Acute Myeloid Leukemia “Cup-Like”: About A Case and Literature Review

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Abstract

Cup-like acute myeloid leukemia (CL AML) is a rare form of acute myeloid leukemia, but its frequency is probably underestimated because it is a poorly understood and little described entity. Characterized by a particular biological profile: hyperleukocytosis, massive blastosis, disseminated intravenous coagulation, nuclei marked by a clear nuclear invagination, relatively stereotyped immunophenotype: CD34− / HLA-DR− / MPO + / CD117 + / CD13 +. Often associated with a normal karyotype, CL AML cytology is highly predictive of molecular abnormalities affecting NPM1 and FLT3.

Keywords: Acute leukemia - cup-like - diagnosis - immunophenotyping - mutation – prognosis.

INTRODUCTION

Acute myeloid leukemia is defined by a malignant proliferation leading to the accumulation in the blood and bone marrow of precursor cells of the myeloid lineage.

Acute myeloid leukemia cup-like, a rare form of AML, has specific cytological, phenotypic, cytogenetic and molecular characteristics distinct from other types of AML. Its diagnosis is based on a bundle of cytological, immunological and genetic arguments.

We report a case of acute cup-like leukemia whose interest lies in the similarities with variant hypogranular acute promyelocytic leukemia.

Observation

A 64-year-old female patient, followed for type 2 diabetes treated with insulin and high blood pressure treated by antihypertensive drugs. Admitted for an incomplete spinal cord syndrome with an anemic syndrome made of asthenia and cutaneous mucosal pallor and a hemorrhagic syndrome made of ecchymotic spots the whole evolving in a context of deterioration of general state.

The blood count reveals a normochromic normocytic anemia at 7 g/dl, a major leukocytosis at 101 G/l and a deep thrombocytopenia at 10 G/l, the blood smear examined objective a 90% swelling of blasts of myeloid appearance with a nuclear invagination.

The bone marrow smear reveals a blastic overwhelming 96% with a nuclear invagination in more than 15% of blasts (Figure 1A &1B), staining with myeloperoxidase returned positive in more than 90% of blasts recalling the myeloid nature (Figure-1C).
Immunophenotyping reveals a population blastic with CD45 +, CD34 -, HLA -, DR -, partial CD117, MPO +, CD13 - and CD33 +, this profile evoked an acute myeloid leukemia "cup-like".

Molecular assyas revealed positive FLT3 and NPM1 mutations in our patient.

The patient received hydro-urea-based cyto-reducing treatment (50 mg / kg / day) without response, then 2 aracytine flashes of 100 mg / day (D1 and D2) with hyperhydration 3L / m² / 24h.

The patient presented on day 11 an infectious syndrome made of fever encrypted at 40 °C, she was put on dual antibiotic therapy (3rd generation cephalosporin + Amikacin). The patient died after 3 days with septic shock.

**DISCUSSION**

The CL-AML is part of acute leukemia classified by the 2016 edition of the classification of hematological tumors of the world health association (WHO) that aims to integrate recent information concerning the clinic, prognosis, morphology, immunophenotyping and genetics [1].

The CL-AML, described for the first time in 1994 [2], is defined according to the authors by the presence of nuclear invagination in at least 5% [3], 7% [4] or more commonly accepted value of 10% blasts [5-7]. In our case, they were detected in more than 15 % of the blasts.

The nuclear invagination is prominent and extends over at least 25% of the nuclear diameter [3, 5-7]. It is then designated by its cup-like appearance or fish mouth. The final stage of nuclear invagination can go as far as clear cleavage, giving a bilobed nuclear appearance [2-7], which can be the source of confusion with variant acute promyelocytic leukemia, with absence or weak expression of CD34 and HLADR as well as a particular morphological aspect of the blasts (prominent nuclear invagination). Thus in our case immunophenotyping was the element of orientation by absence of the expression of CD34 and HL.A.

The formal diagnosis of APL requires identification of a specific genetic mutation of the PML-RARA transcript and is closely correlated with specific immunophenotypic and morphological features [8, 9].

Recently, cup-like were strongly associated with mutations of the nucleophosmin (NPM1), fms-like tyrosine kinase (FLT3)-internal tandem duplication (ITD), and tyrosine kinase domain (TKD) genes as well as with negativity for the MHC class II cell surface receptor HLA-DR [10-14].

These morphological and genetic associations can be used to screen for specific genetic mutations.
However, whether cup-like nuclei are associated with mutation of NPM1 alone or co-occurring mutations of both NPM1 and FLT3 is controversial [10, 11, 14].

In our study, the cytogenetic study has found a combination of the two mutations FLT3 and NMP1.

The bad prognosis related to this form and reported in the literature [14] corresponded to our case, in fact resistance to cytoreductive treatment even before receiving the results of immunophenotyping and cytogenetics was in favor of the diagnosis, which has leads to the search for FLT3 and NPM1 mutations.

**CONCLUSION**

In view of our case report and data from the literature, we recall the interest of recognizing this entity, not only because of the possible cytological confusion with variant acute hypogranular promyelocytic leukemia, but also because of the diagnostic guidance it can provide.

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