Molecular Pitfalls in APL: A Case of Cryptic t(15;17) Translocation Masked by Monosomy 17 and a Marker Chromosome

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Introduction

Acute promyelocytic leukemia (APL) is a subtype of acute myeloid leukemia characterized by abnormal promyelocytes in the bone marrow and the t(15;17) translocation, producing the PML-RARA fusion gene (1).

A minority of cases exhibit variant translocations, in which RARA fuses with alternative genes, or cryptic rearrangements undetectable by standard cytogenetic methods (2).

Over one-third of patients present with other chromosomal abnormalities, which may influence disease progression and treatment response (3).

Aim

To highlight the diagnostic challenges associated with cryptic t(15;17) translocation in APL, and to highlight the significance of integrated cytogenetic and molecular testing for accurate diagnosis and risk assessment.

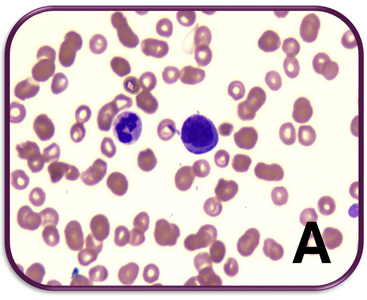
Case Study

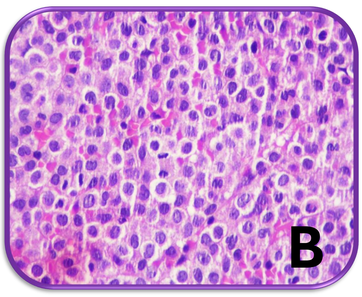
We present the case of a 58-year-old woman with a history of hepatitis C-related chronic liver disease, who presented with pancytopenia. Her bone marrow showed abnormal promyelocytes, with immunohistochemistry positive for myeloperoxidase (MPO) and CD117.

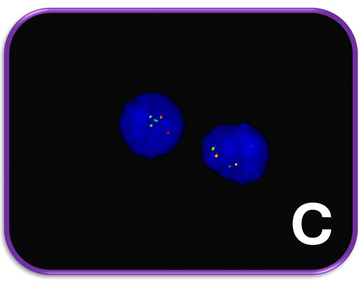
Results

Cytogenetic testing revealed two unusual findings: monosomy 17 (loss of one copy of chromosome 17) and a marker chromosome; however, there was no visible t(15;17). Molecular testing using reverse transcriptase–polymerase chain reaction (RT-PCR) confirmed the presence of the *PML-RARA* fusion, establishing the diagnosis of APL.

Figures







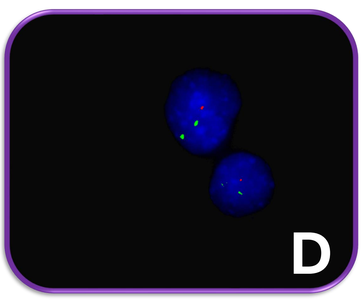


Figure A: Bone marrow aspirate showing abnormal promyelocytes.

Figure B: H & E section of bone trephine biopsy showing diffuse infiltration with abnormal promyelocytes.

Figure C: FISH with PML/RARA probe shows two nuclei with two fusion, one red (PML), and one green (RARA) signal.

Figure D: FISH for TP53 shows deletion of one p53 signal, indicating loss of the TP53 gene.

Discussion

Monosomy 17 in APL is uncommon and may imply tumor protein p53 (TP53) deletion, which has been linked to aggressive illness and a poor prognosis.

Such patients may not respond effectively to standard therapy, requiring intensive clinical surveillance.

RT-PCR is more sensitive than fluorescence *in situ* hybridization (FISH) at detecting complicated PML-RARA rearrangements and monitoring minimal residual disease.

Conclusion

This case emphasizes the value of combining cytogenetic, molecular, and morphological studies for accurate diagnosis and risk assessment in APL, particularly in patients with uncommon or complex chromosomal findings.

References

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