International Journal of Life Science Research Archive

ISSN: 0799-6640 (Online)

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

(CASE REPORT)

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Biphenotypic acute leukemia

K. Lemhouer *, J. Elamouri, M. Braoul, I. tlamçani and M. Amrani Hassani

Department of Hématology, Central Laboratory for Medical Analysis, Hassan II University Hospital Fez, Morocco.

International Journal of Life Science Research Archive, 2023, 04(01), 211–215

Publication history: Received on 01 February 2023; revised on 06 March 2023; accepted on 09 March 2023

Article DOI: https://doi.org/10.53771/ijlsra.2023.4.1.0037

Abstract

Biphenypic leukemia (BAL) is defined by the presence on the same blastic cells of markers belonging to at least two different lines. The incidence is estimated at less than 5% of acute leukemia cases, even if there are disparities in the literature. The morphological aspects of blast cells are variable, aspects of lymphoblasts in 1/3 cases or myeloblasts in other cases. Blast cell flow cytometry distinguishes BAL with co-expression of lymphoid and myeloid markers (L+M) or myeloid markers with lymphoid markers (M+L). BAL with lymphoid markers B and T (B+T) are rarer. Conventional cytogenetic examination makes it possible to highlight more frequently in the BAL type anomalies t(9;22)(q34;q11) in adults, t(12;21)(p13;q22) in children or abnormalities in 11q23, more rarely other cytogenetic abnormalities.

We note the observation of two cases of acute leukemia with their immunophenotypic profile in order to highlight the difficulty of classifying certain acute leukemia with a mixed phenotype and highlight the complementarity of biological analyses for characterization and management of these leukemias.

Keywords: Biphenotypic leukemia; Immunophenotypic; Conventional cytogenetic

1 Introduction

Biphenotypic acute leukemia is defined by the co-expression by blast cells of membrane and cytoplasmic markers belonging to at least two different hematopoietic lineages [1]. In this work, we report the diagnosis of two cases of biphenotypic acute leukemia, emphasizing the capital interest of hematological cytology coupled with blast immunophenotyping.

1.1 Observation No. 1

This is a 64-year-old patient who presents with an anemic syndrome with, on examination, cervical lymphadenopathy evolving in a context of impaired general health. The blood count shows a hemoglobin level at 4.6g/dl, a platelet count at 50G/l and leukocytes at 1,400/mm^3, with 09% neutrophils, 20% lymphocytes, 02% monocytes and 69% circulating blasts. Ag Hbs, Ac Hvc, HIV, TPHA, VDRL serologies are negative.

The myelogram finds a 93% blast invasion characterized by a heterogeneity of shape and size. They are medium to large cells, often rounded nuclei, loose chromatin often nucleolated, sparse cytoplasm and basophilic (Figure 1).

Myeloperoxidase (MPO) cytochemical staining is negative (Figure 2).

* Corresponding author: K. Lemhouer

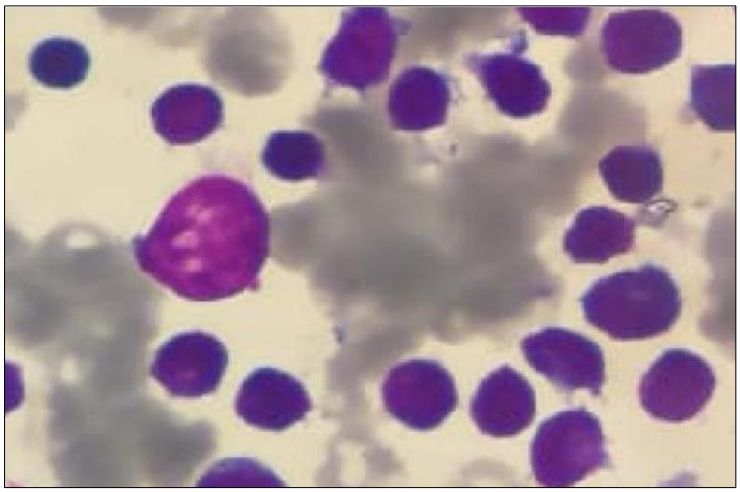

Figure 1 Bone marrow blasts (MGG staining, objective x 100) Department of hematology-central laboratory of medical analysis CHU Hassan II of Fez

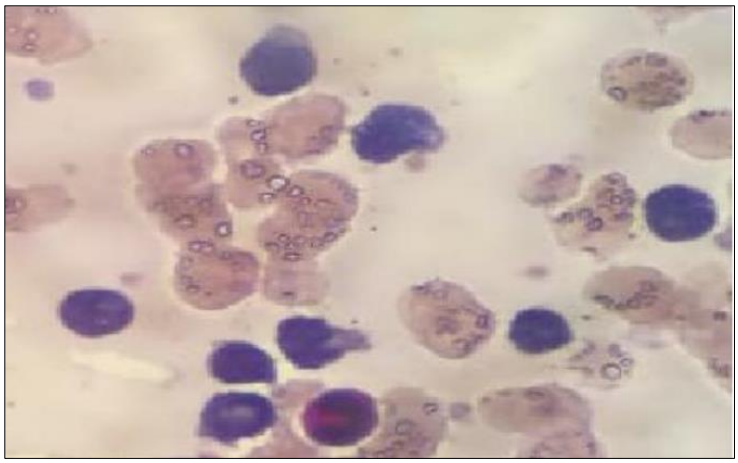

Figure 2 Negative myeloperoxidase (MPO) staining, Department of Hematology-Central Medical Laboratory CHU Hassan II of Fez

The immunophenotypic study of the marrow blood revealed a low expression CD45 population estimated at 84%. A selection panel for classification of acute leukemia was used to target the low-intensity CD45 population, with evidence of an immunophenotypic profile consisting of CD19+ cells; CD79a+; CD22+; IgM-; CD10+; CD3- (intracytoplasmic and surface); CD2-; CD5-; CD7+; MPO-; CD13+; CD33+; CD117+; CD65-; HLADR+; CD34+ (Table I)

Table 1 Results of the cytometric analysis of the different markers

Marqueurs lymphoïdes B	Marqueurs lymphoïdes T	Marqueurs myéloïdes	Marqueurs non spécifiques
CD19 = 37%	CD3 mb = 0.1%	MPO = 2.3%	CD34 = 94%
CD22 = 45%	CD3 ic = 0.8%	CD13 = 91%	HLADR = 00%
IgM = 08%	CD2 = 0.4%	CD33 = 48%	
CD10 = 84%	CD5 = 1.5%	CD65 = 6.5%	
CD79a = 87%	CD7 = 38%	CD117 = 90%	

The cytogenetic study showed the presence of the t(9,21) translocation.

The patient received induction chemotherapy with cytarabine and idarubicin, followed by maintenance treatment with purinethol and methotrexate. The patient died six months after the diagnosis of the disease

1.2 Observation No. 2

This is a 16-year-old girl who presents with an altered general condition with fever without tumor syndrome. The blood count shows a hemoglobin level at 5.1g/dl, a platelet count at 151g/l and leukocytes at 18.80g/l with 5% neutrophils, 57% lymphocytes, 2% monocytes and 36 % large blasts with high nucleo-cytoplasmic ratio, rounded to oval nucleus, loose and nucleolated chromatin and basophilic cytoplasm. The myelogram finds 53% blast invasion made up mostly of blasts of the same type as those of the blood (figure 3)

Cytochemical staining for myeloperoxidase (MPO) is positive (Figure 4)

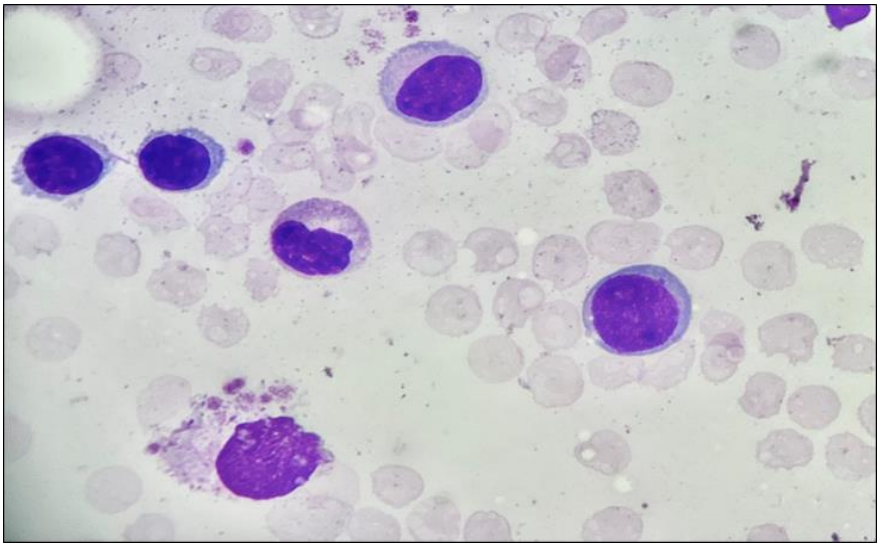

Figure 3 Bone marrow blasts (MGG staining, objective x 100) Hematology Department-Medical Analysis Laboratory-CHU Hassan II of Fez

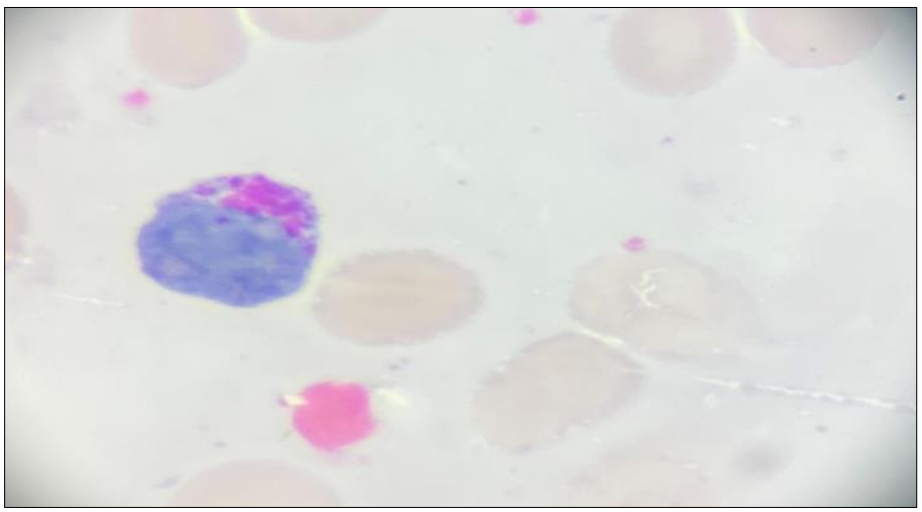

Figure 4 Negative myeloperoxidase (MPO) stain Hematology Department-Medical Analysis Laboratory-CHU Hassan II of Fez

The immunophenotypic study by flow cytometry of the medullary blood revealed the presence of a blast cell population of mixed B/myeloid phenotype. The immunophenotypic profile composed of: CD13+/ CD19+/ CD22+/ CD33+/ CD34+/ CD79a+/ CD117+ HLA-DR+/ MPO+ and CD45+ dim.

The other markers analyzed are negative: cCD3, sCD3, CD7, CD10, CD20 and TdT.

Cytogenetic examination showed the t (8;21)(q22;q22) translocation.

The patient received induction chemotherapy with cytarabine and idarubicin, followed by maintenance treatment with purinethol and methotrexate.

The evolution was marked by complete remission with normalization of the blood count and end of treatment medullogram containing less than 5% of blasts

2 Discussion

The terminology of biphenotypic acute leukemias is often confusing. Indeed, it should be distinguished from leukemias aberrantly expressing one or more markers of a different lineage and which are mistaken for biphenotypic acute leukemia [1]. This terminological ambiguity could in some way explain their varied incidences. Thus, for some authors, their frequency is a little over 3.6% [2], for others, this frequency does not exceed 2% [3,4]. Morphologically, on all the blasts, we recognize the myeloid nature of part of the blasts on their differentiation elements (granulation and Auer bodies). In fact, the appearance of acute biphenotypic leukemias is heterogeneous, as is the case with other types of leukemia. The appearance of the blasts evokes either lymphoblasts in about 1/3 of cases or more frequently myeloblasts [5]. The appearance of LAM 1 found would be in agreement with the international literature. Myeloperoxidase staining is essential, it demonstrates the granular component that is sometimes undetectable in conventional cytology [6]. Given the difficulty in diagnosing acute biphenotypic leukemia in cytology, immunophenotyping remains unavoidable and their definition is strictly immunological [7].

Few studies have analyzed and compared the cytological presentations of BAL compared to other LA. In a series of 23 patients with BAL, Owaidah et al. show that 13 cases have a mixed morphology associating small and large blasts, including 10 cases with cytoplasmic granulations and 1 case with Auer bodies; 6 cases present with small undifferentiated blasts and 4 cases with large blasts. Based solely on cytological criteria (May-Grünwald Giemsa staining and determination of myeloperoxidase), the authors make the following diagnoses (FAB classification): LAM2 (7 cases), LAM0 (1 case), LAM1 (4 cases) , LAM4 (1 case), ALL1 (5 cases), ALL2 (4 cases) and ALL3 (1 case) [8].

In our study, cytology found small blasts (observation 1 classified LAL), and large blasts (observation 2 classified LAM2).

Cytogenetic abnormalities are frequently found. Among them, the most common in adults and associated with a poor prognosis is the Philadelphia chromosome resulting from the t(9;22) (q34;q11) translocation. This translocation is represented by the BCR/ABL rearrangements. On the other hand, translocations (12;21) (p13;q22) or TEL-AML rearrangements have a good prognosis and often occur in children [1]. The individualization of this form of leukemia is important given its unfavorable prognosis [7]. Thus, the complete remission rate and the median survival time are enormously reduced.

3 Conclusion

The management of acute leukemia has benefited from considerable progress. Diagnosis and classification of biphenotypic forms of acute leukemia are now routinely possible. The combination of cytology, cytochemistry, cytogenetics, molecular biology and flow cytometry techniques certainly makes it possible to propose a rational approach to the management of acute leukaemias, in particular biphenotypic forms.

Compliance with ethical standards

Disclosure of conflict of interest

No conflict of interest.

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.

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