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Case Report

Extensive Splenic Infarction in a Pediatric Patient with Acute Promyelocytic Leukemia: A Case Report Highlighting Dual Hemostatic Dysregulation

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Abstract

Background: Acute promyelocytic leukemia (APL) is characterized by a life-threatening coagulopathy, traditionally associated with hemorrhagic complications. However, thrombotic events, including arterial infarction, are increasingly recognized as significant contributors to morbidity during induction therapy.

Case Presentation: We report a 16-year-old male diagnosed with APL who developed extensive splenic infarction two weeks after initiation of all-trans retinoic acid (ATRA). He presented with persistent fever and left upper quadrant pain. Abdominal imaging revealed a large subcapsular splenic infarct without evidence of macrovascular thrombosis. Despite improving blood counts and resolution of initial cytopenias, systemic inflammation and coagulopathy persisted. ATRA was temporarily discontinued due to suspicion of differentiation syndrome, which may have delayed disease control. With resumption of ATRA and addition of arsenic trioxide (ATO), along with supportive care, the patient achieved complete hematologic remission with undetectable minimal residual disease (MRD) at day 50.

Conclusion: Thrombotic complications such as splenic infarction can occur in APL even during early treatment, emphasizing the dynamic and dual nature of hemostatic dysregulation. Clinicians should maintain a high index of suspicion for non-infectious causes of fever and abdominal pain in APL patients. Early recognition and uninterrupted targeted therapy are critical to resolving the underlying prothrombotic state and improving outcomes.

Keywords:
Acute promyelocytic leukemia
Coagulopathy
Thrombosis
Splenic infarction
Disseminated intravascular coagulation
All-trans retinoic acid

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1. INTRODUCTION

Acute promyelocytic leukemia (APL), a distinct subtype of acute myeloid leukemia (AML) classified as AML-M3 in the French-American-British (FAB) classification, is a molecularly defined disease driven by the t(15;17)(q24;q21) translocation, resulting in the PML::RARA fusion oncogene (1) .This genetic aberration disrupts retinoic acid receptor alpha (RARA) signalling, leading to a block in myeloid differentiation and uncontrolled accumulation of abnormal promyelocytes in the bone marrow and peripheral blood (2).

APL is characterized by a life-threatening coagulopathy, typically manifesting as disseminated intravascular coagulation (DIC) and hyperfibrinolysis, which predisposes patients to severe hemorrhagic complications—most notably intracranial hemorrhage—the leading cause of early death. Paradoxically, thrombotic events, though less common, are increasingly recognized as significant contributors to morbidity and mortality. The hemostatic imbalance in APL arises from multiple mechanisms: (1) tissue factor–mediated activation of coagulation; (2) overexpression of annexin A2 on the leukemic cell surface, promoting plasmin generation and fibrinolysis; and (3) direct proteolytic degradation of coagulation factors, including fibrinogen and von Willebrand factor (3).

Prior to the advent of targeted therapies, APL was associated with high early mortality and poor prognosis. However, the introduction of all-trans retinoic acid (ATRA) and arsenic trioxide (ATO) has revolutionized its management, transforming APL into the most curable subtype of AML (4).

Despite these advances, early death due to hemorrhage during the initial days of therapy remains the principal barrier to cure. Therefore, prompt clinical suspicion and immediate initiation of ATRA upon diagnosis—without waiting for confirmatory molecular or cytogenetic testing—are critical to improving outcomes (5). Aggressive supportive care, including timely replacement of platelets, cryoprecipitate (or fibrinogen concentrate), and fresh frozen plasma to correct coagulopathy, is essential during the induction phase. Historically, heparin and antifibrinolytic agents were used, but current evidence does not support their routine use, and they are generally not recommended (6).

Thrombotic complications, including venous thromboembolism and arterial events such as splenic infarction, although uncommon, have been increasingly reported, underscoring the dynamic and complex nature of the coagulopathy in APL (7).

Herein, we report a case of APL presenting with abdominal pain and radiologically confirmed splenic infarction, highlighting the dual risk of hemorrhage and thrombosis in this disease.

2. CASE PRESENTATION

A previously healthy 16-year-old male with no significant medical history presented with one week of persistent fever, chills, diffuse extremity pain, and a 4-kilogram weight loss over three weeks. He reported spontaneous gingival bleeding during tooth brushing one week prior to admission. On examination, vital signs were stable. Cardiopulmonary auscultation was normal. The spleen tip was palpable below the left costal margin, consistent with mild splenomegaly; no hepatomegaly was noted.

Initial laboratory findings revealed: WBC 2,000/μL (lymphocytes 51%, PMNs 43%), Hb 7.5 g/dL, MCV 63 fL, platelets 76,000/μL, LDH 578 U/L, uric acid 5.4 mg/dL, and markedly elevated CRP. Intravenous ceftriaxone was initiated for suspected infection, but fevers persisted. Transthoracic echocardiography was normal. Abdominal ultrasound showed splenomegaly (craniocaudal diameter: 140 mm) with normal liver echotexture. Given ongoing fever, cytopenias, and splenomegaly, peripheral smear and bone marrow aspiration (BMA) were performed. Peripheral smear revealed >90% abnormal promyelocytes with bilobed nuclei and granulocytic precursors, along with severe thrombocytopenia (<20,000/μL). BMA confirmed acute promyelocytic leukemia, hypogranular variant. Molecular testing detected the PML::RARA fusion transcript. ATRA was immediately started, and the patient was discharged for outpatient follow-up.

Two weeks later, he returned with worsening left upper quadrant pain and persistent fever. On readmission: WBC 16.4 × 10^9/L (PMN 83%), Hb 8.1 g/dL, platelets 35,000/μL, CRP 193 mg/L. ATRA was discontinued due to concern for differentiation syndrome, and broad-spectrum antibiotics (ceftriaxone) were continued. After six days without improvement, he was referred to our tertiary center.

At admission: WBC 2.1 × 10^9/L (neutrophils 50%, lymphocytes 48%), Hb 9.7 g/dL, platelets 129,000/μL, CRP 175 mg/L, LDH 895 U/L, ESR 108 mm/hr, INR 1.45, PTT 36.8 s. D-dimer was elevated (1.3 μg/mL), and fibrin degradation products (FDPs) were positive. Blood cultures, viral panel (EBV, CMV, HIV, HBV/HCV), and autoimmune screening were negative. Empiric antimicrobial therapy was escalated to vancomycin and meropenem. ATRA was restarted and ATO was added. Chest X-ray was unremarkable. Abdominal ultrasound

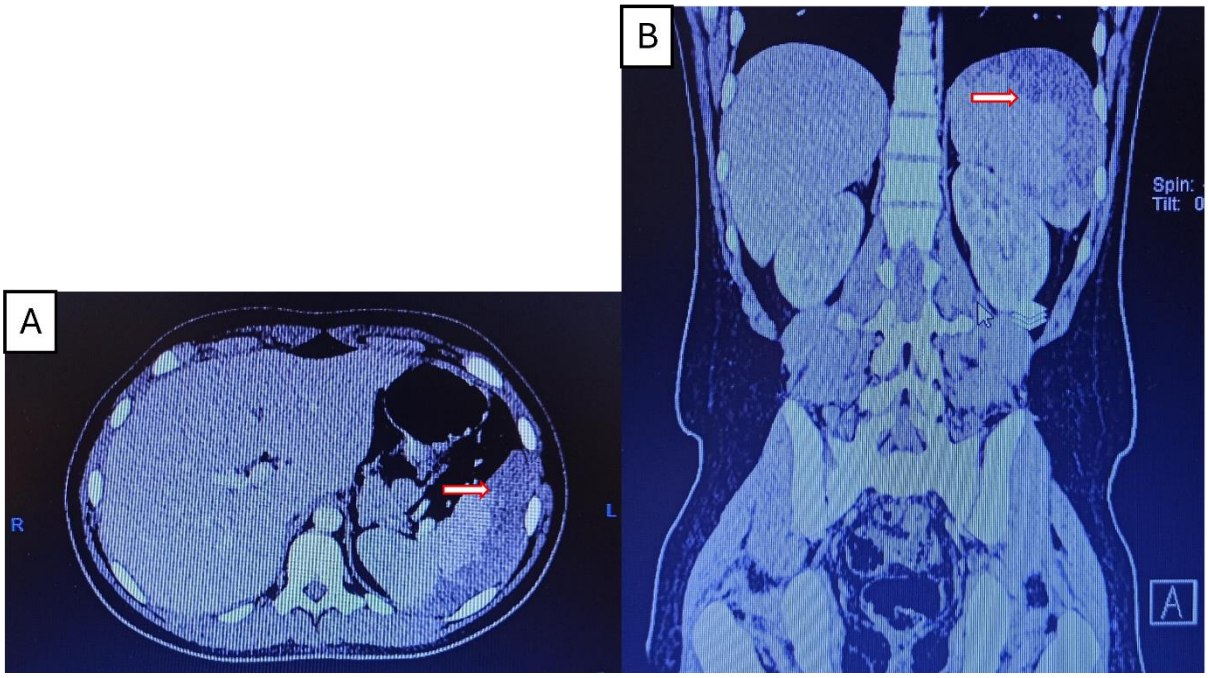

Figure 1. Contrast-enhanced CT images demonstrating extensive peripheral splenic infarction.
(A) Axial view shows a large non-enhancing area (arrow) in the upper pole of the spleen, consistent with infarction.
(B) Coronal view confirms the subcapsular and peripheral distribution of the infarct. No evidence of splenic vein or artery thrombosis was observed on vascular imaging.

showed splenomegaly (145 mm) with a 124 × 21 mm peripheral hypoechoic lesion suggestive of infarction. No splenic vein thrombosis was seen on Doppler. Contrast-enhanced CT of the abdomen confirmed splenomegaly (143 mm) with extensive non-enhancing peripheral subcapsular areas consistent with splenic infarction (**Figure 1**). Splanchnic Doppler studies showed patent splenic and portal veins with normal flow. No abscess or infectious focus was identified.

Due to clinical deterioration and persistent fever, dexamethasone was initiated for possible differentiation syndrome, and fluconazole was started for antifungal prophylaxis. Over the following days, symptoms improved and fever resolved.

Eleven days after resuming ATRA/ATO, follow-up ultrasound showed reduced spleen size (137 mm) and a stable hypoechoic lesion (84 × 24 × 23 mm, ~26–27 mL) with no Doppler flow—consistent with organizing infarct. Repeat labs showed marked improvement: WBC 4.3 × 10^9/L, platelets 261,000/μL, CRP 8.7 mg/L, LDH 359 U/L, ESR 14 mm/hr.

The patient was discharged in stable condition on ATRA and ATO. One week later, imaging confirmed stable infarct and normal vasculature. At day 50, bone marrow evaluation showed complete hematologic remission with undetectable PML::RARA by quantitative RT-PCR.

3. DISCUSSION

Acute Promyelocytic Leukemia (APL), classified as the M3 subtype in the French-American-British (FAB) system, is a distinct form of acute myeloid leukemia (AML) (8). A hallmark clinical feature of APL is its associated coagulopathy, which historically led to frequent severe hemorrhagic complications (9). Notably, APL exhibits exceptional sensitivity to differentiation therapy with agents such as all-trans retinoic acid (ATRA). This paradigm-shifting treatment approach has transformed APL from one of the most lethal AML subtypes into its most curable form (10).

This case illustrates the dual hemostatic dysregulation in APL, where life-threatening hemorrhage coexists with a prothrombotic state that can lead to arterial infarction—even

during early targeted therapy. Our patient developed extensive splenic infarction despite partial hematologic recovery, highlighting that normalization of blood counts does not immediately resolve the underlying coagulopathy.

Thrombotic events in APL are underrecognized but increasingly reported. Mechanisms include tissue factor (TF) overexpression on leukemic promyelocytes, promoting thrombin generation and microthrombosis, and annexin A2-mediated plasmin activation, driving hyperfibrinolysis and bleeding (11). This paradoxical state may persist during ATRA-induced differentiation, especially in the context of systemic inflammation and endothelial activation (12).

The development of splenic infarction in our patient raises several important points:

1. Fever in APL is not always infectious: Persistent fever during induction should prompt evaluation for non-infectious etiologies, including leukostasis, differentiation syndrome, or sterile infarction.
2. Imaging is crucial: Abdominal pain with splenomegaly warrants ultrasound or CT, particularly when infection is unlikely.
3. Avoid premature discontinuation of ATRA: Stopping ATRA based on fever alone—without respiratory compromise or clear signs of differentiation syndrome—may delay disease control and prolong coagulopathy (13).
4. Balanced management of coagulopathy: While anticoagulation was avoided due to recent thrombocytopenia and bleeding risk, close monitoring is essential. In stable patients with confirmed thrombosis and recovering platelets, low-molecular-weight heparin may be considered cautiously (14).

Our patient's gradual improvement following resumption of ATRA and addition of ATO underscores that controlling the underlying leukemia remains the cornerstone of managing APL-associated coagulopathy.

4. CONCLUSION

Thrombotic complications such as splenic infarction, though rare, should be considered in APL patients presenting with abdominal pain, splenomegaly, and persistent inflammation. This case highlights the complexity of hemostatic dysregulation in APL and reinforces the need for vigilant monitoring, early imaging, and uninterrupted targeted therapy to mitigate early morbidity and mortality.

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Conflict of interest

The authors declare that they have no competing interests.

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Ethical statement

The study was conducted in accordance with the Declaration of Helsinki. Written informed consent was obtained from the patient and his legal guardian.

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