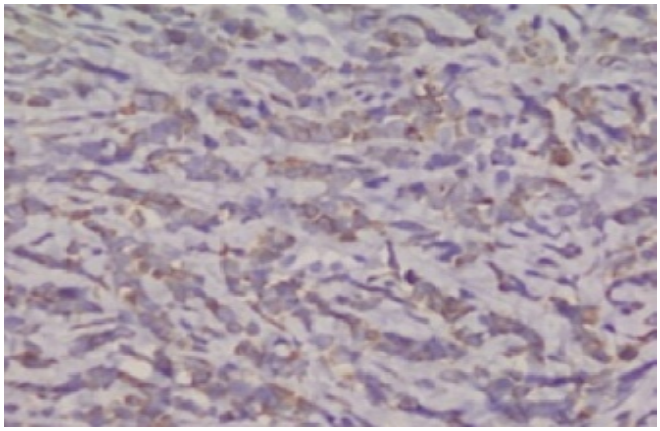

Fig .10

Case 3

- A 10 year old male patient presented with fever for last 1 month and pain abdomen since 15 days.Physical examination showed pallor,cervical lymphadenopathy.On systemic examination he had mild hepatosplenomegaly.
- Routine blood tests revealed heamoglobin of 9g/dl,total leukocyte count of 11,000/cumm and N-48%,L-45%,E-02%,atypical cells-05% with platelets-60,000/cumm.
- On peripheral blood smear examination,red cells were normocytic,normochromic with mild anisopoikilocytosis and few nucleated RBC.WBC showed atypical cells and thrombocytopenia was present.
- On blood test it was diagnosed to be bicytopenia with presence of atypical cells.Then the patient was subjected to bone marrow aspiration cytology.
- Bone marrow analysis yielded hypercellular marrow with erythroblast-60%,myeloblast-30% and promyelocyte-10%.
- Flow cytometry revealed blasts were positive for Glycophorin A and CD71.CD117 was expressed weakly.

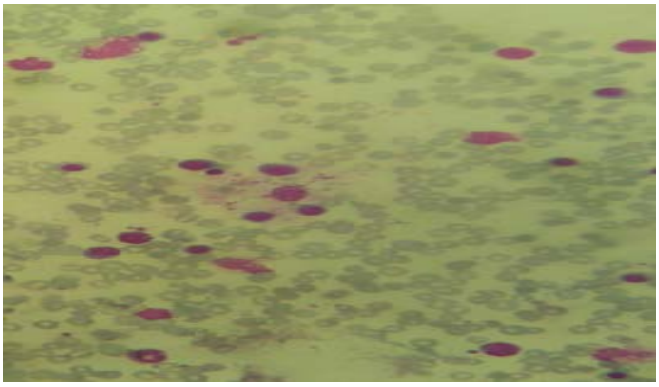

Fig. 11: Bone marrow aspirate showing numerous erythroid precursor at varying stage of maturation and myeloblast

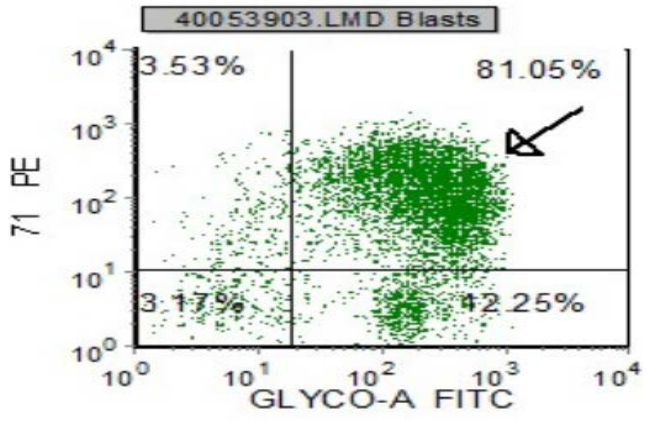

Fig. 12:

Bone marrow biopsy-Predominant population of erythroid precursor,few with dysplastic features were present.

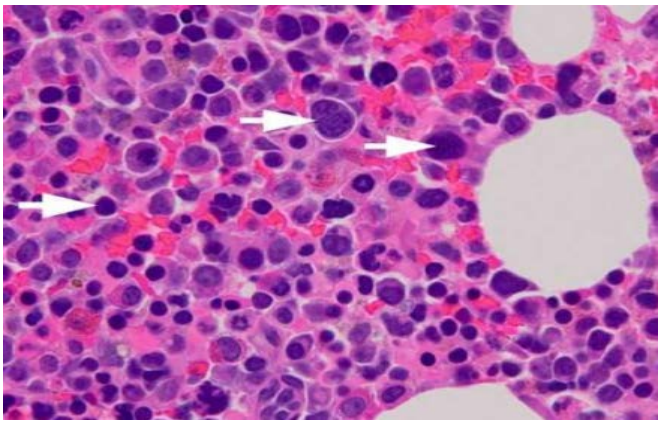

Fig. 13:

- On the basis of results obtained,diagnosis of Acute erythroleukemia was made.

Case 4

- A 20 years old male patient presented with on and off fever for last 1 month and was also a known case of Down syndrome.On physical examination,pallor was present.There was no lymphadenopathy and organomegaly.
- Laboratory investigations revealed heamoglobin of 5g/dl,total leukocyte count of 85,000/cumm with 60% of blasts,neutrophil 30%,lymphocytes 7%,eosinophil-03% and platelets-7lacs/cumm,MCV-82fl,MCH-29pg,MCHC-34g/dl.
- Bone marrow aspirate was dry tap so bone marrow biopsy was done which showed marked proliferation of megakaryocytes with few dysplastic forms.
- These blasts were positive for PAS.

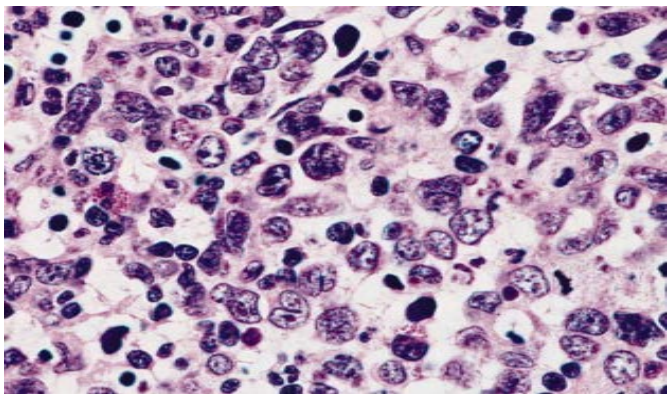

Fig.14: Bone marrow biopsy showing extensive infiltration by megakaryoblasts with sparse cytoplasm,frequent convoluted nuclei with distinct nucleoli

- Immunophenotyping revealed expression of CD41 and CD61.
- On basis of above investigations,diagnosis of Acute myeloid leukemia M7 associated with Down syndrome was made

Discussion

Acute myeloid leukemia is one of the common haematological malignancies encountered with varied

clinical and haematological presentation.[7]It is more lethal than chronic myeloid leukemia,a disease that affects same myeloid cells,but at a different pace.It prevents bone marrow cells from properly maturing,causing an accumulation of immature myeloblast cells in the bone marrow.[7]

Usually patients present with symptoms because of cytopenias, organomegaly, lymphadenopathy and bone pain. Children with myeloid leukemia can present a wide variety of symptoms.In some instances,the patient may present with an unusual signs and symptoms.[8]

The exact etiology for leukemia is not known. However, genetic, viral,chemicals,drugs and environmental factors play a role.[9]

Children with down syndrome have a 10 to 20-fold increased risk of developing acute leukemia. The incidence of acute megakaryoblastic leukemia in Down's syndrome is estimated to be 400 times that in normal children.[10]

AML with maturation (FAB AML-M2) comprises 10-15% of all AML cases. Myeloid sarcoma is accumulation of immature myeloid cells in extramedullary area.It is seen in 1-5% of AML cases.[11]

Acute myelomonocytic(M4)leukemia is most commonly characterized by weakness,bleeding and a diffuse erythematous skin rash and frequently presents with extramedullary involvement including liver,spleen,lymph nodes, gingiva, skin, eyes, meninges, bladder,CNS.

The incidence of acute erythroid leukemia is rare and ranges from 3% to 8%.The most common complaint in patients with erythroid leukemia is severe anaemia,which is present in most of the patients.The presence of hepatosplenomegaly varies between 20-40%.[11]

According to widely used WHO criteria,the diagnosis of AML is based on the presence of at least 20% myeloid cells in the bone marrow.

FAB classification requires a blast percentage of atleast 30% in bone marrow or peripheral blood for diagnosis of AML.

Conclusion

As we can see from the cases discussed,there is a varied presentation of acute myeloid leukemia.Myeloid sarcoma is especially seen in AML-M2 subtype. The first clue to diagnose AML is typically an abnormal result on a complete blood count. While an excess of abnormal white blood cells(leukocytosis)is a common finding with the leukemia,and leukemic blasts are sometimes seen,AML can also present with isolated decrease in platelets,red blood cells or leukopenia.

A presumptive diagnosis of AML can be made by examination of peripheral blood smear when there are circulating leukemic blasts,a definitive diagnosis usually requires an adequate bone marrow aspiration and biopsy.As an acute leukemia,AML progresses rapidly and is typically fatal within weeks or months if left untreated therefore proper evaluation to make early diagnosis is necessary.

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