UNMASKED BY COAGULOPATHY: NPM1-MUTATED AML WITH APL-LIKE FEATURES

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INTRODUCTION

A subset of non-APL acute myeloid leukemia (AML) shares the immunophenotype of acute promyelocytic leukemia (APL) — absence of CD34 and HLA-DR — without the defining PML::RARA fusion. This "APL-like" phenotype occurs in ~10–17% of AML and is strongly linked to NPM1 mutation, FLT3-ITD, and cup-like nuclear morphology.

This CD34−/HLA-DR− subgroup carries a significantly higher risk of disseminated intravascular coagulation (DIC) and inferior survival — even among patients otherwise classified as favorable risk — underscoring the need for early recognition and vigilance.

AIM

To describe a case of NPM1-mutated AML with an APL-like (CD34−/HLA-DR−) immunophenotype complicated by fulminant DIC and multifocal arterial cerebral infarction prior to treatment initiation, and to illustrate the rationale for empiric ATRA administration despite a negative PML::RARA result.

CASE DESCRIPTION

- 55-year-old woman presented with persistent cytopenias and 56% circulating blasts.
- Flow cytometry: 57% myeloblasts, CD34−/HLA-DR−, MPO+, CD33+.
- Molecular panel: NPM1 mutation (VAF 42.6%), 2 FLT3-ITD mutations, IDH2 mutation; normal karyotype; PML::RARA negative.
- Before induction: headaches, visual changes, dysarthria. MRI showed multifocal cerebral infarcts; CTA showed high-grade right cerebellar artery stenosis.
- Labs revealed overt DIC: D-dimer >20,000 ng/mL, fibrinogen 116 mg/dL, platelets 50×10^9/L, with active PICC-site bleeding.

CLINICAL COURSE & OUTCOME

Immunophenotype at Diagnosis:

Flow cytometry — 57% myeloblasts

Positive: MPO, CD33, dim CD38/CD117, subset CD64

Negative: CD34, HLA-DR, CD1a, CD2, CD3, CD5, CD7, CD10, CD13, CD14, CD19, CD20, CD22, TdT, CD79a

PML::RARA RT-PCR: negative

Key Findings

- **Diagnosis:** NPM1-mutated AML with a CD34−/HLA-DR− (APL-like) immunophenotype; ELN 2022 intermediate risk given FLT3-ITD co-mutation.
- **Coagulopathic complication:** Fulminant DIC with multifocal arterial cerebral infarction — a rare presenting thrombotic event in AML-associated DIC.
- **Treatment response:** Empiric ATRA + 7+3 + midostaurin achieved complete morphologic remission by day 22, with no further thrombotic or bleeding complications.
- **Post-consolidation:** Residual IDH2/DNMT3A mutations at low VAF, consistent with clonal hematopoiesis; patient proceeding to azacitidine maintenance and allogeneic HSCT evaluation.

Discussion

- The CD34−/HLA-DR− immunophenotype identifies a biologically distinct AML subgroup predisposed to DIC and thrombosis, independent of PML::RARA status.
- Arterial stroke as a presenting thrombotic complication of AML-associated DIC is rare, underscoring the severity of coagulopathy in this subgroup.
- Absence of PML::RARA should not preclude empiric ATRA when clinical deterioration mirrors APL.
- A low threshold for coagulopathy surveillance and ATRA initiation is warranted in CD34−/HLA-DR− NPM1-mutated AML.

ACKNOWLEDGEMENTS

The authors thank the patient for granting permission to share her clinical course, and the UConn Health Division of Hematology-Oncology for their care and support of this case report.

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