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Case Report

Acute Myeloid Leukemia Cup-Like: About a Case

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Abstract: Cup-like acute myeloid leukemia is a rare type of AML with specific and distinct cytological, phenotypic, cytogenetic, and molecular characteristics compared to other AMLs. We will report through this observation the aspects of this pathological entity.

Keywords: Hematology, Myeloid Leukemia, Myeloid Leukemia Cup, Like.

INTRODUCTION

Acute myeloid leukemia (AML) is a malignant hematological disorder characterized by excessive and acute clonal proliferation of myeloid lineage precursors, with maturation gaps. Cup-like acute myeloid leukemia is a rare type of AML with specific and distinct cytological, phenotypic, cytogenetic, and molecular characteristics compared to other AMLs. Its diagnosis relies on a combination of cytological, immunological, and genetic arguments, and its prognosis is very bleak. Recognizing this entity is important to avoid confusion with acute promyelocytic leukemia, thus guiding molecular study.

CASE REPORT

We report the case of a 26-year-old patient with no significant medical history.

He has presented with asthenia and deterioration of general condition for six months. The clinical examination reveals no lymphadenopathy, hepto-splenomegaly, or bleeding syndrome. The biological assessment shows hyperleukocytosis associated with anemia and thrombocytopenia. The leukocyte differential check on blood smear shows 96% medium-sized blasts with a very high nuclear-cytoplasmic ratio, nuclei with irregular contours and fine chromatin, often nucleolated showing a cup-like inclusion, the cytoplasm is slightly basophilic, sometimes granular (Figure 1 and 2).

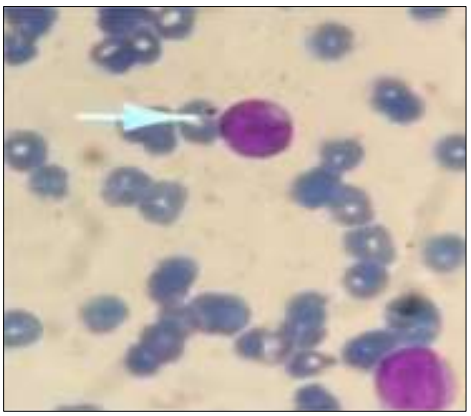

Figure 1: Cup-like blasts on blood smear, MGG

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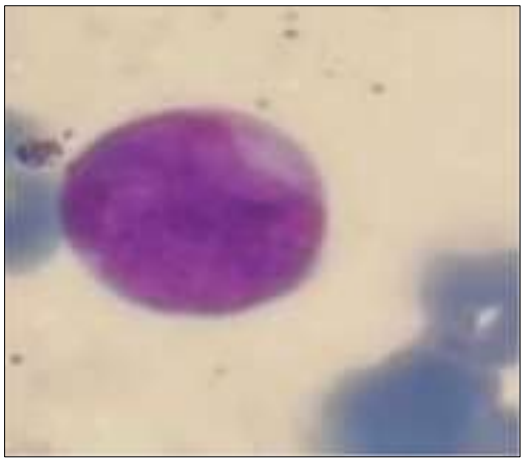

Figure 2: Cup-like blasts on blood smear, MGG

The hemostasis assessment shows normal levels of prothrombin time, activated partial thromboplastin time, and fibrinogen. The myelogram reveals a very rich marrow with massive blast infiltration comprising 90% with an appearance comparable to circulating blasts in peripheral blood, with a cup-like appearance in more than 20% of the blasts (Figure 3).

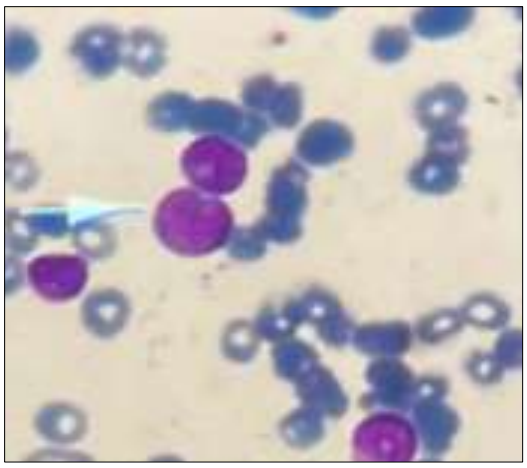

Figure 3: Cup-like blasts on bone marrow smear, MGG

The complementary assessment includes:

- A cytochemical reaction to myeloperoxidase, very positive in over 90% of the blasts (Figure 4).

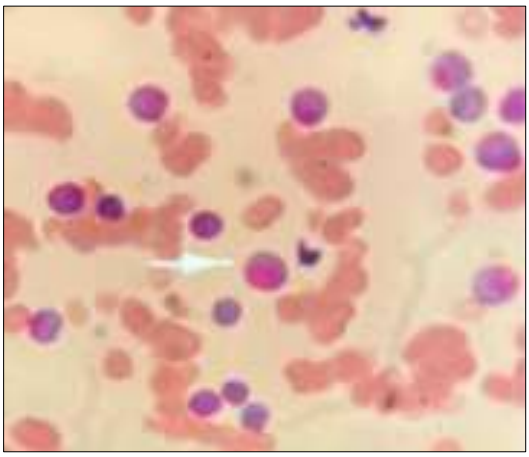

Figure 4: Very positive myeloperoxidase reaction on marrow smear

- A bone marrow immunophenotyping, which highlights a myeloid blast proliferation MPO +, CD33 +, CD45 +, partial CD117, CD13-, CD34-, HLA-DR. • Molecular exploration by NGS showed the presence of FLT3 and NPM1 mutations. The patient received induction treatment with Idarubicin, followed by 2 boluses of Ara-C 100 mg/day (Day 1 and Day 2) with hyperhydration of 3L/m2/24h. The evolution was marked by the onset of an infection on day 10.

DISCUSSION

The cup-like AML is classified among hematological neoplasms according to the WHO 2016. This classification aims to integrate clinical, morphological, immunophenotypic, genetic, and prognostic parameters. Cup-like AML was initially described in 1942 and is defined by the presence of at least 10% of blasts with cup-like nuclear invagination, which is consistent with our case where more than 20% of blasts had cup-like invaginations [1, 2].

Nuclear invagination is prominent and extends over at least 25% of the nucleus diameter. It is described as a cup-like or cup-shaped invagination. In the extreme state of nuclear invagination, a bilobed appearance of the nucleus can be observed, which may be confusing with acute promyelocytic leukemia variant, characterized by the absence of CD 34 and HLA DR expression; therefore, immunophenotyping is an important element for guidance. The diagnostic confirmation of acute promyelocytic leukemia requires the identification of specific genetic mutation of PML RARA, and is closely correlated with immunophenotypic and morphological appearances [3, 4].

Recently, the cup-like appearance has been strongly associated with mutations of the nucleophosmin (NPM1) genes, fms-like tyrosine kinase (FLT3)-internal tandem duplication (ITD), and tyrosine kinase domain (TKD), as well as the negativity of HLA DR, MHC II cell receptors. These morphological and genetic associations allow for the search for specific genetic mutations; however, the cup-like appearance is the result of either the NPM1 mutation alone or the co-mutation of NPM1 and FLT3. In our case, molecular analysis confirmed the presence of both FLT3 and NPM1 mutations, which is an indicator of poor prognosis in the literaturev [5].

CONCLUSION

The cup-like LAM is a rare form of LAM, its frequency is likely underestimated because it is a poorly known and described entity. In light of our case and the data from the literature, we emphasize the importance of recognizing this entity, not only due to the possible cytological confusion with acute promyelocytic leukemia variant, but also because of the diagnostic direction it can provide and the poor prognosis it may entail.

Conflict of Interest: The authors declare that they have no conflict of interest.

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