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Acute Biphenotypic Leukemia about a Case

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Case Report

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Abstract: Acute biphenotypic leukemias (LAB) are defined by the presence on the same blast cells membrane and cytoplasmic markers belonging to at least two different hematopoietic lineages. We report the case of an infant of 22mois with LAB highlighting the capital interest of hematological cytology, immunophenotyping and cytogenetic study.

Keywords: Acute leukemia; myeloperoxidase; immunophenotyping.

INTRODUCTION

Acute biphenotypic leukemia is a rare and heterogeneous form of acute leukemia and represents only 5% of cases. It is defined by the presence on the same blast cells of membranous and cytoplasmic markers belonging to at least two different hematopoietic lineages [1-4].

In this work, we report the diagnosis of a case of acute biphenotypic leukemia in an infant, highlighting the vital interest of hematological cytology associated with blast cell immunophenotyping and cytogenetic study.

OBSERVATIONS

It is a 22-month-old infant, admitted for a fever of 39 ° C, cutaneo-mucous pallor, a hemorrhagic syndrome made of bruises on the anterior aspect of the left arm, evolving in a context of alteration of the general condition.

The hemogram revealed bicytopenia (hemoglobin: 4.5g / dl, platelets: 11G / L) and hyperleucocytosis at 46.96G / L with 0% neutrophils, 50% lymphocytes, 29% monocytes and 21% agranular blasts. The myelogram found a blast infiltration estimated at 73% made of blasts of undifferentiated appearance without maturation and the same appearance of those found in the peripheral blood. (Figure-1 and 2)

Myeloperoxidase staining on spinal smear was negative (Figure-3), thus suggesting two diagnoses: acute lymphoblastic leukemia, acute myeloid leukemia undifferentiated type M0. In this case, immunophenotyping of bone marrow blasts is needed to make a difference. Table I shows a summary of the flow cytometry analysis results.

This immunological profile corresponds to acute biphenyl leukemia with lymphoid B and myeloid markers (Table-2). The cytogenetic study has shown complex abnormalities in chromosome 11.

Table-1: Summary of Flow Cytometry Analysis Results

CD19	99,2%	MPO	9,6%	DR	1,1%
CD79a	92,8%	CD33	39,6%	TDT	44%
CD22	66,8%	CD13	83,4%	CD10	99,5%
IgM	98%	CD15	43,2%	CD34	84,4%
CD3s	0%	CD117	0,9%		
CD3-I	4,9%	CD7	0,8%		
CD2	0,25%	CD14	0%		
CD5	1,64%	CD65	27%		

Table-2: EGIL immunoassay system [1] A score strictly greater than 2 makes it possible to define membership in a lineage

Score	Lines and markers			Points awarded		
	B	T	My	B	T	My
2	CD79a CD22cyt IgM cyt	CD3 AntiTCR(αβ) Anti-TCR(γδ)	Anti-MPO	2 2 2	0 ND	0
1	CD19 CD20 CD10	CD2 CD5 CD8	CD117 CD13 CD33 CD65s	1 ND 1	0 0 ND	0 1 1 1
0,5	Tdt CD24	Tdt CD7 CD1a	CD14 CD15 CD64	0,5 ND	0 0 ND	0 0,5 ND

Table-3: Frequency of the LAB according to series [6-13]

Study	Number of patients Having LA	Number of patientsLAB	Frequency %
Al seraihy *et al.* [6]	633	24	3,7
Gujral *et al*. [7]	2689	32	1,2
JE-HWAN *et al.* [8]	1554	33	2,1
Mikulic *et al*. [9]	535	21	3,9
Xu X-Q *et al*. [10]	452	21	4,6
Owaidah *et al*. [11]	676	23	3,4
Killik *et al.* [12]	693	25	3,6
Rubio *et al.* [13]	811	39	4,8

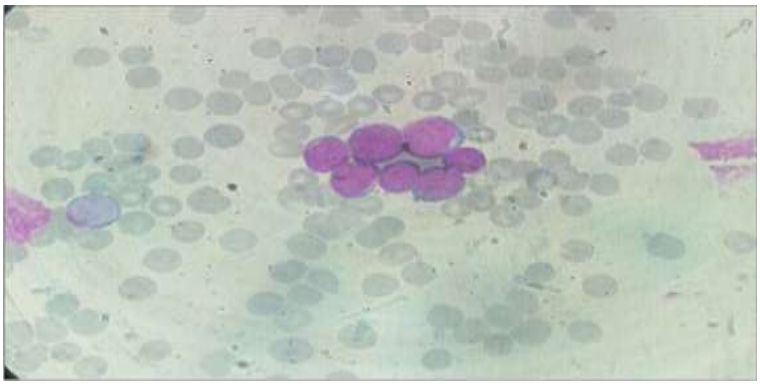

Fig-1: Blood smear (May-Grunwald-Giemsa-Objective × 100) showing 7 agranular blasts with mixed morphology (medium and large)

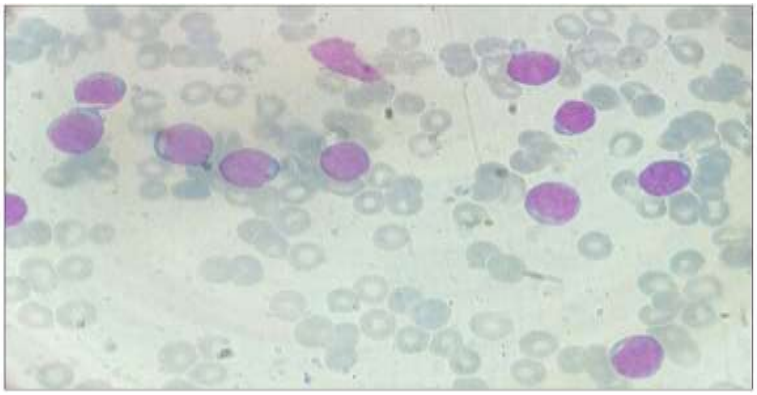

Fig-2: Medullary smear (MGG-objective × 100) showing agranular blasts of the same appearance as those found in the blood smear

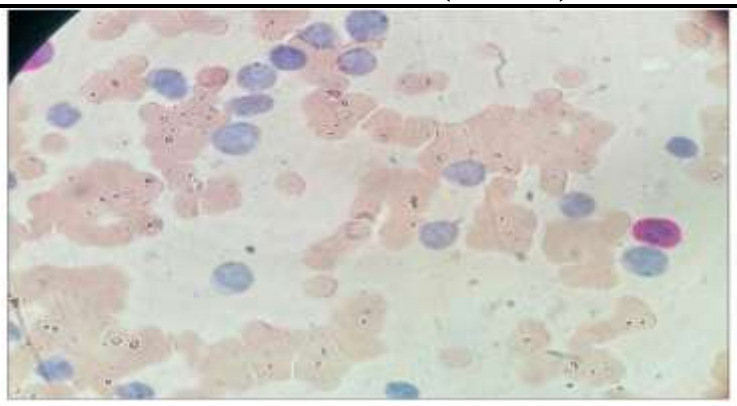

Fig-3: Myelogram + reaction to myeloperoxidase negative medullary blasts (MGG × 100)

DISCUSSIONS

The generalization of the LA phenotype allows in the great majority of cases to classify them according to the belonging to the myeloid or lymphoid lineage of the blast cells involved [5] .However, a small percentage of cases remains difficult to classify, either because of the absence of expression of markers specific to the lines (undifferentiated LA), or because of the simultaneous expression of myeloid and lymphoid markers (LAB or biclonal). The European Group for the Immunological Classification of Leukemias (EGIL) proposes a set of diagnostic criteria for the LAB; indeed, an LA is defined as biphenotypic when the calculated score is strictly greater than 2 for each line involved [2, 4].

The LAB remains a rare entity with an incidence that varies between 1.2 and 4.8% depending on the series (Table-3) [5-9, 12-14].

On a morphological level, rare studies are interested in comparing the cytological presentations of the LAB compared to the other LA.The series of Gujral et al [7] shows that 16cas have a mixed morphology made up of blasts of different sizes (small, medium and large) with cytoplasm of average abundance and presence of some granulations; 15cases have a monomorphic blast population considered as LAL1 or LAL2 according to FAB, and a case with myeloblasts and auer bodies. In our observation, the cytological appearance coupled with MPO staining favored an LAL2 according to FAB.

This morphological presentation was present in the series previously described in half of the LAB cases. However, the FAB LAM2 presentation was the most dominant in the study by Owaidah et al. These studies thus prove the significant heterogeneity of this clinical entity on the cytological level. Thus, immunophenotyping remains unavoidable to quickly correct the diagnosis of LAB [1-3].

For this, EGIL proposes a diagnostic score to differentiate LAB from other types of LA. A LAB is defined by a score strictly greater than 2 for markers of the myeloid lineage and a score greater than 2 for those of the lymphoid B / T line. Thus, the LAB can be divided into 4 subgroups; the myeloid-B phenotype is frequently found with an incidence ranging between 47 and 72% depending on the series, followed by lym T / myeloid (24%), lym B / T and triligne phenotypes are very rare [6,7,10].

There is no pathognomonic chromosomal abnormality at LAB. However, several studies have shown that there are common cytogenetic abnormalities, such as the Philadelphia chromosome that results from translocation t (9; 22) (q34; q11). Its incidence seems high between 28 and 35% depending on the series [11, 6]. This abnormality is associated with a poor prognosis. Indeed, Kullik *et al* [12] in their study showed that children younger than 15 years with a Philadelphia negative chromosome had comparable survival to control patients with AML or LAL, unlike those with a Philadelphia positive. Other cytogenetic abnormalities found in the literature: traslocation (12; 21) (p13; q22), TEL-AML rearrangements that are of good prognosis and often occur in children [1], abnormalities of the 11q23 region. and chromosome 5 are also reported. A new cytogenetic abnormality was found in a 6 year old child with LAB; it is a fusion spliced MLL gene fusion with CT45A2 [14], describe the child died 28 months after diagnosis. As for our study, the cytogenetic study has shown complex abnormalities in chromosome 11.

LAB in children is associated with a generally good prognosis [6] with survival comparable to patients with ALL and better than those with AML.

CONCLUSION

LAB is a rare clinical entity. The systematic use of blast immunophenotyping associated with the cytogenetic study and molecular biology remains essential for better diagnostic, prognostic and therapeutic management of acute leukemias and more particularly biphenotypic forms.

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