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Hematology

Unusual Morphology in Acute Myeloid Leukemia: The Cup-Like Variant – Case Report and Literature Review

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Abstract | **Case Report**

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.

Keywords: Cup Like, Acute Leukemia, Immunophenotyping, Blastosis.

INTRODUCTION

Acute myeloid leukemia (AML) is a hematologic malignancy marked by the clonal proliferation of immature myeloid precursors in the bone marrow, resulting in ineffective hematopoiesis and rapid marrow failure. Although AML accounts for approximately 1.2% of all new cancer diagnoses in the United States, it remains the most common form of acute leukemia in adults [1]. From a pathophysiological standpoint, AML arises from acquired genetic mutations in hematopoietic stem and progenitor cells, which lead to uncontrolled proliferation and a block in differentiation. This process is often preceded by preleukemic states such as clonal hematopoiesis of indeterminate potential (CHIP) [2]. Management of AML has evolved significantly in recent years, with the advent of targeted therapies and less intensive regimens tailored to elderly or unfit patients. Multidisciplinary approaches—including early integration of palliative care—are increasingly emphasized to improve patient outcomes and quality of life [3].

In this context, we report a clinical case of AML with an uncommon morphological presentation—so-called "cup-like" nuclei—and discuss its diagnostic and therapeutic implications in light of current literature.

CASE REPORT

We report the case of a 62-year-old woman with a medical history of well-controlled hypertension and seasonal allergic rhinitis. She had no known hematologic conditions and no family history of cancer or autoimmune diseases.

The patient presented to the emergency department with complaints of increasing fatigue, easy bruising, and bleeding gums for the past week. She also reported mild lower back pain and a subjective fever without chills.

On physical examination, she appeared pale and had scattered petechiae on her lower limbs. There was no hepatosplenomegaly or lymphadenopathy. Her vital signs were stable, with a temperature of 37.8°C.

Initial laboratory findings were as follows:

- Hemoglobin: 8.5 g/dL
- Platelets: 21 × 10^9/L
- White blood cell count: 105 × 10^9/L with 83% circulating blasts
- Prothrombin time: 42%
- D-dimers: markedly elevated

These findings were consistent with acute leukemia complicated by disseminated intravascular coagulation (DIC).

Peripheral blood smear revealed medium-to-large blasts with basophilic cytoplasm and nuclei showing deep invaginations, giving a “cup-like”

morphology (Figure1). Bone marrow aspirate confirmed hypercellularity with over 90% blast infiltration.

Immunophenotyping showed a stereotypical pattern:

- CD34: negative
- HLA-DR: negative
- MPO: positive **(Figure2)**
- CD117: positive
- CD13 and CD33: positive

Cytogenetic analysis revealed a normal karyotype. Molecular studies identified an NPM1 mutation and a FLT3-ITD mutation with high allelic ratio.

Induction chemotherapy was initiated with cytarabine and daunorubicin (7+3 protocol).Supportive measures included transfusions, antibiotics, and treatment of coagulopathy. During the first week of treatment, she developed febrile neutropenia complicated by septic shock and worsening DIC. She developed multiorgan failure, including acute respiratory distress syndrome and refractory hypotension. She died on day 10 of induction therapy.

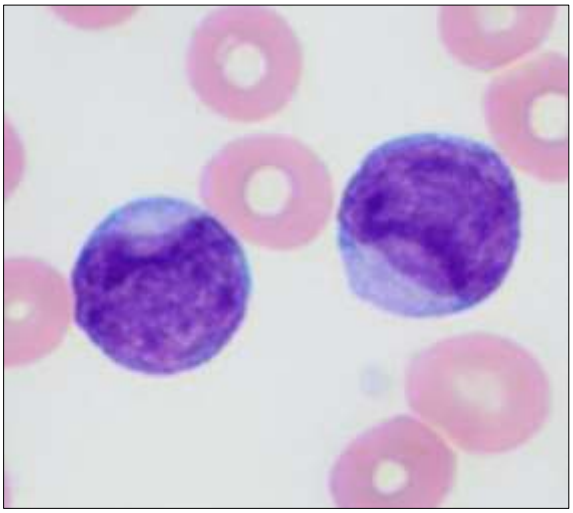

Figure 1: Blasts with cup-like nuclear morphology

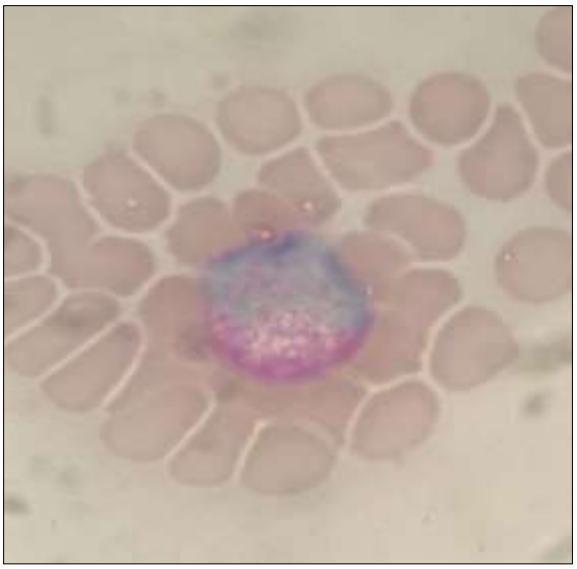

Figure 2: Blast appearance with negative MPO staining

DISCUSSION

Acute myeloid leukemia (AML) is a genetically heterogeneous clonal disorder characterized by the proliferation and accumulation of myeloid blasts in the bone marrow and peripheral blood, resulting in ineffective hematopoiesis and bone marrow failure [1, 2]. Among the less frequent morphological variants, cup-like AML has gained increasing attention due to its distinct cytological features and strong molecular associations.

Cup-like AML is defined by the presence of blasts with deep, prominent nuclear invaginations forming a characteristic “cup-like” appearance under light microscopy. This morphological pattern is strongly

associated with NPM1 mutations and FLT3-ITD mutations, which confer both diagnostic and prognostic implications [4, 5]. In fact, the presence of cup-like nuclei has been reported to have a high positive predictive value for NPM1 mutations, especially in cases with a normal karyotype [6, 7].

The immunophenotype of cup-like AML is relatively stereotyped and includes CD34-, HLA-DR-, MPO+, CD117+, CD13+, and CD33+ expressions, which can aid in early diagnostic orientation even before molecular confirmation [4-8].

Clinically, patients with cup-like AML often present with hyperleukocytosis, coagulopathy, and in many cases, disseminated intravascular coagulation (DIC), which significantly increases the risk of hemorrhagic and thrombotic complications [9]. A recent study also reported a high incidence of **a**cute cerebral infarctions in patients with this AML subtype, likely due to both leukostasis and a hypercoagulable state [9].

Therapeutically, standard induction regimens (e.g., cytarabine plus anthracyclines) remain the cornerstone of initial treatment. However, the identification of FLT3-ITD mutations has led to the integration of targeted agents such as midostaurin, which improves overall survival when combined with chemotherapy [9]. Despite these advances, patients with high FLT3 allelic burden and DIC remain at elevated risk for early mortality, particularly in the presence of infectious or thrombotic complications.

In the presented case, the patient exhibited classic features of cup-like AML, including marked leukocytosis, DIC, and an NPM1/FLT3-ITD mutation profile. Despite prompt initiation of induction therapy and supportive care, she developed febrile neutropenia complicated by septic shock and multiorgan failure, resulting in early death. This highlights the aggressive course and high early mortality risk associated with this AML subset, underscoring the need for rapid diagnosis, molecular stratification, and close multidisciplinary management.

In conclusion, cup-like AML represents a morphologically and genetically distinct form of AML with important diagnostic and prognostic significance. Early recognition of its characteristic features should prompt urgent molecular testing and tailored therapeutic strategies to mitigate its severe complications.

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