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Acute Promyelocytic Leukemia or Acute Myeloid Leukemia with Mutated *NPM1*?

Akut Promyelositik Lösemi veya *NPM1* Mutasyonlu Akut Myeloid Lösemi?

Maximiliano Cloobs-Venezia[1], Jimena Dejesus[1], Cecilia Malusardi[2], Mariángeles Auat[2], Alejandra Altube[2]

[1]*Medical Staff, University of Buenos Aires, Hematology Division, Hospital de Clínicas "José de San Martín," Buenos Aires, Argentina*
[2]*Flow Cytometry Laboratory, University of Buenos Aires, Hematology Division, Hospital de Clínicas "José de San Martín," Buenos Aires, Argentina*

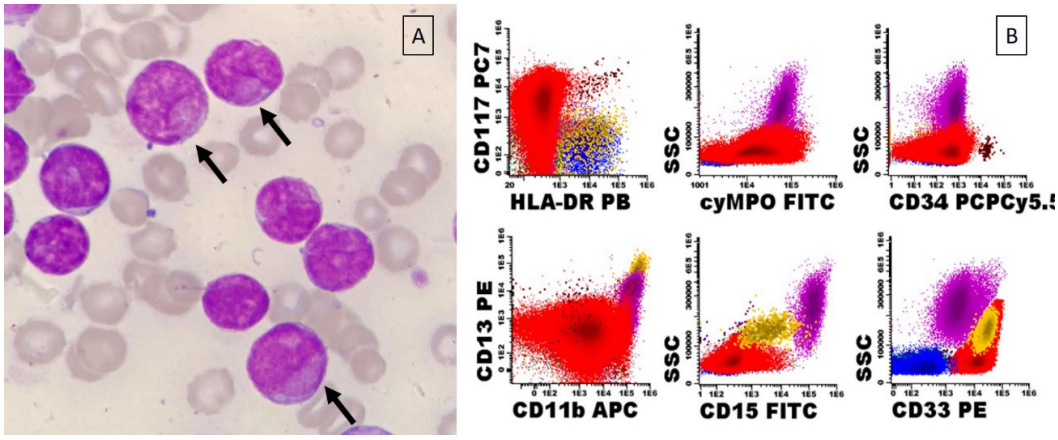

Figure 1. A) Peripheral blood smear with cup-like blasts (black arrows). May-Grünwald-Giemsa staining. B) Dot plots showing the immunophenotype of blasts (red dots). Normal myeloid precursors (brown dots), neutrophils (purple dots), monocytes (yellow dots), and lymphocytes (blue dots) present in the sample are also shown.

A 76-year-old woman was admitted to our hospital and laboratory results showed a high white blood cell (WBC) count of $527x10^9$/L, hemoglobin of 104 g/L, platelet count of $45x10^9$/L, fibrinogen of 1.77 g/L, and prolonged prothrombin time.

A peripheral blood smear revealed blasts with prominent nuclear indentations (cup-like blasts) (Figure 1A).

Immunophenotyping by multiparametric flow cytometry (MFC) showed 95% abnormal cells with low side scatter (SSC); heterogeneous expression of CD13, CD117, CD64, and MPO; bright expression of CD33; and absence of CD34, HLA-DR, and CD15 (Figure 1B). This immunophenotype pattern is related to abnormal promyelocytes.

However, fluorescence in situ hybridization analysis using dual-color dual-fusion probes revealed the absence of the *PML/RARA* fusion gene. Molecular studies identified the presence of the *NPM1* exon 12 gene mutation. *FLT3* and *CEBPA* mutations were not detected. In light of these findings, a diagnosis of acute myeloid leukemia with mutated *NPM1* (acute myeloid leukemia [AML]-NPM1) was made.

Address for Correspondence/Yazışma Adresi: Alejandra Altube, M.D., University of Buenos Aires, Hematology Division, Hospital de Clínicas "José de San Martín," Buenos Aires, Argentina
E-mail : altubea@hospitaldeclinicas.uba.ar ORCID: orcid.org/0000-0003-4380-6779

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Blasts of this subtype of AML can have immunophenotypic features of myeloid or monocytic differentiation. Some cases with myeloid differentiation can exhibit an acute promyelocytic leukemia-like ("APL-like") immunophenotype [1,2]. Thus, distinguishing between AML-NPM1 and APL can be challenging, especially with the hypogranular variant of APL, which usually presents itself with higher WBC counts and lower SSC by MFC than the classical form of APL. It is noteworthy that the presence of cup-like blasts is associated with *NPM1* mutations [3].

It is well known that MFC plays an important role in identifying highly suggestive cases of APL. However, the immunophenotypic profile associated with abnormal promyelocytes might be present in other types of AML. Therefore, AML-NPM1 may be suspected when the immunophenotype resembles that of APL in the absence of the *PML-RARA* fusion gene.

Keywords: Flow cytometry, Acute myeloid leukemia, *NPM1* mutation, Acute promyelocytic leukemia

Anahtar Sözcükler: Akım sitometri, Akut myeloid lösemi, *NPM1* mutasyon, Akut promyelosit lösemi

Authorship Contributions

Surgical and Medical Practices: M.C-V., J.D.; Design: M.A., A.A.; Data Collection or Processing: C.M., M.A., A.A.; Analysis or Interpretation: M.C-V., J.D., C.M., M.A., A.A.; Literature Search: M.C-V., J.D., C.M., M.A., A.A.; Writing: M.A., A.A.

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