Double the Challenge: A Rare Case of Twin Pregnancy in a Woman with Acute Promyelocytic Leukemia

Neusha Zadeh, OMS-IV[1], James Dugan, M.D.[2]
Campbell University Jerry M. Wallace School of Osteopathic Medicine, Lillington, NC 27546
[1]Medical Student, Campbell University [2]Medical Doctor, Novant Health Cancer Institute - Forsyth

Abstract

We describe a 31-year-old woman at 17 weeks gestation with a twin pregnancy presented with chest discomfort, palpitations, and dizziness. Bone marrow biopsy confirmed acute promyelocytic leukemia (APL) with t(15;17). She started on all-trans retinoic acid (ATRA) and daunorubicin with dexamethasone prophylaxis for differentiation syndrome (DS).

ATRA was held for 4 days after severe DS symptoms and restarted following stabilization. Hemoglobin and platelets were maintained above 8 g/dL and 50,000/mm³, and she received supportive care including antiemetics, antimicrobial prophylaxis, and psychiatric support. Delivery occurred at 29 weeks due to preeclampsia, after which she transitioned to ATRA and arsenic trioxide (ATO).

This case underscores the feasibility of treating APL during a twin pregnancy with ATRA and anthracycline chemotherapy in the second trimester, highlights the diagnostic challenge of DS in pregnancy, and emphasizes early recognition and multidisciplinary management to optimize maternal and fetal outcomes.

Introduction

APL is a subtype of acute myeloid leukemia characterized by the PML-RARA fusion protein [t(15;17)] and represents a hematologic emergency.[1]

- Standard first-line therapy includes ATRA and ATO.[2]
- Initiation of treatment increases the risk of DS, a potentially life-threatening complication marked by fever, hypotension, and respiratory failure.[3,4,5]
- In pregnancy, APL treatment requires careful balancing of maternal survival and fetal safety, as both ATRA and ATO are known teratogens.[1,2,6]

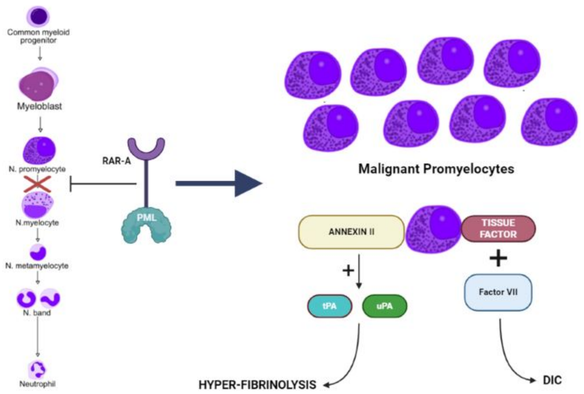
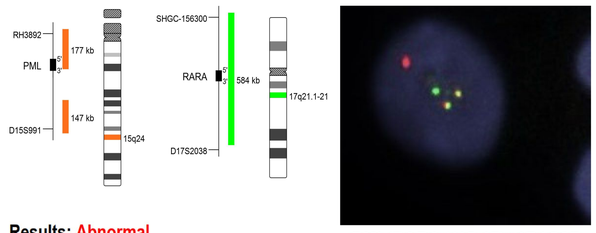


Figure 1. Pathophysiology of APL PML-RARA–mediated maturation arrest at the promyelocyte stage, driving coagulopathy through hyperfibrinolysis and tissue factor activation.[6]

History of Present Illness

A 31-year-old woman at 17 weeks gestation with a twin pregnancy presented with chest discomfort, palpitations, and dizziness. Past medical history included schizoaffective disorder, anxiety, and bipolar disorder. Laboratory evaluation revealed pancytopenia and bone marrow biopsy demonstrated 57% pro myeloblasts with t(15;17) translocation, confirming APL.



Interpretation:

	INTERPRETATION	SIGNAL PATTERN	ABNORMALITY IDENTIFIED	%
PML/RARA t(15;17)	Detected	1R1G2F	t(15;17)	63.0%

Figure 2. Notable Admission Lab Results PML-RARA FISH Results Fluorescence in situ hybridization (FISH) detected the PML-RARA t(15;17) translocation in 63% of analyzed cells, consistent with APL.

Induction therapy with ATRA and daunorubicin was initiated with intravenous dexamethasone for DS prophylaxis. Four days into therapy, ATRA was held due to severe DS symptoms and restarted following stabilization. Hemoglobin and platelets were maintained above 8 g/dL and 50,000/mm³, respectively.

	Differentiation Syndrome (DS)	Severe Preeclampsia	Infection / Sepsis
Onset	Days–weeks after starting ATRA/ATO	After 20 wks gestation	Any time
Blood Pressure	May be elevated (capillary leak)	Elevated (≥140/90 mmHg)	Variable, often low in septic shock
Respiratory	Dyspnea, hypoxia, pulmonary infiltrates	Pulmonary edema possible	Dyspnea if pneumonia/sepsis
Fever	Common	Rare	Common
Neuro	Headache, confusion (less common)	Headache, visual changes, seizures	Confusion/AMS possible
Labs	Leukocytosis, ↑ creatinine, abnormal LFTs possible	Proteinuria, ↑ LFTs, thrombocytopenia	Leukocytosis or leukopenia, positive cultures
Key Clues	**Temporal link to APL therapy, responds to steroids**	**HTN + proteinuria, no chemo link**	**Positive cultures, improves with antimicrobials**

Table 1. DS vs. Pregnancy Complications Comparison of differentiation syndrome, severe preeclampsia, and infection/sepsis, highlighting overlapping features and distinguishing clues in pregnant patients with APL.[3,4,5]

Supportive care included antiemetics, antimicrobial prophylaxis, and psychiatric support. At 29 weeks, preeclampsia prompted preterm delivery, after which she transitioned to an ATRA and ATO regimen.

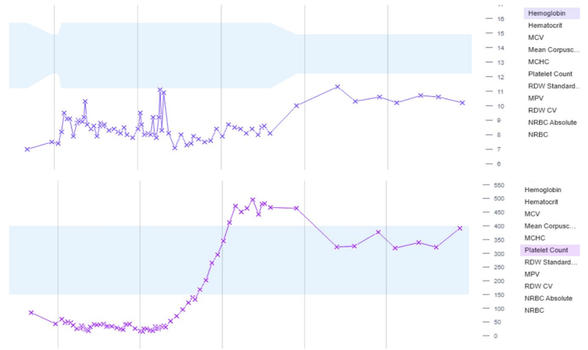


Figure 3. Hemoglobin and Platelet Trends During APL Treatment and Pregnancy Hemoglobin and platelet count trends in a pregnant patient with APL, highlighting treatment-related declines, transfusion support, and recovery patterns over time.

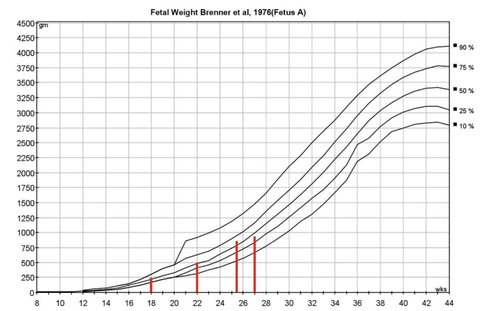


Figure 4. Fetal Growth Curve for Twin A Estimated fetal weight measurements plotted against gestational age, showing growth trajectory between the 10th and 50th percentiles.

Plan

- Continue ATRA and anthracycline induction during second trimester with vigilant monitoring for DS.
  - Dexamethasone prophylaxis initiated; ATRA temporarily held and restarted after DS resolution.
- Maintain hemoglobin > 8 g/dL and platelet count >50,000/mm³ with transfusion support as needed.
  - Provide comprehensive supportive care
- Psychiatric support throughout hospitalization.
- Monitor for and manage pregnancy-related complications (e.g., preeclampsia, preterm labor).
- Post-delivery transition to consolidation therapy with ATRA and ATO.
- Multidisciplinary coordination between hematology/oncology, maternal-fetal medicine, and neonatology for maternal and fetal outcomes.

Discussion

Acute promyelocytic leukemia (APL) is a distinct subtype of acute myeloid leukemia characterized by the t(15;17) translocation and the PML-RARA fusion gene.[1,2,3] Prompt recognition is critical, as untreated carries a high risk of early mortality from disseminated intravascular coagulation and other coagulopathies.[4,5,6] The availability of targeted therapy with all-trans retinoic acid (ATRA) and arsenic trioxide (ATO) has transformed APL into one of the most curable leukemias, but management in pregnancy requires careful balancing of maternal benefit with fetal safety.[1,2]

Differentiation syndrome (DS) is one of the most feared complications of ATRA therapy, occurring in up to 25% of patients and characterized by fever, dyspnea, pulmonary infiltrates, and hypotension. In pregnancy, the overlap of DS symptoms with other obstetric complications, such as preeclampsia or infection, which can delay recognition and treatment.[5] In this case, DS presented with respiratory compromise and cerebral venous sinus thrombosis, prompting temporary cessation of ATRA. Reintroduction after stabilization allowed for completion of induction therapy.[4]

In pregnant patients with unexplained cytopenias, especially in the second or third trimester, APL should remain on the differential.[1,2] Awareness of its presentation and potential complications may improve timely diagnosis and survival for both mother and child.

Key Takeaways:

- Early diagnosis and treatment initiation are paramount in APL in pregnancy to reduce the risk of early hemorrhagic death.
- Complication recognition, particularly DS, requires vigilance, as symptom overlap with pregnancy-related disorders is common.
- Multidisciplinary management optimizes maternal and fetal outcomes, balancing the urgency of leukemia treatment with gestational considerations.

Citations

1. Santolaria, A., Perales, A., Montesinos, P., & Sanz, M. A. (2020). Acute Promyelocytic Leukemia during Pregnancy: A Systematic Review of the Literature. Cancers, 12(4), 968.
2. Ni, W., Deng, K., Chen, Y., et al., (2023). Pregnant woman with acute promyelocytic leukemia delivers healthy twins and is cured successfully: A case report. Experimental and therapeutic medicine, 25(5), 206.
3. Giannakaki, A. G., Giannakaki, M. N., Oikonomou, E., et al., (2024). Leukemia in pregnancy: Diagnosis and therapeutic approach (Review). Molecular and clinical oncology, 21(5), 79.
4. Droc, G., Stancioaica, M. C., Soare, et al., (2023). Acute Promyelocytic Leukemia and Severe Differentiation Syndrome in Pregnancy-A Management Challenge. Life (Basel, Switzerland), 13(5), 1141.
5. Rego, E. M., & De Santis, G. C. (2011). Differentiation syndrome in promyelocytic leukemia: clinical presentation, pathogenesis and treatment. Mediterranean journal of hematology and infectious diseases, 3(1), e2011048.
6. Woods, A. C., & Norsworthy, K. J. (2023). Differentiation Syndrome in Acute Leukemia: APL and Beyond. Cancers, 15(19), 4767.