International Journal of Life Science Research Archive

ISSN: 0799-6640 (Online)

Journal homepage: https://sciresjournals.com/ijlsra/

(CASE REPORT)

Check for updates

Acute megakaryoblastic leukemia (AML7) about a case

Kadiri Meryem [1, 2, *], Tlamçani Imane [1, 2] and Amrani Moncef [1, 2]

[1] *Department of Hematology, Central Laboratory for Medical Biological Analysis, CHU Hassan II, Fez, Morocco.*
[2] *Faculty of Medicine and Pharmacy Sidi Mohammed Benabdallah, Fez, Morocco.*

International Journal of Life Science Research Archive, 2024, 06(02), 040–044

Publication history: Received on 31 March 2024; revised on 06 May 2024; accepted on 09 May 2024

Article DOI: https://doi.org/10.53771/ijlsra.2024.6.2.0050

Abstract

Acute myeloid megakaryoblastic leukemia (AML7) is a rare and severe form of acute myeloid leukemia. Its diagnosis is based essentially on cytometric and cytogenetic data, given the complexity of morphological diagnosis. Myelofibrosis and osteolytic lesions may be a particular feature of AML7.

Treatment with chemotherapy is considered, but the outcome is often unfavorable. The gold standard of treatment is bone marrow transplantation.

Our article reports the case of an infant diagnosed with acute megakaryoblastic leukemia initially revealed by a bone marrow failure syndrome and aggravated by a cerebro-orbital extension with osteolytic lesions of the orbital cavity, treated with chemotherapy with a good clinical-biological evolution.

Keywords: Leukemia; Megakaryoblasts; Medullogram; Myelofibrosis; Immunophenotyping

1 Introduction

Acute megakaryoblastic leukemia (AML7) represents a subtype of acute myeloid leukemia according to the Franco-American-British (FAB) classification.

It is a very rare entity whose incidence varies according to the authors: for some, it represents 8 to 15% of acute myeloid leukemias (AML); for others, it accounts for only 1.2% of all AMLs [1,2]. Although well known, AML7 may be frequently misdiagnosed as acute myelosclerosis, given its frequent association with myelofibrosis [2].

AML7 occurs at any age, accounting for 2% of adult AMLs and 7-10% of pediatric AMLs [1,2].

The clinical presentation of AML7 can be variable. Some patients present with symptoms of a myeloproliferative disorder, with tumor syndrome appearing to be the most frequent form of revelation [2].

Morphological diagnosis of AML7 is based on the presence of 20% or more Blasts in the bone marrow (BM), at least half of which are megakaryoblasts, according to the FAB classification. Cytochemical staining with myeloperoxidase (MPO) is negative in AML7. Morphological diagnosis may nevertheless be difficult, requiring cytometric and cytogenetic criteria. Chromosome 3 abnormalities are common, and an association with Down's syndrome has been described [3,4].

Survival after treatment with conventional chemotherapy is extremely poor [2, 5].

* Corresponding author: Kadiri Meryem

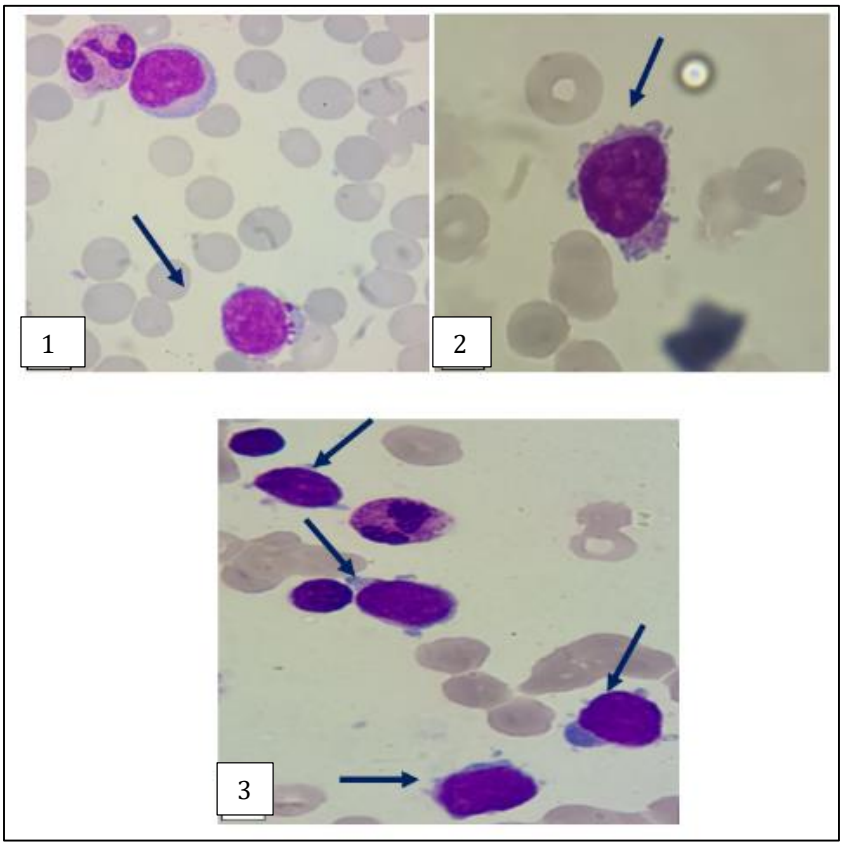
The aim of our study is to review the clinical, biological, morphological, cytometric and cytogenetic features of AML7, based on data from the literature.

2 Observation

This was a two-year-old female infant from a non-consanguineous marriage with good psychomotor development and no notable pathological history. She was referred for management of a haemorrhagic and anaemic syndrome evolving in a context of altered general condition.

The onset of the disease was marked one month before the consultation, by the onset of an anemic syndrome consisting of mucocutaneous pallor and generalized asthenia manifested by hypotonia and motor slowing. The symptomatology worsened ten days later with the appearance of ecchymotic spots on the lower limbs.

Clinical examination revealed a patient in fairly good general condition, pale, hemodynamically and respiratorily stable, and apyretic. The examination also revealed splenomegaly (SMG) and bilateral cervical adenopathy (ADP) measuring 1.5cm in diameter. The child also presented with ecchymotic spots on both lower limbs, with bilateral palpebral infiltration. The ophthalmological examination was difficult to perform, given the extensive palpebral infiltration.



Figures 1, 2, 3 Medullary smear stained with May-Grunwald-Giemsa and read under the light microscope at x 100 objective showing medium-sized blasts with unbound and nucleated chromatin and basophilic cytoplasm with budding on hypocellular marrow

The haemogram showed pancytopenia with normochromic normocytic anaemia (Hb 6.5 g/dl), neutropenia (PNN 260 e/mm3) and thrombocytopenia (Plq 45,000).

Blood smear revealed 16% circulating blasts. The bone marrow was hypocellular, heterogeneous and low in megakaryocytes, with hypoplasia of the granular and erythroblastic lineages. Blasts are present with an average of 40% (Fig 1, 2, 3). These are small to medium-sized blasts with irregularly contoured nuclei, unbound and nucleolated chromatin and sparse, basophilic cytoplasm containing budding. Cytochemical staining with myeloperoxidase is negative (Fig 4).

Central Laboratory Hematology Department, Fez University Hospital

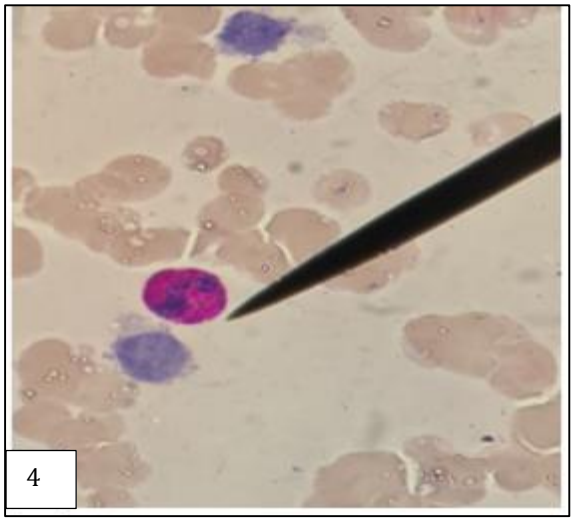


Figure 4 Microscopic appearance of a bone marrow smear with Myeloperoxidase staining showing undifferentiated blasts.

Hematology Department, Central Laboratory, Fez University Hospital

Flow cytometric immunophenotyping (Beckam Coulter/Navios EX 2L6C) of bone marrow blood from a 23% blast population was consistent with acute myeloid leukemia with a megakaryocytic component: CD42a 86%, CD4b CD61 88% and CD42b 28%.

The bone marrow karyotype showed chromosomes with clonal structural abnormalities: interstitial deletion of the long arm of chromosome 9 associated with a derivative of chromosome 5, the site of a double abnormality (a paracentric inversion of the long arm associated with a (t 5 ;17) translocation). The rest of the laboratory work-up was unremarkable, with no hypercalcemia.

The evolution of the symptoms was marked by the appearance of ptosis associated with ophthalmic paralysis, prompting a cerebro-orbital CT scan and ophthalmological examination. The cerebro-orbital CT scan showed signs of metastatic homeopathic pathology in the orbital, meningeal and cervical lymph nodes, as well as osteolytic lesions of the maxillary sinus walls, orbital floor and papyraceous laminae, and focal thrombosis of the superior longitudinal sinus.

Therapeutically, the patient received palliative treatment based on platelet and red blood cell transfusions. For her leukemia, the AML-MA 2011 protocol was administered. During the treatment period, clinical improvement was noted: regression of infiltration, ptosis and ocular paralysis with persistence of hemorrhagic manifestations and pancytopenia with regression of the blast count to 4%.

The end of treatment was marked by a clinical and biological improvement: disappearance of clinical signs and normalization of blood count parameters, with the presence of 2% blasts on the control medullogram.

3 Discussion

AML7 is a very rare condition, first discovered in 1931 by Von Bros [6], the incidence of which varies according to the author: for some, it represents 8 to 15% of acute myeloid leukemias (AML); for others, such as TALLMAN et al (in a sample of 20 patients), it accounts for only 1.2% of all AMLs [1,2]. It occurs at all ages, accounting for 2% of adult AML and 7-10% of childhood AML [1,2]. It has 2 frequency peaks, before the age of 3 and in adulthood [7,8].

AML7 can be associated with Down syndrome or trisomy 21, or diagnosed de novo without trisomy 21 or apparent predisposition [9]. The development of Down's syndrome-associated AML7s is based on a 3-step mechanism of tumor progression, each associated with the acquisition of genetic alterations that accumulate to include: constitutive trisomy of chromosome 21 associated with a predisposition to leukemias; somatic mutations in the GATA1 gene associated with a transient myeloid syndrome diagnosed at birth; and additional mutations affecting genes encoding signaling pathway

intermediates and/or epigenetic regulators [10]. In the group of patients with novo AML7, global cytogenetic and genomic analyses showed, in the majority of cases, the presence of chromosomal alterations responsible for the expression of fusion oncogenes [11,12]. The first recurrent anomaly identified was a translocation between chromosome 1 and chromosome 22, visible in conventional cytogenetics, and encoding the OTT-MAL fusion protein, which includes almost all of both OTT and MAL proteins [13].

The clinical presentation of AML 7 can be variable. Some patients present with symptoms of a pre-existing myeloproliferative disorder: hepatosplenomegaly, anemic and infectious syndrome secondary to biologic bi- or pancytopenia [2]. The presence of adenopathies, whether or not associated with hepatosplenomegaly, forming a tumor syndrome common to all acute leukemias, may be the most frequent form of revelation, along with the clinical signs mentioned above. As in the literature, our patient presented with a typical leukemia picture of anemic, hemorrhagic and tumoral syndrome.

Bone and musculoskeletal pain are common in acute leukemia. In a study by Rogalsky et al, 20.6% of a series of 107 patients had bone and musculoskeletal pain at the time of diagnosis [14]. These clinical signs are often related to bone abnormalities of diffuse osteoporosis and osteolysis. These lesions are common to all acute leukemias. In acute megakaryoblastic leukemia, the most common bone signs are periosteal reaction, clear metaphyseal bands and pathological fractures [6,7, 15]. Our patient had no bone or musculoskeletal pain, but the CT scan showed lytic bone lesions in the orbital region.

According to Oki et al, myelofibrosis is present in around 60% of cases of AML7 suspected clinically by difficulties with bone marrow aspiration “dry tapping” [2, 16]. It is confirmed by anatomopathological study.

Myelofibrosis and bone lesions are explained by the increased production of megakaryocytic cytokines, which activate fibroblast proliferation, collagen synthesis and osteogenesis [15,17,18].

It is difficult to confirm AML7, but the morphology of blasts on the medullogram, essentially the presence of budding, basophilia of the cytoplasm, fragmentation of megakaryocytes and multinucleation are recurrent without being pathognomonic of megakaryoblastic leukemia [19]. Cytoplasmic budding is the morphological sign most suggestive of AML7 in our patient.

The definitive diagnosis of AML7 is based on immunophenotyping, in which CD41, CD42 and CD61 antigens are expressed, as in the case of our patient.

Confirmation of our patient's diagnosis of AML7 was based on the results of immunophenotyping, which showed the presence of platelet antigens CD42a, CD41b, CD61 and CD42b.

Progression under chemotherapy was marked by a clinical and biological improvement with regression of the blast rate to 2%, in contrast to several studies reporting a poor prognosis and therapeutic response [5,20].

4 Conclusion

Acute myeloid megakaryoblastic leukemia is a difficult diagnosis to make, given the non-specificity of the clinical symptoms associated with a cytology that is sometimes not very suggestive, despite the particular morphological signs of blasts. However, a clinic characterized by the presence of bone signs, myelofibrosis and blasts with cytoplasmic budding may guide the diagnosis, which is only confirmed by immunophenotyping to detect platelet antigens on the surface of blasts.

Compliance with ethical standards

Disclosure of conflict of interest

No conflict of interest to be disclosed.

Statement of ethical approval

The present research work does not contain any studies performed on animals/humans subjects by any of the authors’.

Statement of informed consent

Informed consent was obtained from all individual participants included in the study.

References

[1] Yahyaoui A, Zahid H, El khazraji A, Labrini F, Hadef R, Messaoudi N. Acute megakaryoblastic leukemia: about a case and review of the literature. Haematology and immuno-haematology laboratory of the Hôpital militaire d'instruction Mohamed V Rabat Morocco. 2016

[2] Tallman MS, Neuberg D, Bennett JM, Francois CJ, Paietta E, Wiernik PH, Dewald , G, Cassileth PA, Oken MM, Rowe JM. Acute megacaryocytic leukemia: the Eastern Cooperative Oncology Group experience. Blood 2000; 96: 2405–2411.

[3] Pui C-H, Williams DL, Scarborough V, Jackson CW, Price R, Murphy S. Acute megakaryoblastic leukemia associated with intrinsic platelet dysfunction and constitutional ring 2 chromosome in a young boy. Br J Haematol 1982; 50: 191–200.

[4] San Miguel JF, Gonzalez M, Canizo MC, Ojeda E, Orfao A, Caballero MD, Moro MJ, Fisac P, Lopez Borrasca A. Leukemia with megakaryoblastic involvement: clinical, hematological and immunological characteristics. Blood 1988; 72: 402–407

[5] RUIZ-ARGUELLES GJ, LOBATO-MANDIAZABAL E, SAN MIGUEL JF, et al. Long term treatment results for acute megakaryoblastic leukemia patients. A multicenter study. Br J Haematol 1992; 82:671– 675.

[6] Von Boros J, Korenyi A. ''A case of acute megakaryoblastic leukemia, at the same time some remarks on the problem of acute leukemia''. Medicine, vol. 118, pp. 697–718, 1931.

[7] Athale UH, Razzouk B, Raimondi SC, et al. Biology and outcome of childhood acute megakaryoblastic leukemia: a single institution's experience. Blood 2001; 97:3727–32.

[8] Windeban, K, Tefferi A, Smithson W et al. Acute megakaryocytic leukemia (m7) in children.MayoClinProc 1989;64:1339–51.

[9] Teyssier A, Lapillonne H, Pasquet M *et al.* Acute megakaryoblastic leukemia (excluding Down syndrome) remains an acute myeloid subgroup with inferior outcome in the French ELAM02 trial. Pediatr Hematol Oncol 2018; 34: 425–427.

[10] Roberts I, Izraeli S. Haematopoietic development and leukaemia in Down syndrome. Br J Haematol 2014; 167: 587–599.

[11] Thiollier C, Lopez C, Gerby B *et al.* Characterization of novel genomic alterations and therapeutic approaches using acute megakaryoblastic leukemia xenograft models. J Exp Med 2012; 209 : 2017–2031.

[12] Rooij J, Branstetter C, Ma J *et al.* Pediatric non-Down syndrome acute megakaryoblastic leukemia is characterized by distinct genomic subsets with varying outcomes. Nat Genet 2018; 49: 451–456.

[13] Bernard O, Mercher T. Activation of the Notch pathway by OTT-MAL in acute megakaryoblastic leukemia. Med Sci (Paris) 2009; 25 : 676–678.

[14] Chambona F, Paillarda P et al. Megakaryoblastic acute leukemia: Bone and joint manifestations in a 7-month-old child.

[15] Athale, U., Kaste, S., Razzouk B., et al. Skeletal manifestations of pediatric acute megakaryoblastic leukemia. J Pediatr Hematol Oncol 2002; 24:561–5.

[16] Oki Y, Kantarjian H, Zhou X et al. Adult acute megakaryocytic leukemia: an analysis of 37 patients treated at m.d. anderson cancer center. Blood 2006; 107:880–4

[17] Abrahamsson J, Swolin B, Mellander L. Bone marrow fibrosis and radiological changes of the long bones in children with acute megakaryocytic leukaemia. Acta Paediatr 1998; 87:1093–6.

[18] Alioglu B, Tuncay I, Ozyurek E, et al. Bone fracture: an unusual presentation of acute megakaryoblastic leukemia. Pediatr Hematol Oncol 2009; 26:62–9.

[19] Anoop P, Lancaster D, Atra A. Osteolytic presentation of pediatric acute megakaryoblastic leukemia. Pediatr Hematol Oncol 2011; 28:526–8

[20] Muler J, Valdez R, Hayes C, Kaminski M. Acute megakaryocytic leukemia presenting as hypercalcemia with skeletal lytic lesions. Eur J Haematol 2002: 68: 392–396. # Blackwell Munksgaard 2002.