

Acute Megakaryoblastic Leukemia in Infants (About a Case)Mahha Mariam¹, Tlemçani Imane¹, Hendi Rajae¹, Bouramdane Sanae², Benmiloud Sara², Hida Moustapha², Amrani Hassani Moncef¹¹Department of hematology, university hospital Hassan II, 30000 Fes, Morocco²Department of pediatry, university hospital Hassan II, 30000 Fes, Morocco**Case Report*****Corresponding author**

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Abstract: Acute megakaryoblastic leukemia, or type 7 (AML 7), is a rare entity defined by a proliferation of blasts of which at least 50% are megakaryoblasts. It represents 0.5 to 2% of acute leukemias (LA) in children and 3 to 10% of acute myeloid leukemias (AML). Patients may have nonspecific symptoms. His diagnosis is based on the presence in the blood or in the marrow of blasts with typical morphology and expressing specific platelet antigens. This observation describes the clinical case of a 19-month-old infant with pancytopenia. The diagnosis of AML7 was made based on explorations of peripheral blood, myelogram, and immunophenotypic analysis. Chemotherapy has been started, with a poor therapeutic response. The patient died in a state of septic shock. We recall through a literature review the clinical, histological and immunophenotypic features of acute megakaryoblastic leukemia.

Keywords: Acute megakaryoblastic leukemia, Cytology, Immunophenotyping.

INTRODUCTION

Acute megakaryoblastic leukemia or acute myeloid leukemia 7 (AML7) according to the Franco-American British classification (FAB); is defined by a proliferation of blasts greater than 20%, of which at least 50% are megakaryoblasts. It is poorly prognostic and very rare, representing 2% of adult AML and 7-10% of AML of the child.

The clinical picture of AML7 includes signs of bone marrow failure: pallor, infection and hemorrhage, organomegaly (splenomegaly, lymphadenopathy), and sometimes mediastinal germ cell tumors.

The biological diagnosis is oriented by the presence of pancytopenia at the hemogram, and especially the morphology of blasts in the myelogram. Confirmation of the diagnosis of AML 7 is by flow cytometry (CMF) which confirms the blast surface expression of at least one platelet-specific marker: CD41, CD42, or CD61.

We report a case of AML 7 diagnosed in the hematology laboratory of the CHU HASSAN II of Fez and we recall through a review of the literature the clinical and biological characteristics of acute megakaryoblastic leukemia.

OBSERVATION

This is a 19-month-old female infant who has had a well-attended pregnancy at 40 weeks of amenorrhea, with good adaptation to extrauterine life at birth.

The history of the disease dates back to 15 days with the progressive onset of anemic syndrome in a context of unencrypted fever and deterioration of the

general condition. The clinical examination revealed lower limb ecchymotic stains, with lenticular cervical lymphadenopathy, without hepatosplenomegaly or gingival hypertrophy.

The haemogram showed bicytopenia with a hypochromic artemenative macrocytic deep-hemorrhagic anemia (Hb: 3.7g / dl, VGM: 100fl, MCHC: 30.8g / l), thrombocytopenia at 6G / L and leukocytosis at 41G / L. The tumor lysis balance is positive with: Uric acid: 116 mg / l LDH: 3052 Kaliemia: 5.2 mmol / l.

The blood smear revealed the presence of circulating blasts estimated at 28%. The myelogram revealed a hemodiluted marrow, quite rich, with absence of megakaryocytes, infiltrated by 40% of undifferentiated blasts of medium size, chromatin fine nucleolate, with agranular basophilic cytoplasm and can show buds or pseudopods, with hypoplasia of the erythroblastic (4%) and granular (14%) lineage. Cytochemical staining with myeloperoxidase is negative. Immunophenotyping revealed the expression of CD 61+ platelet glycoproteins at 78%, CD 42a + at

94%. The CD36 + antigen is 75% positive. The evolution was fatal, the infant died during the first

phase of treatment.

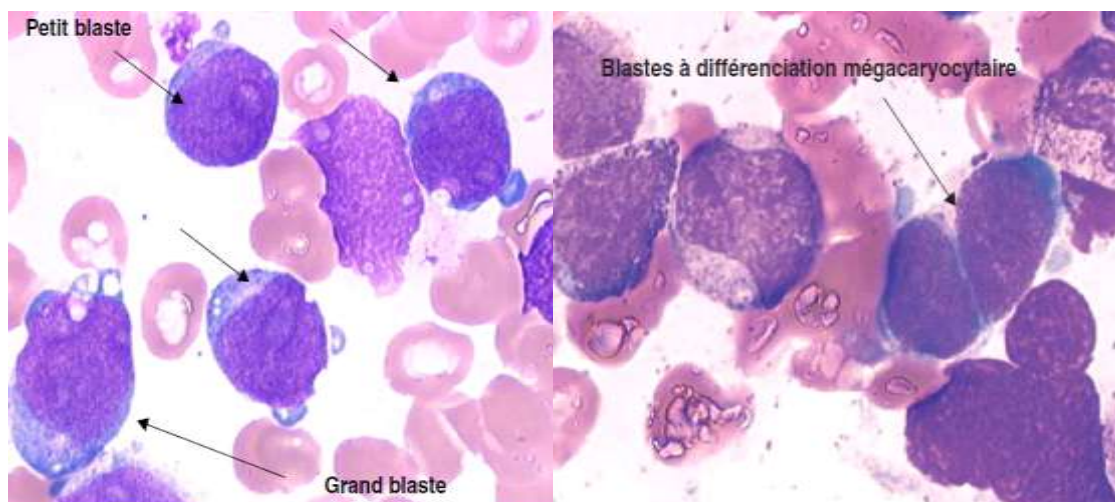


Fig-1& 2: blood smear stained with May Grünwald Giemsa (light microscopy $\times 100$) showing the blasts of the megakaryocytic line [7]

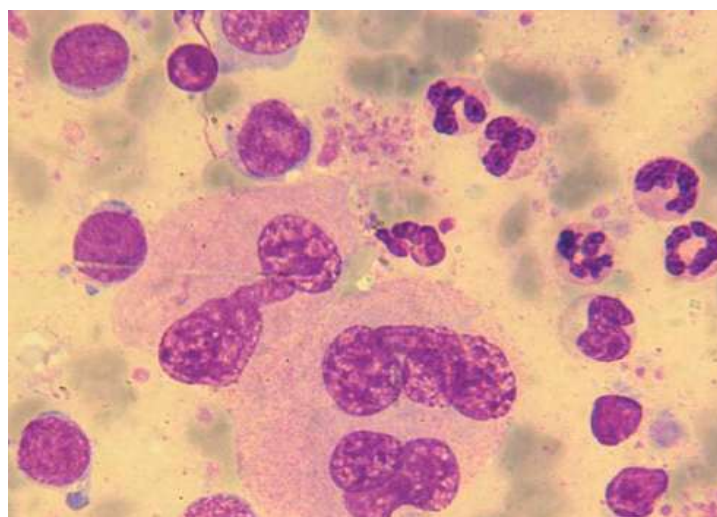


Fig-3: Medullary smear showing dystrophic megakaryocytes [7]

DISCUSSION

Acute megakaryoblastic leukemia (AML 7) was described in 1985 by the French-American-British group (FAB) 50 years after its description by Von Boros *et al* in 1931. It is rare and accounts for 3 to 5% of cases. LAM. It is more commonly seen in young age. It responds very little to chemotherapy; the transplant is often considered in first remission. In 2000, in the new WHO classification, this entity remains individualized in group 4 [1-3].

Hematologically, patients are classically cytopenic with often *de novo* thrombocytopenia. There is no hepato splenomegaly except in some forms of the child with t (1; 22). This is consistent with the clinical picture of our patient who presented a syndrome of bone marrow failure without tumor syndrome [4].

During diagnosis, the difficulty lies in the cytology of megakaryoblasts and the identification of their variable morphology (size, density of chromatin). There are two types:

- Undifferentiated blasts of variable size, with immature nuclei, fine chromatin, plurinucléolés and highly basophilic cytoplasm may contain fine azurophilic granules often localized. The cytoplasmic membrane is characteristic by the formation of rounded protuberances.
- Megakaryocytic differentiation blasts that are either regularly rounded, often very small and lymphocytoids, or conversely large sizes and clearly polyploid. Megakaryocytes are dystrophic, sometimes arranged in large and cohesive groups (Figure: 1; 2; 3) [5, 6].

Medullary aspiration generally provides poor hypocellular smears with cellular fragility preventing

accurate assessment of blast infiltration and making osteomedullary biopsy (BOM) essential. The biopsy shows hypercellularity, blast infiltration and the presence of myelofibrosis. In our case, the marrow is quite rich and hemodiluted with absence of megakaryocytes. The BOM was not performed. The diagnosis is confirmed by immunophenotyping showing the negativity of lymphocyte markers B and T, and the positivity of myeloid markers CD34, CD117, CD13 and CD33. Megacaryoblasts express one or more platelet glycoproteins: GP IIb / IIIa (CD41), GP IIIa (CD61) and more rarely GP Ib (CD42). Blasts do not express myeloperoxidase (MPO). In our patient, we report negativity of lymphoid markers with positivity of myeloid markers and markers of the platelet lineage on the blastic clone, which made it possible to retain the diagnosis of AML7. The only specific cytogenetic abnormality of AML-7 is t (1; 22) (p13; q13) translocation with the presence of OTT-MAL transcript. It is found in 25% of AML-7, the latter was also found in the series of Dastugue *et al.*, only in children. The Down Syndrome Down Syndrome is associated with a high risk of developing LAM-7. In our patient, we could not perform the karyotype. The infant died at the beginning of treatment [7, 8].

CONCLUSION

AML7 is a rare leukemia, hence the importance of knowing its clinical characteristics, cytomorphological blast and immunophenotypic. The treatment is based on intensive multi-agent chemotherapy and, in some cases, a bone marrow transplant. Nevertheless, the evolution remains unfavorable with an overall survival rate of 35-60%. New therapies need to be developed to increase the likelihood of a cure for this serious illness.

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