A case of acute megakaryoblastic leukaemia (FAB M7), a rare type of acute myeloid leukemia (AML), in a teenager

Philip O Olatunji1, Omotola T Ojo1, Fatai O Bello1, Binta Y Bakare1, Ayodeji O Olatunji2

1. Department of Haematology and Blood Transfusion, Olabisi Owanbanjo University Teaching Hospital, Sagamu, Ogun State, Nigeria
2. Department of Radiology, Olabisi Owanbanjo University Teaching Hospital, Sagamu, Ogun State, Nigeria

Abstract
Acute Megakaryoblastic Leukaemia (AML, M7) is a rare type of acute myeloid leukaemia (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. Patients may present with a broad variety of symptoms including low-grade fever, easy bruising, and life-threatening conditions. We report a rare case of AML, M7 in a 19-year-old lady who presented with weakness and fatigue. She was diagnosed as a case of AML, M7 on the basis of peripheral blood finding, bone marrow examination report, radiological findings and immunophenotyping.

Key words: acute myeloid leukaemia, acute megakaryocytic leukaemia, immunophenotyping, myelosclerosis

Introduction
Acute Myeloid Leukaemia (AML) is a group of heterogeneous hematological malignancies 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 leukaemic 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. It accounts for 80% of the acute leukaemias in adults and 15-20% of the acute leukaemias in children. AML constituted 4.9% of all haematological cancers with annual incidence of 1.2 per million in Ilorin, Nigeria. Patients may present with a broad variety of symptoms including anaemia, low-grade fever, easy bruising. Hepatomegaly or splenomegaly occurs in about 30% of the patients with lymphadenopathy being extremely uncommon. A presumptive diagnosis of AML can be made via examination of the peripheral blood smear when there are circulating leukaemic blasts, but a definitive diagnosis usually requires an adequate bone marrow aspiration with immunophenotyping.

In the French-American-British (FAB) Classification, subtype 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 megakaryoblastic changes. The AML classified as acute megakaryocytic leukaemia is M7 and is characterized by the presence of megakaryocytic antigens demonstrated by flow cytometry, immunohistochemistry or the presence of platelet peroxides.
Case of acute megakaryoblastic leukemia

There were giant forms of platelets on the film. The bone marrow aspiration yielded a dry tap which necessitated a bone marrow biopsy. The bone marrow imprint showed increased immature mononuclear cells with abundant basophilic cytoplasm containing vacuoles and hyperchromatic and pleomorphic nuclei. Some of the immature mononuclear cells had cytoplasmic blebs and constituted over 90% of nucleated cells (Figure 2).

The overall picture was in keeping with AML, most likely Acute Megakaryoblastic Leukaemia (AML, M7), which was confirmed by immunophenotyping (carried out by Safety Molecular Pathology Laboratory, Enugu) of peripheral blood with positivity for CD 33, CD41 and CD 61. CD41 and CD61 are megakaryocyte specific antigens, and CD33 is a myeloid marker. The percentage positivity and micrographs are shown in Table 1 and Figures 3 and 4. The biochemical parameters such as uric acid, bilirubin, creatinine, liver enzymes were normal. X-rays of tibia and fibula showed increased fibrosis (figure 5).

She was admitted and resuscitated with empirical intravenous antibiotic, intravenous fluid and a transfusion with 5 units of fresh whole blood because the facility for blood component therapy was not available to cater for anaemia and thrombocytopaenia that the patient had. Therapy was initiated thereafter with cytarabine and daunorubicin (7+ 3) regimen.

Table 1: Percentage positivity of CD33, CD41, CD

<table>
<thead>
<tr>
<th>CD Marker</th>
<th>% Positivity</th>
</tr>
</thead>
<tbody>
<tr>
<td>CD33</td>
<td>46</td>
</tr>
<tr>
<td>CD41</td>
<td>24</td>
</tr>
<tr>
<td>CD61</td>
<td>20</td>
</tr>
</tbody>
</table>

*CD – Cluster of differentiation

Repeat FBC on the seventh day of induction showed PCV of 17.7%, WBC of 0.38 X 10⁹/L and platelet of 22 X 10⁹/L. Peripheral blood film revealed leucopenia, thrombocytopaenia and there was no abnormal mononuclear cell. She was transfused with 2 more units of fresh whole blood. A repeat bone marrow aspiration was done for assessment of remission. Marrow was aspirated with ease and blasts were less than 5%. She was then scheduled for consolidation therapy. Her parents requested for discharge from the hospital due to financial constraint with the promise to return after purchasing the chemotherapeutic drugs. She was discharged and is yet to return to care.
Discussion

AML M7 is a rare subtype of leukemia accounting to 1.2% of cases of adult AML, compared to 3-10% of childhood AML. It is as under M7 in the French-American-British classification. The patient was a 19-year old female with clinical features similar to other types of AML except for organomegaly noted infrequently in adults which was the case with our patient. In our patient, symptoms of anemia were easy fatiguability and breathlessness. Cytopenias are usually present but 30% of patients have platelet counts in excess of 1000 x 10^9/L. In our patient, biciphotypaemia (PCV-10.8%, WBC-4.1x 10^9/L, platelet count- 50 x 10^9/L) was found. Osteosclerosis was found in our patient in line with osteosclerotic and osteolytic lesions described in few case reports. This might be due to production of platelet-derived growth factor (PDGF) and transforming growth factor β with their attendant fibroblastic activity. Myelofibrosis has been hypothesized to be a reactive phenomenon secondary to myeloid disorders. It has been postulated that defective or abnormal megakaryocytes and the release of growth factors such as platelet-derived growth factor (PDGF), and transforming growth factors (TGF)-β are responsible for the development of myelofibrosis. PDGF is a major mitogen for connective tissue cells such as fibroblasts and smooth muscle cells. TGF-β consists of a family of proteins and has broad effects on many types of cells, including fibroblasts and osteoblasts.

The diagnosis depends on the expression of at least one platelet antigen (CD41, CD42b, and CD61) on the leukemic cells. In our patient, peripheral film showed immature mononuclear cells with cytoplasmic blebs. Bone marrow aspiration was difficult probably due to intense myelofibrosis which has been documented in most patients. Bone marrow biopsy imprint examined for cytology was relied upon for initial diagnosis.

Non-specific, cytogenetic abnormalities are more frequent (>90%) in AML, M7 than in other subtypes of AML. Cytogenetic analysis was not carried out due to non-availability of the facility. AML, M7 may present as de novo leukemia, secondary leukemia after chemotherapy, or transformed myeloproliferative disorders and myelodysplastic syndromes. Our patient had clinical and haematologic remission and remains stable but neutropenic before discharge against medical advice. This is consistent with the previously observed remission and long term survival in spite of generally poor prognosis of AML, M7.

Conclusion

To our knowledge, this is the first case of AML M7 in the literature in our environment. The lesson here is that proficiency in morphologic diagnosis remains the window through which uncommon diagnosis can be confirmed by molecular technology particularly in resource-limited settings.

Acknowledgement

Safety Molecular Pathology Laboratory, Enugu, for immunocytochemical diagnosis through CD33, CD41 and CD61

Conflict of Interest

The authors declare no conflict of interest.

References
