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Biphenotypic Acute Leukemia: Description of a Case and Literature Review

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Authors' contributions

This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.

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Case Study

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ABSTRACT

Introduction: "Ambiguous lineage acute leukemias" including biphenotypic acute leukemia are subtypes of acute leukemia (AL) generally representing less than 5% of all acute leukemias. We report a case of biphenotypic acute leukemia (T and B) diagnosed in the clinical hematology department of Dakar.
Observation: This was a 17-year-old female patient, with no specific pathological history, referred for exploration of a bicytopenia associated with hyperleukocytosis that appeared 2 months before. The clinical examination showed an alteration of general state of health (PS WHO 3), an anemic syndrome, a sepsis with a pulmonary focus and a tumor syndrome (nodes and splenomegaly). The blood count showed a hyperleukocytosis of 94.15 G/L, an anemia of 3.7 g/dl normochromic normocytic aregenerative and a thrombocytopenia of 14 G/L. The blood smear showed 34% of

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blasts cells. The myelogram study showed an acute lymphoblastic leukemia. Immunophenotyping revealed partly T-type blasts (CyCD3+; sCD3-; CD7+; heterogeneous CD2 and CD5), B cells (CD19+ and CD79a+) and absence of aberrant myeloid markers. Replacement therapy with blood products (red blood cells and platelets concentrates) was provided to the patient. The short-term evolution was marked by a worsening of the clinical presentation and a mortality at day 3 of hospitalization.

Conclusion: Bi-phenotypic acute leukemia is a very rare cytological entity with a poor prognosis. Systematization of flow cytometry in our countries with limited resources would help to better diagnose AL.

Keywords: Acute leukemia; biphenotypic; flow cytometry.

1. INTRODUCTION

Most acute leukemias can be classified into a specific lineage, namely acute lymphoblastic leukemia (ALL) or acute myeloid leukemia (AML) based on morphological, cytochemical and immunophenotypic characteristics of blast cells. With the widespread use of flow cytometry, acute leukemias that express antigens of different lineages are increasingly recognized [1,2]. These may be leukemias with two distinct populations of blasts, each from a different lineage, or with a single population of blasts expressing several lineage markers. The two groups have been referred to as bilineage acute leukemias and biphenotypic acute leukemias (BAL), respectively. All these cases are classified as "ambiguous lineage acute leukemias" in the World Health Organization 2008 classification system [3].

In an effort to unify the definition of AMLs, the European Group for Immunological Classification of Acute Leukemias (EGIL) has proposed guidelines for scoring lineage-specific antigens commonly used in the lineage assignment of acute leukemia [4].

According to this scoring system, LABs are rare, generally accounting for less than 5% of all acute leukemias [5-9]. Most are of combined myeloid/B-cell or myeloid/T-cell lineage, whereas B-cell/T-cell LABs are extremely rare. It is important to recognize LAB because they are uniformly associated with a poor prognosis with conventional therapies [3, 8,10].

We report a case of biphenotypic (T and B) acute leukemia diagnosed at the clinical hematology department of the CNTS in Dakar.

2. CASE PRESENTATION

The patient was 17 years old, with no particular pathological history, no exposure to toxins and no notion of phytotherapy. She was referred for exploration of a bicytopenia associated with hyperleukocytosis that appeared 2 months before admission. On admission, the clinical examination showed an altered general condition (WHO statue performance coted 3), an anemic syndrome with poor hemodynamic tolerance and no external bleeding; a sepsis with a pulmonary point of call (left basal pulmonary condensation syndrome); a tumor syndrome with bilateral and asymmetric nodes located at cervical, axillary and inguinal measuring 2 to 4 cm and a painless splenomegaly with a splenic overhang of 2 cm at the level of the left mid-clavicular line. The blood count showed a major hyperleukocytosis of 94.15 G/L associated with an anemia of 3.7 g/dl normochromic normocytic aregenerative (Reticulocyte count: 34G/L) and a thrombocytopenia of 14 G/L. The blood smear showed anisopoikylocytosis with the presence of 34% of blasts. In view of these results, associated with the clinical context, the myelogram, bone marrow immunophenotyping and some biological parameters were requested. The myelogram showed a very rich type V marrow invaded by medium-sized blast cells with a high nucleocytoplasmic ratio; their chromatin was loose and nucleated and their cytoplasm was sparse and very basophilic. This cytologic appearance was in favor of a type II acute lymphoblastic leukemia according to the FAB classification (Fig. 1). Immunophenotypic complement further refined the diagnosis by showing partly T-type blasts with CyCD3 + and sCD3-. The majority of other T markers were negative: CD1a, TdT, CD4, CD8 while CD2 and CD5 were heterogeneous. In addition, CD7 was highly expressed, associated with an absence of aberrant myeloid markers. B cells were also found in this blast population with the presence of CD19 and CD79a. In sum, the immunophenotypic appearance was consistent with T and B acute lymphoblastic leukemia according to the EGIL classification (Fig. 2). The

workup showed a spontaneous tumor lysis syndrome, which was managed as an emergency. She was treated with hematological resuscitation, including transfusions of packed red blood cells and platelets, combined with bi-antibiotic therapy for the lungs. The outcome was marked by a deterioration of the clinical condition after 2 days of hospitalization with the apparition of a hemorrhagic syndrome of great abundance associated with a melena and a diffuse non-infiltrated petechial purpura. Death occurred on the third day of hospitalization.

3. DISCUSSION

Acute lymphoblastic leukemia (ALL) is a rare hematologic malignancy; its incidence increases in childhood and is therefore rare in adults [11]. It is a heterogeneous disease with simultaneous evaluation of several surface and intracellular markers at diagnosis helping to identify subtypes of acute lymphoblastic leukemia [4]. These subtypes have different prognoses and require different therapeutic strategies.

On the other hand, biphenotypic acute leukemia is a very rare subtype of acute leukemia (AL). Its prevalence among patients with ALL depends on the diagnostic criteria used. A retrospective meta-analysis of 7,627 cases of ALL in pediatric and adult populations reported 213 (2.8%) and 119 (1.6%) cases of biphenotypic acute leukemia according to EGIL and WHO 2008 criteria, respectively [12]. The case of our 17-year-old patient is one of the first cases of bi phenotypic acute leukemia diagnosed in Senegal. This is currently possible thanks to the availability and systematic performance of immunophenotyping in the diagnostic workup of acute leukemia. Clinically, our patient presented with bone marrow failure syndrome and tumor syndrome as observed in patients with other types of ALL [12]. Nevertheless, studies have shown that AML is more frequently associated with central nervous system involvement than AML and ALL [13,14]. On bone marrow smear, our case presented a very rich marrow invaded by medium-sized blasts of lymphoid appearance; however, the morphological appearance of AML is heterogeneous. As in all AMLs, the marrow contains more than 20% blasts, the appearance of which suggests either lymphoblasts in about 1/3 of cases or, more frequently, myeloblasts [9]. This cytological heterogeneity is coupled with immunophenotypic techniques for a better characterization of acute leukemias. Only flow cytometry examination is likely to identify AML by demonstrating an EGIL "immunological score" greater than 2 in at least two lineages.

This score identifies several subgroups of AML. The first group corresponds to a co-expression of lymphoid and myeloid markers (L+M). These LAB are the most frequent and the expression of myeloid markers is in order of frequency CD33, CD13 and CD11b. Based on MPO expression, it is usual to distinguish between L+M MPO+ LAB and LAB with myeloid and lymphoid (M+L) MPO + markers. LAB with B and T lymphoid markers (B+T) are rarer as are LAB with B+T lymphoid and myeloid markers (B+T+M) [15].

Our patient was able to perform flow cytometry which showed T and B lineage markers with negativity of myeloid markers. She had not been able to undergo cytogenetic testing due to the high cost and unavailability of the test in Senegal. Cytogenetic testing would reveal more frequent t(9;22) (q34;q11) or p190 BCR/ABL rearrangements in LAB. Ph1-positive ALL is more frequent in adults than in children and is associated with the expression of CD19, CD34 and CD10. Their poor prognosis justifies innovative treatments and the role of tyrosine kinase inhibitors appears to be important. In contrast to t(9;22) (q34;q11), t(12;21)(p13;q22) or TEL-AML1 rearrangements are very frequent in children and have a relatively good prognosis [16]. AMLs associated with abnormalities at 11q23 are associated with CD19 and CD34 expression but not with CD10 expression. Finally, other recurrent but non-specific cytogenetic abnormalities have also been described in LAB [17].

Our patient, naïve to any background treatment, died of signs of disease progression including a hemorrhagic syndrome complicated by anemia. A study has shown that biphenotypic acute leukemia is considered to have a poor prognosis [18]. Given its low incidence, there is little information in the literature on treatment outcomes. Published data suggest poor treatment outcomes, both in terms of probability of achieving complete remission and overall survival (OS), compared to AML or ALL [19, 20]. A study of treatment in 35 children with AML meeting EGIL criteria showed comparable outcomes to AML but poorer overall survival than in pediatric ALL [21].

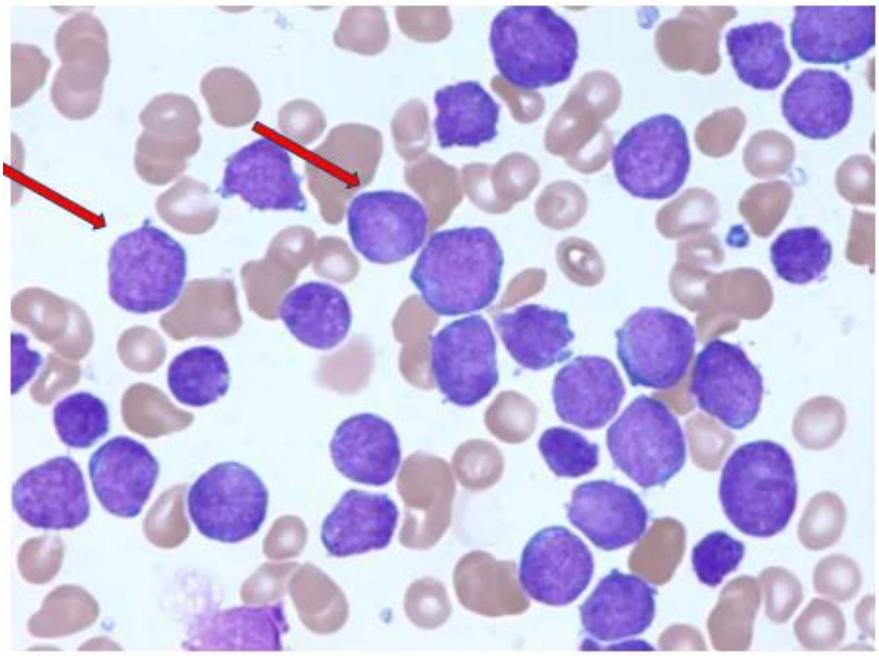

Fig. 1. Medullary smear stained with May Grunwald Giemsa, magnification x 100: lymphoblasts (red arrow)

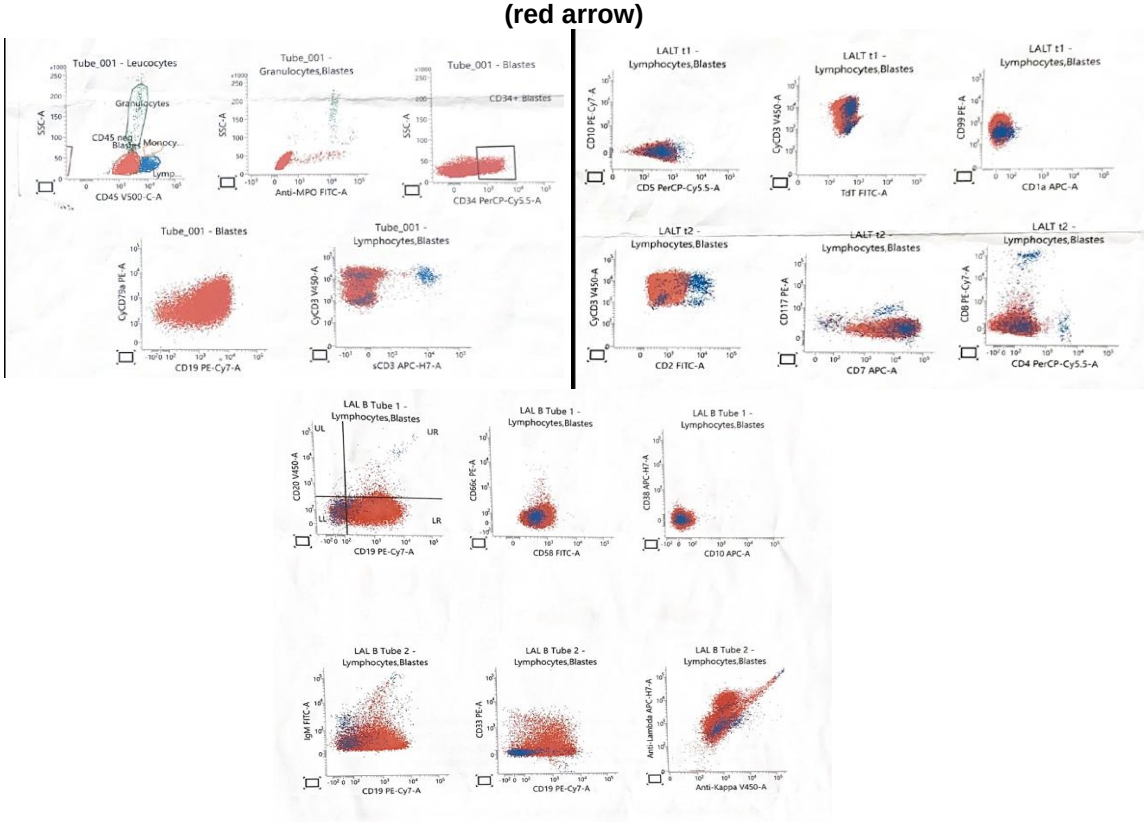

Fig. 2. Medullary immunophenotyping

4. CONCLUSION

Acute biphenotypic leukemia is a very rare cytological entity with a poor prognosis. The systematization of flow cytometry in our countries with limited resources would allow to better diagnose these hematological malignancies.

CONSENT

As per international standard or university standard, parental(s) written consent has been collected and preserved by the author(s).

ETHICAL APPROVAL

As per international standard or university standard written ethical approval has been collected and preserved by the author(s).

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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