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CASE REPORT

A Rare Cytogenetic Presentation of Acute Myeloid Leukemia (AML-M2) Mimicking Acute Promyelocytic Leukemia

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SUMMARY

Background: **Acute myeloid leukemia (AML) with the t(8;21)(q22;q22) mutation, which produces the AML1/ETO fusion gene on chromosome 8q22, is a specific subtype of AML categorized as AML t(8;21) in the WHO classification and AML-M2 in the FAB classification. This subtype is typically linked to a positive prognosis, although variant additional chromosomal abnormalities are often observed.**
Methods: **We report a rare case of this category with unusual karyotype and morphologic characteristic mimicking APL.**
Results: **A diagnosis of acute myeloid leukemia (AML-M2) was made through comprehensive diagnostics.**
Conclusions: **Recognition of the morphological variation is helpful in diagnosis. In addition, further research is needed to better understand the molecular mechanisms underlying unusual rearrangements and their clinical significance.**
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KEYWORDS

acute myeloid leukemia, AML t(8;21), AML-M2, AML1/ETO fusion

INTRODUCTION

Acute myeloid leukemia (AML) is a heterogeneous disease, and the diagnostic karyotype is a significant independent prognostic indicator. It helps identify biologically distinct subsets of the disease and is widely used to guide different risk-adapted treatment approaches [1]. The t(8;21)(q22;q22) chromosomal abnormality is a common non-random cytogenetic anomaly in AML and is strongly linked to the French-American-British (FAB) subtype M2 in the WHO classification. It has distinct clinical and morphologic features associated with a favorable prognosis, including a high remission rate and a long median survival. Approximately 3% - 4% of AML cases are associated with the variant t(8;21)(q22;q22). The balanced reciprocal translocation t(8;21)(q22;q22) is linked to around 6% of AML-M1 cases and up to 92% of AML-M2 cases. This translocation also reported in a small portion of M0, M1, and M4

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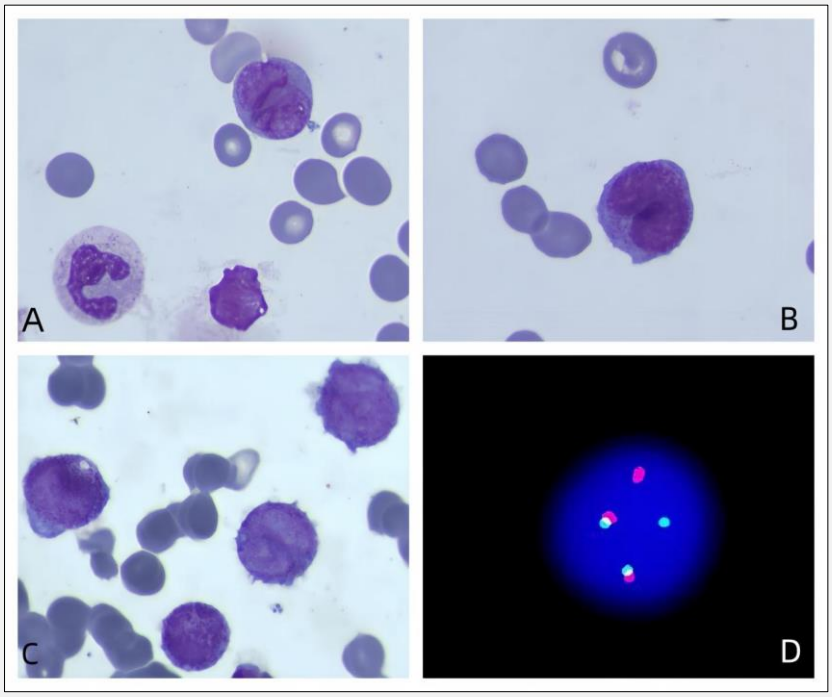

Figure 1. A, B) Blasts were identified in peripheral blood smears. C) Bone marrow aspirate smears showed 30% abnormal cells with prominent hypergranular cytoplasm and kidney-shaped or bilobed nuclei, suggesting acute promyelocytic leukemia (APL). Auer rods were seen (Wright-Giemsa stain, 100 x objective). D) Molecular evidence of the AML1::ETO (RUNX1-RUNX1T1 fusion gene positivity by fluorescent in situ hybridization showing double fusion signals in blast cells.

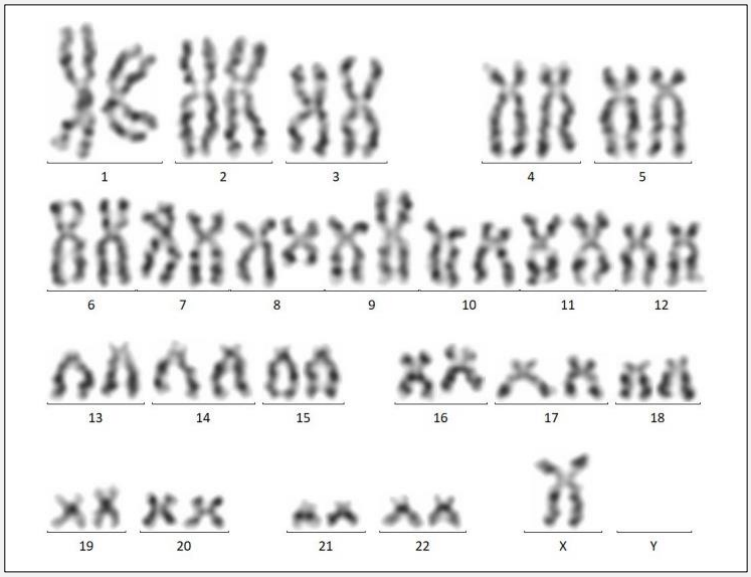

Figure 2. The finding of the chromosome karyotype analysis was as follows: 45,X,-Y,t(8;9)(q22;p24)[20].

subtypes [2,3]. The t(8;21)(q22;q22) chromosomal abnormality results in the fusion of the AML1 gene from chromosome 21q22 with the ETO gene on chromosome 8q22. It is important to note that clinically, AMLs with t(8;21) are associated with good responses to chemotherapy [4]. Herein, we report a rare case of this category with unusual karyotype and morphologic characteristic mimicking APL.

CASE REPORT

A 77-year-old man was hospitalized due to persistent fatigue, chest tightness and shortness of breath following physical activity for the past month. The initial laboratory results revealed a white blood cell count of 32 x 10^9/L, a hemoglobin concentration of 41 g/L, and a platelet count of 9 x 10^9/L. The prothrombin time was 12.3 seconds, the D-dimer level was 0.89 mg/L, and the fibrinogen level was 7.10 g/L. Blasts were identified in peripheral blood smears (Figure 1A, B). Bone marrow aspirate smears revealed 30% abnormal cells with prominent hypergranular cytoplasm and nuclei that were kidney-shaped or bilobed, and Auer rods were seen, indicating a diagnosis of acute promyelocytic leukemia (APL) (Figure 1C). Myeloperoxidase was strongly positive. Flow cytometry analysis showed these promyelocytes were positive for CD34, CD33, CD117, HLA-DR, CD38, CD56, CD13, myeloperoxidase, and CD19 (partial), and were negative for CD5, CD7, CD 10, CD11b, CD15, CD16, CD64, CD22, cCD79a. However, the diagnosis of APL was ruled out by the absence of the PML::RARA gene fusion detected by real-time polymerase chain reaction. The finding of the chromosome karyotype analysis was as follows: 45,X,-Y,t(8;9)(q22;p24)[20] (Figure 2). Subsequently, AML1::ETO (RUNX1-RUNX1T1) positivity was confirmed using the fluorescence in situ hybridization method (Figure 1D). Finally, a diagnosis of acute myeloid leukemia (AML-M2) was made. After undergoing low-dose HA regimen (Homoharringtonine, cytarabine) chemotherapy, the patient developed bone marrow suppression. Relatives of the patient requested discharge from the hospital on their own initiative.

DISCUSSION

The chromosomal translocation t(8;21)(q22;q22) is found in 92% of all cases of AM-M2, and in some cases of AML-M4, and less commonly in M0 and M1 (6%). In a small proportion of acute myeloid leukemias (AMLs), complex variants of the t(8;21)(q22;q22) translocation may involve the AML1 rearrangement or AML1/ETO fusion translocation. Variants showing good response to therapy as in typical t(8;21)(q22;q22) cases but others have reported that variants have a worse prognosis [2]. All documented cases have shown the breakpoint on chromosome 8 at q(22), the site of the ETO gene. Numerous studies have highlighted the significance of the der(8) chromosome, which carries the AML1/ETO fusion gene, in the pathogenesis of AML-M2. Molecular techniques such as FISH or SKY can aid in identifying the specific chromosomes involved in the concealed form of the variant t(8;21)(q22;q22) [5]. In addition, in this case, the morphological variation mimicking APL also put us in a diagnostic dilemma. Recognition of the potential for this morphological variation allows us to minimize misdiagnosis. Regrettably, the case was lost to follow-up. Further studies are needed to investigate the molecular mechanisms underlying these unusual rearrangements, and their clinical significance may be determined through larger studies with longer follow-up periods.

CONCLUSION

This case highlights the significance of employing a range of detection methods for a comprehensive diagnosis, including morphology, immunophenotyping, cytogenetic and molecular examination.

Informed Consent:
Informed consent was obtained from the patient.

Declaration of Interest:
The authors declare no competing interests.

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