A Rare Case of Acute Myeloid Leukemia with a monocytic variant presenting as pyrexia of unknown origin in a young adolescent male.

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Abstract

Acute Myeloid Leukemia(AML) is characterized by a clonal proliferation of myeloid precursors with a reduced capacity to differentiate into more mature cellular elements. As a result, there is an accumulation of leukemic blasts or immature forms in the bone marrow, peripheral blood, and occasionally in other tissues, with a variable reduction in the production of normal red blood cells, platelets, and mature granulocytes. The increased production of malignant cells, along with a reduction in these mature elements, results in a variety of systemic consequences including anemia, bleeding, and an increased risk of infection.

In our case report, an 18-year-old boy came with complaints of high-grade fever for one month associated with fatigue. Blood reports were suggestive of pancytopenia and the peripheral smear consisted of abnormal blast cells. The case was further dealt with with a bone marrow examination and a diagnosis of acute myeloid leukemia was made and treated further.

Keywords: clonal proliferation of myeloid precursors, high-grade fever, atypical blast cells; pancytopenia.

INTRODUCTION

The most prevalent acute leukaemia in adults is acute myeloid leukaemia (AML), which is diagnosed in about 21,450 people yearly in the US and is responsible for almost 11,000 fatalities. Acute myeloid leukemia (AML; formerly called acute myelogenous leukemia) refers to a diverse group of aggressive hematologic malignancies involving the proliferation of myeloid blasts committed to the granulocytic, monocytic, erythroid, or megakaryocytic lineages.

AML accounts for 80 percent of acute leukemias in adults; the median age at diagnosis is 65 years. By contrast, Acute Myeloid Leukemia(AML) represents <10 percent of acute leukemias in children <10 years.

Presentation – Patients generally present with symptoms of fatigue, bleeding, or bruising due to cytopenias. Less commonly, patients present with fever, respiratory or neurological symptoms due to leukostasis, cutaneous or other extramedullary collections of leukemic blasts (chloroma), or metabolic complications of AML. Some patients are asymptomatic and are first detected by abnormal laboratory studies.

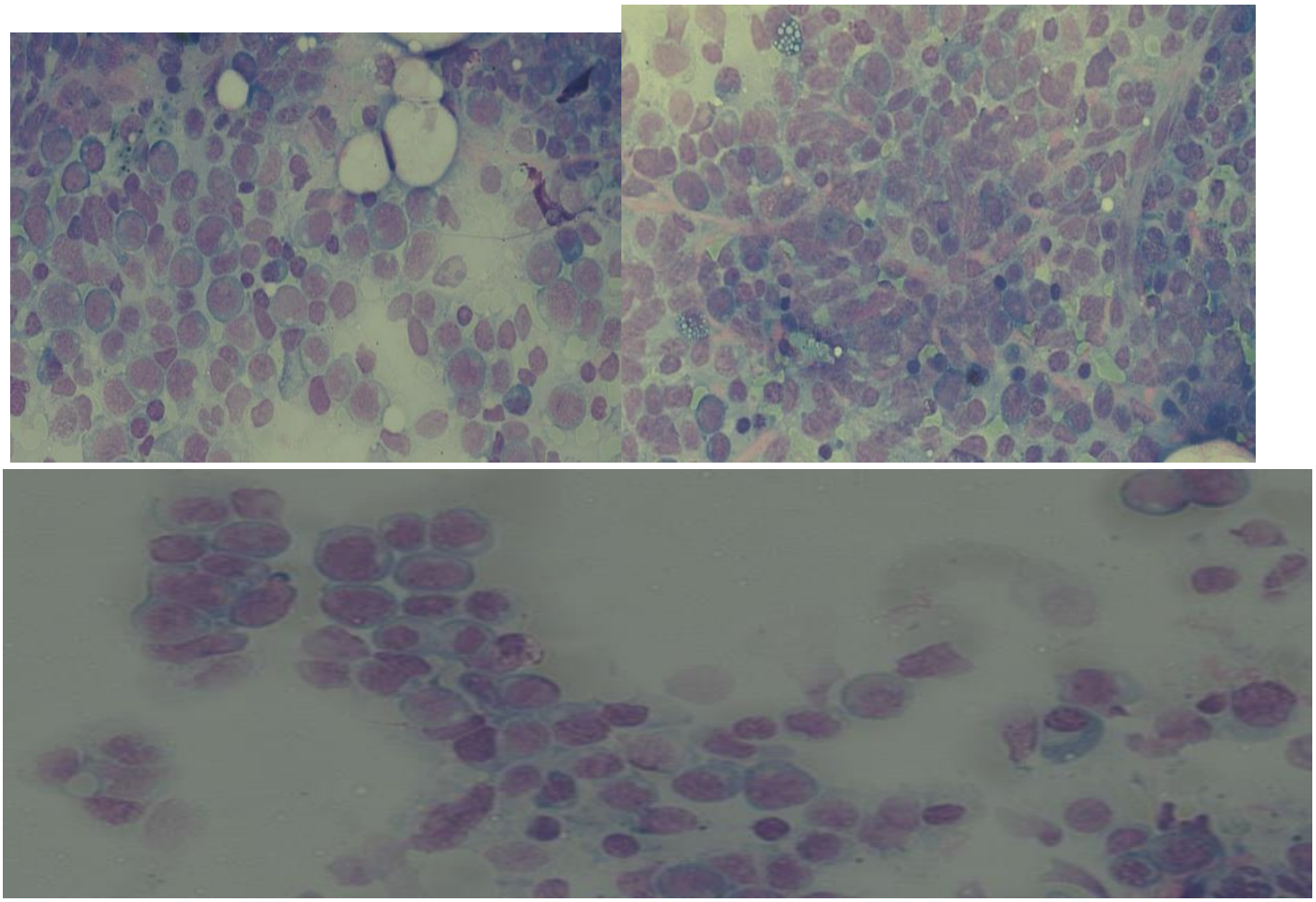
Although it is a diverse disease with a wide range of manifestations, the majority of those who are affected have a poor prognosis. Unfortunately, the 5-year overall survival rate for patients over 65 years old is still poor, at fewer than 5%. The landscape of AML is starting to alter, though, as new and better treatments become available

CASE REPORT

An 18-year-old male, student, a right-handed person, from a lower socio-economic background, came with chief complaints of fever with chills for 1 month, associated with dry cough and generalized weakness. Fever was high grade, intermittent, with 4-5 spikes/day with chills. No history of cold/rash/bleeding tendencies/nausea/vomiting/loose stools/burning micturition. Past History -The patient had no history of similar complaints in past. The patient had shown to numerous doctors and sought different medications and was subjected to many investigations, but the patient had no relief from fever and all extended fever profiles came to be negative except hemogram suggestive of severe pancytopenia with atypical cells in smear and was referred to our hospital for further management and to find out the cause of disease. No history of Diabetes, Hypertension,

Tuberculosis, or Malignancy. No past surgical history. No past history of vaccination. No significant personal or family history. The patient was already transfused with blood products for pancytopenia but pancytopenia persisted. Clinical Examination: Febrile – 100 F, Pulse was 88/min in the right upper limb, BP was 110/80mmHg measured in the supine position in the right upper limb, SpO2 was 95 % on room air, and BSL- 128mg/dL. Pallor was present, rest no icterus, cyanosis, clubbing, lymphadenopathy, or edema was present. Systemic Examination: On CVS examination, ECG was suggestive of Sinus Tachycardia. CNS examination: Higher mental functions examination, Patient was conscious, and oriented to time, place, and person. Cranial nerve examination: All cranial nerve examinations were normal. Motor and Sensory examinations were normal. No signs of meningitis are present. Respiratory and Per Abdomen examinations were normal.

Lab Investigations:- Hb was 7.4; TLC was 19200; platelet was 3000; Liver Function Tests, Renal Function Tests, serum protein levels, electrolytes, iron studies, B12, and folic acid levels were all normal. Bleeding and clotting time was normal. ANA by IF was negative. Extended fever profiles including tuberculosis, dengue, malaria, typhoid, rickettsia, brucella, Leptospira, and scrub typhus all were negative. Covid and H1N1 RT-PCR were also negative. Stool and urine examination including stool, blood, and urine cultures all were negative. CRP was 130 / ESR was 96. Peripheral Blood Smear showed 70% atypical cells with a high N: C ratio with scant greyish blue cytoplasm□ suggestive of leukemia.



All the above images show smear made from bone marrow biopsy, shows cells of monocytic series of Monoblasts having a roughly circular nucleus, delicate lacy chromatin, and abundant, often basophilic cytoplasm. And promonocytes having a more convoluted nucleus, and their cytoplasm contains metachromatic granules.

Chest x-ray was normal.

HRCT Thorax showed a normal study.

USG(A/P) s/o minimal ascites.

2D ECHO was normal.

CECT(A/P) s/o hepatosplenomegaly with minimal ascites.

Bone Marrow Aspirate and Biopsy s/o Acute Myeloid Leukemia.

Bone Marrow Flow Cytometry s/o Acute Myeloid Leukemia with Monocytic Variant.

DISCUSSION:

AML is the most common acute leukemia in adults and accounts for approximately 80 percent of cases in this age group [1,2]. AML has been associated with environmental factors (eg, exposure to chemicals, radiation, tobacco, chemotherapy) and genetic abnormalities (eg, trisomy 21; Fanconi anemia; Bloom's syndrome; familial mutations of CEBPA, DDX41, RUNX1).

Patients with AML generally present with symptoms related to complications of pancytopenia (eg, anemia, neutropenia, and thrombocytopenia), including weakness and easy fatigability [2], infections of variable severity, and/or hemorrhagic findings such as gingival bleeding, ecchymoses, epistaxis, or menorrhagia [3]. The most frequent side effect among AML patients is infection. During the neutropenic stage, prevention with a broad range of antibacterial, antifungal, and antiviral medicines is recommended. When signs or symptoms of infection appear in people with acute leukemia, they should all be treated aggressively and considered of as functionally neutropenic. Neutropenic fever is regarded as an oncologic emergency since it can cause sepsis, shock, and death very quickly. To lower morbidity and mortality in these patients, it is crucial to accurately recognize and treat early indications of sepsis. Fever is a clear indication of infection and may be the only symptom in AML patients. Chills, rigors, tachycardia, tachypnea, hypotension, lethargy or altered mental status, chilly extremities, and reduced urine are other instances of early sepsis symptoms. Any confluence of these clinical symptoms is alarming in AML patients, necessitating very close observation and quick action.

Complete blood count (CBC) – CBC usually reveals leukocytosis due to malignant blasts, but the leukocyte count may be low or normal with few or no blasts detected; most patients have normochromic, normocytic anemia and thrombocytopenia. Blood smear – Myeloblasts characteristically appear as immature cells with large nuclei, prominent nucleoli, variable amounts of cytoplasm, and faint granulation, and may have Auer rods with Wright Giemsa staining. The microscopic appearance of blasts can vary with the category of AML. Bone marrow (BM) examination – BM is generally hypercellular with ≥20 percent blasts and replacement of normal, maturing cells. There may be substantial fibrosis in some cases. Diagnosis – AML is generally diagnosed by morphologic, cytochemical, immunophenotypic, and cytogenetic/molecular analysis of bone marrow; in some cases, AML can be diagnosed from blood or a chloroma.

Criteria for the diagnosis of AML include:

1. Diagnostic cytogenetic/molecular features – The following cytogenetic/molecular features are sufficient to diagnose AML: AML with t(8;21)(q22;q22); RUNX1-RUNX1T1, AML with inv(16)(p13.1q22) or t(16;16)(p13.1;q22); CBFB-MYH11, APL with t(15;17)(q24.1;q21.1); PML-RARA

2. Myeloid sarcoma – A tumor mass of myeloid blasts that effaces normal tissue architecture at a site outside of the BM.

3. Others – In the absence of the features listed above, the diagnosis of AML requires, Blasts – ≥20 percent blasts in bone marrow or blood. Myeloid immunophenotype – Documentation of myeloid lineage of blasts by flow cytometry and/or immunohistochemistry.

Acute monoblastic and monocytic leukemia (FAB M5A and M5B) — This category accounts for 15 percent of AML, NOS [4], and 5 to 10 percent of total AML. More than 80 percent of bone marrow cells are of the monocytic lineage (monoblasts, promonocytes, and monocytes) and <20 percent are of the granulocytic lineage [5]. Promonocytes are considered blast equivalents for determining the blast percentage. Auer rods are rare and hemophagocytosis may be present.

1. M5A – In monoblastic leukemia (M5A) >80 percent of bone marrow cells are monoblasts. Monoblasts are large with abundant, moderately to intensely basophilic cytoplasm and may demonstrate pseudopod formation, scattered fine azurophilic granules, and vacuoles. Nuclei are round with delicate lacy chromatin and one or more large prominent nucleoli.

2. M5B – In monocytic leukemia (M5B), promonocytes and mature monocytes predominate, but with <80 percent monoblasts. Promonocytes are large with less basophilic and sometimes more obviously granulated cytoplasm with occasional large azurophilic granules and vacuoles. The nucleus is irregular with a delicately convoluted configuration [6].

Almost all cases express HLA-DR, myeloid antigens are variably expressed, and there is usually the expression of ≥2 markers of monocytic differentiation (eg, CD14, CD4, CD11b, CD11c, CD64, CD68, CD36, lysozyme).

Differential diagnosis – AML must be distinguished from other bone marrow failure states (eg, aplastic anemia, nutritional deficiencies, myelofibrosis) and from lymphoid leukemia, chronic myeloid leukemia, myelodysplastic syndromes (MDS), and a leukemoid reaction (non-malignant leukocytosis due to an extreme response to infection).

CONCLUSION:

Children and adolescents with AML should be treated in the context of a clinical trial whenever possible. Trials are designed to compare potentially better therapy with that which is currently accepted as standard. New technologies, such as next-generation sequencing, that can more deeply interrogate AML at the genomic and epigenomic level have the potential to identify novel biomarkers that can enhance risk stratification and potential therapeutic targets. Although cure rates for children and adolescents with AML have approached 70 percent, outcomes for children with adverse prognostic biologic features and refractory or relapsed disease remain poor. Novel therapies for high-risk patients are needed. Children and adolescents treated for AML should also be monitored closely for long-term complications of treatment regimens and require regular follow-up throughout their lives. In our case, the patient had a severe course of disease progression such that the patient succumbed to death even before the therapy for AML could be started.

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Conflict of Interest - None

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Patient consent for publication – The patient provided consent for her information to be published.

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