Massive splenomegaly in acute erythroid leukaemia (FAB Class-M6): An unusual Presentation

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Abstract

AML-M6 has a peak incidence in the seventh decade with slight male preponderance, and can also present at a younger age. The usual features are anaemia, thrombocytopenia, malaise, fatigue, easy bruising, epistaxis and petechiae. Splenomegaly may occur in 20-40 % of the cases but massive splenomegaly is rare presentation and have been only reported once in humans and once in animals. A 22 year Asian female, presented with fatigue, pallor, mild jaundice, exertional dyspnoea ,epigastric pain, tender right hypochondrium and massive splenomegaly. Investigations revealed anaemia and thrombocytopenia, tear drop cells, basophilic stippling, piokilocytosis and anisochromia; increased uric acid and LDH. Abdominal ultrasound showed enlarged liver (22cm) and spleen (20cm). Bone marrow aspiration revealed 51% erythroid and 24% non-erythroid precursors, depressed leukopoeisis and megakarypoeisis. Erythroblasts were PAS and CD71 positive and also reacted to Antihaemoglobin-Antibody. This report highlights characteristic features and diagnostic criteria of erythroleukaemia, differential diagnosis of massive splenomegaly and their rare association.

Keywords: AML M-6, Massive Splenomegaly, Erythroleukaemia, Hepatomegaly.

Introduction

Acute Erythroid Leukaemia (FAB-M6) can present at a young age with unusual clinical features like massive splenomegaly. Erythroleukaemia is a rare form of acute myeloid leukaemia (AML), which comprises abnormal proliferation of erythrocyte precursors. More than 50% of the nucleated marrow cells are abnormal nucleated red blood cells. Erythroid leukaemia makes up around 5 percent of AML cases and is classified as M6 in the French-American British (FAB) classification. The median age of AML M6 is in the range of 60 to 70 years, with a bimodal distribution having a small peak before 20 years and a much wider peak in the seventh decade of life.[1] The incidence increases with age with approximately 1.3 and 12.2 cases per 100,000 population with age less than 65 years and more than 65 years, respectively. The female: male ratio is approximately 3:5.[2] AML has been associated with environmental factors (eg, exposure to chemicals, radiation, tobacco, or chemotherapy drugs), genetic abnormalities (eg, trisomy 21, Fanconi's anaemia, Bloom's syndrome), and other benign (eg, paroxysmal nocturnal haemoglobinuria) and malignant (eg, myelodysplastic syndrome and myeloproliferative disorders) haematologic diseases.[3] The signs and symptoms usually seen on presentation are constitutional including fatigue, pallor, weakness,loss of well-being, dyspnoea on exertion and palpitations, reflecting anaemia but cannot be correlated to the severity of anaemia. Other early features include easy bruising, petechiae, epistaxis, bleeding gums, conjunctival haemorrhages, and prolonged bleeding, due to thrombocytopenia. Infrequently, gastrointestinal, urogenital, bronchopulmonary, or central nervous system bleeding may occur at the onset of disease.[3]

Case Presentation:

A 22 year old pale looking young Asian female presented to Out-Patient Department (OPD) of Mayo Hospital, Lahore with shortness of breath and fatigue on mild exertion for 3 months, and moderate epigastric pain for 3 weeks. She was normotensive and normoglycaemic and had never experienced similar shortness of breath before which was increasing progressively and was relieved by taking rest. She also gave a history of epigastric pain for last 3 weeks; it was mild present persistent and had no relation with eating. It radiated to both flanks and was aggravated by change in posture, on activity and deep inspiration. She had no history of dyspepsia, gastroesophageal reflux disease and lower respiratory tract infection in the recent past. Similarly, she had no previous history of orthopnoea, paroxysmal nocturnal dyspnoea, oedema, nausea, vomiting, diarrhoea, burning micturation, dysuria or urinary obstruction. She was unmarried, had a regular menstrual cycle of 5/28 days with normal blood loss. She had no history of ischaemic heart disease and tuberculosis. She had no history of any hospitalization, or any severe illness. Her socio-economic status was poor.

On Examination, the patient was vitally stable with Pulse of 80/min, regular; Respiratory rate of 24/min; Temperature was 99°F and blood pressure 125/80 mm of Hg. She was pale and had mild jaundice. Neither thyroid nor any group of Lymph nodes i.e., cervical, supra-clavicular, axillary, para-aortic and inguinal was palpable. Rest of general physical

examination (GPE) was unremarkable. She had normal vesicular breathing and there were no added sounds. Her neurological and cardiovascular examination was also normal. On abdominal examination, positive findings included abdominal protuberance and tenderness at right hypochondrium. Liver was enlarged with lower border 16cm below right costal margin in mid-clavicular line. Spleen was also enlarged with lower border below 12cm from the left costal margin in the mid-clavicular line. Rest of the abdomen was resonant and there was no sign of ascities.

Laboratory investigations showed microcytic, hypochromic anaemia (Hb 9.2g/dL, RBC count 3.42 x $10^6/\mu L/mm^3$, Hct 31%, MCV 91.8 fL, MCH 26.9pg, MCHC 29.3g/dL); severe thrombocytopenia (Platelet count 18 x $10^3/\mu L/mm^3$); but normal white blood cell (WBC) count (4.7 x $10^3/\mu L/mm^3$). Peripheral blood film examination showed blast cells (3%), myelocytes (3%) and meta-myelocytes (9%), and the erythrocyte morphology showed marked anisocytosis, poikilocytosis, anisochromia, and basophilic stippling. Her fasting and random blood glucose levels obtained at various occasions were in normal range (90 mg/dL and 118 mg/dL respectively). Her liver functions tests were normal (Bilirubin 0.8 mg/dL, Total Proteins 7.1gm/dL, Albumin 4.1 gm/dL, Globulin 3.0 gm/dL, Alkaline Phosphatase 98 units/L, ALT 17 units/L, AST 21 units/L). The urine complete examination was normal and so were the renal function tests (urea 11.0 mg/dL, creatinine1.1 mg/dL, BUN/Creatinine Ratio 10). Her serum uric acid (10.2 mg/dL) were raised suggesting hyperuricemia, and serum electrolytes were also normal (Sodium 142 mEq/L, Potassium 3.9 mEq/L, Bicarbonate 22 mEq/L, Calcium 8.7 mEq/L, Chloride 103 mEq/L, and Magnesium 1.6 mEq/L), while serum Lactate Dehydrogenase level (186 units/L) was raised. Viral markers for hepatitis B and C, ANA and RA factor were also negative. Her PT (14 sec) was normal and APTT (40 sec) was 12 seconds prolonged.

Abdominal ultrasonography revealed enlarged liver and spleen; 22cm and 20cm respectively. There was no abdominal lymphadenopaty and ascites. There were multiple focal defects in the right lobe of liver.

Bone marrow aspiration revealed hyper-proliferation of erythroid cells comprising 51% of nucleated marrow cells; Leukopoeisis and Megakarypoeisis were suppressed. Blast cells constituted 24% of non-erythroid component. These blast cells were medium to large sized with scanty cytoplasm, open chromatin nuclei and prominent nucleoli. Additional special test indicate that erythroblasts were strongly PAS positive and CD71-positive, they also reacted with antihemoglobin antibody. Bone marrow findings were consistent with acute myeloid leukaemia FAB-M6 (acute erythroid leukaemia).

Discussion

AML M6 was diagnosed on the basis of clinical signs and symptoms, investigations and bone marrow aspiration picture. Following findings were particularly consistent with the diagnosis of erythroleukaemia and ruled out other diagnosis. The features include anemia and thrombocytopenia which are present in almost all cases of erythroleukaemia.[3] It was also augmented by the peripheral blood picture which showed marked anisocytosis, poikilocytosis, anisochromia, and basophilic stippling of erythrocytes.[4] Erythroblasts were strongly PAS positive which is found in almost all the AML M6 cases.[5] The immunophenotype of erythroblasts was CD71.They also reacted with antihemoglobin antibody, also consistent with AML M6.[6] Bone marrow aspiration confirmed our diagnosis of AML M6 by showing erythroid precursors comprising more than 50% of the total nucleated marrow cells. Bone marrow aspiration also showed blast cells comprising ? 20% of non-erythroid population. These findings correspond to diagnostic criteria of AML-M6.[1] We could find only one citation reporting massive splenomegaly in AML M-6 in human subjects.[7] Shirani D has recently reported similar results in cats.[8]

Conclusion

This case presents a rare finding of the association of massive splenomegaly with AML M6 which has been reported only once in humans and cats.

References

1. Greer JP, Foerister J, Rodgers G, Paraskevas F, Glader B, Arber DA, et al. Wintrobe's Clinical Hematology. Philadelphia: Lippincott Williams & Wilkins; 2008.
2. Larson RA, Anastasi J. Clinical manifestations, pathologic features, and diagnosis of acute myeloid leukaemia. 12th ed. (Online) (Cited …). Available from URL: www.uptodate.com/contents/wrote.
3. Kaushansky K, Lichtman MA, Kipps TJ, Seligsohn U, Prchal JT. William's Hematology: McGraw-Hill. (Online) 2008 (Cited 2010 Sept 20). Available from URL: http://www.accessmedicine.com/resourceTOC.aspx?resourceID=69.
4. Domingo-Claros A, Larriba I, Rozman M, Irriguible D, Vallespi T, Aventin A, et al. Acute erythroid neoplastic proliferations. A biological study based on 62 patients. Haematologica 2002; 87: 148-53.
5. Davey FR, Abraham N Jr, Brunetto VL, MacCallum JM, Nelson DA, Ball ED, et al. Morphologic characteristics of erythroleukaemia (acute myeloid leukaemia; FAB-M6): a CALGB study. Am J Hematol 1995; 49: 29-38.
6. Goldberg SL, Noel P, Klumpp TR, Dewald GW. The erythroid leukaemias: a comparative study of erythroleukaemia (FAB M6) and Di Guglielmo disease. Am J Clin Oncol 1998; 21: 42-7.
7. Cuneo A, Ferrant A, Michaux JL, Demuynck H, Boogaerts M, Louwagie A, et al. Philadelphia chromosome-positive acute myeloid leukaemia: cytoimmunologic and cytogenetic features. Haematologica 1996; 81: 423-7.
8. Shirani D, Nassiri SM, Aldavood SJ, Seddigh HS, Fathi E. Acute erythroid leukaemia with multilineage dysplasia in a cat. Can Vet J 2011; 52: 389-93.
9. Provan D. Oxford handbook of clinical and laboratory investigation. 2nd ed. Oxford ; New York: Oxford University Press; 2005.
10. Longo DL, Harrison TR. Harrison's hematology and oncology. New York: McGraw-Hill Medical; 2010.