CASE REPORT

CYPRUS
JOURNAL OF MEDICAL SCIENCES

DOI: 10.4274/cjms.2025.2024-164
Cyprus J Med Sci 2025;10(5):343-346

A Unique Case of Acute Promyelocytic Leukemia with Disseminated Intravascular Coagulation and Spontaneous Tumor Lysis Syndrome

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Abstract

Acute promyelocytic leukemia (APL) is a rare and specific subtype of acute myeloid leukemia involving characteristic genetic translocations and the accumulation of abnormal promyelocytes. Severe coagulopathy is common and can result in disseminated intravascular coagulation (DIC), a major early cause of death. Furthermore, tumor lysis syndrome is a life-threatening complication of hematologic malignancies that typically develops after treatment initiation. Spontaneous tumor lysis syndrome (STLS) occurring prior to the initiation of treatment is an exceedingly rare event in cases of APL. We present a rare case of a 25-year-old male who developed STLS along with DIC before any treatment. Metabolic imbalances consistent with STLS, including hyperkalemia and hyperuricemia, were identified as laboratory findings, along with evidence of DIC. The patient was treated with all-trans retinoic acid and arsenic trioxide along with supportive measures against metabolic imbalances and coagulopathy. However, the patient's condition quickly deteriorated despite prompt therapeutic intervention, and the patient died of multiorgan failure within one week of admission. The outcome of this case emphasizes the importance of early recognition and aggressive management of complications, such as (example 1) and (example 2), in APL, with a high mortality risk when both complications are present. More research is needed to better understand the pathophysiology and treatment strategy for STL Sin APL.

Keywords: Disseminated intravascular coagulation, spontaneous tumor lysis syndrome, acute promyelocytic leukemia, coagulopathy, multiorgan failure

INTRODUCTION

Acute promyelocytic leukemia (APL), or M3 in the French-American-British system, is a special subtype of acute myeloid leukemia characterized by the t(15;17) translocation, creating the *PML-RARA* fusion gene.[1] Coagulopathy is a common finding in APL patients and most frequently takes the form of disseminated intravascular coagulation (DIC), which is present in more than 80% of newly diagnosed patients and is a major cause of early death before treatment.[2]

The pathophysiology of DIC in APL involves the release of procoagulant factors, such as tissue factors and cancer procoagulants, from leukemic promyelocytes. This initiates the coagulation cascade, leading to excessive fibrin formation, the consumption of clotting factors, and a clinical phenotype characterized by both thrombosis and hemorrhage.[3] Rapid diagnosis and initiation of all-trans retinoic acid (ATRA) therapy are important. ATRA not only induces remission but also controls coagulopathy.[4]

Another life-threatening complication of chemotherapy is spontaneous tumor lysis syndrome (STLS), which usually develops in patients with hematologic malignancies. Massive tumor cell breakdown is characterized by the release of intracellular components, including

To cite this article: Alamin AA, Bashir FA, Mohamed IA. Unique case of acute promyelocytic leukemia with disseminated intravascular coagulation and spontaneous tumor lysis syndrome. Cyprus J Med Sci. 2025;10(5):343-346

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Received: 09.01.2025
Accepted: 19.02.2025
Epub: 29.09.2025
Publication Date: 09.10.2025

potassium, phosphate, and uric acid.[5] This causes metabolic imbalances such as hyperkalemia, hyperphosphatemia, hyperuricemia, and even potential renal failure. STLS is a rare entity in which tumor lysis occurs without therapeutic intervention, indicating a high tumor burden. APL patients are extremely rare among those with STLS, which is a real diagnostic and therapeutic challenge.[6] Cases of DIC and STLS coexisting in APL patients are rare, and both conditions demand timely but contrasting therapeutic procedures. Treatment for DIC consists of supportive measures, such as platelet transfusions and cryoprecipitation, plus ATRA, to induce promyelocyte maturation. In contrast, STLS management is characterized by aggressive hydration, urate-lowering therapies, and close monitoring of electrolyte imbalances.[7] In this report, we present a rare case of a newly diagnosed APL patient who developed DIC and STLS, at the same time, which complicates the management of these life-threatening conditions. We present the case of a patient who most likely has APL complicated by both DIC and STLS. Early diagnosis and multidisciplinary treatment are highly important to avoid fatal outcomes, particularly in the setting of more aggressive leukemic phenotypes.

CASE REPORT

An otherwise healthy 25-year-old male presented with fatigue, weakness, and easy bruising for one week. He was pale, with petechial and ecchymotic rashes on physical examination. Pancytopenia was detected via laboratory findings, including a white blood cell count of 1,500/µL (80% promyelocytes), a hemoglobin level of 7 g/dL, and a 20,000/µL platelet count. Coagulation studies revealed coagulopathy, demonstrated by an elevated prothrombin time (18 s), activated partial thromboplastin time (60 s), and D-dimer level (2.0 µg/mL). Electrolyte abnormalities consistent with STLS were also noted: hyperkalemia (6.5 mmol/L), hyperphosphatemia (6.0 mg/dL), and hyperuricemia (10.0 mg/dL) (Table 1).

A peripheral blood smear and bone marrow aspirate confirmed the diagnosis of APL with numerous abnormal promyelocytes containing Auer rods (Figure 1).

The diagnosis of APL was confirmed through flow cytometry and chromosomal analysis (Figure 2). Standard induction therapy for APL for this patient included ATRA (45 mg/m²/day orally) and arsenic trioxide (ATO) (0.15 mg/kg/day intravenously). Supportive care consists of red blood cell transfusions, platelet transfusions, intravenous fluids, and medications to resolve electrolyte imbalances. Hyperuricemia was treated, and renal complications were prevented with rasburicase. Interventions were performed while the patient was in critical condition due to coagulopathy from DIC and STLS complications. The patient was admitted to the hospital and received the outlined therapy. Despite the interventions, one week after admission, the patient developed acute kidney injury (AKI) and multiorgan dysfunction, leading to death. Written informed consent was obtained from the patient for the publication of clinical details and images. Identifying information has been anonymized where possible, and any potentially identifying images or details are included with explicit consent.

DISCUSSION

In untreated patients, DIC often complicates APL and is the most common cause of early mortality. In APL, DIC arises from leukemic promyelocytes releasing procoagulants such as tissue factor, triggering excessive fibrin formation, clotting factor consumption, and a dual phenotype of thrombosis and hemorrhage.[3] Although DIC is a well-known APL complication, STLS is very uncommon. However, STLSs are frequently observed in rapidly proliferating malignancies e.g., burkitt lymphoma, but are uncommon in untreated APLs.[6] In this case, the patient presented with metabolic derangements characteristic of TLS, such as hyperkalemia, hyperphosphatemia, and hyperuricemia, at the time of diagnosis. The rapid breakdown of tumor cells in patients with STLS causes metabolic disturbances and AKI.[5]

This case provides a rare instance of STLS in APL, emphasizing several unique insights. While STLS is typically associated with malignancies such as burkitt lymphoma[8], its occurrence in APL is uncommon because of slower tumor turnover. These findings suggest that certain aggressive APL phenotypes may predispose patients to STLS, emphasizing the importance of identifying high-risk subtypes. The metabolic derangements, such as hyperkalemia, hyperphosphatemia, and hyperuricemia observed before treatment initiation, could serve as early warning signs of STLS in APL patients. This case demonstrates the difficulty of managing both conditions simultaneously. The challenge of balancing aggressive hydration and electrolyte management for patients with STLS, with control of coagulopathy in DIC, requires careful attention. The simultaneous presence of DIC and STLS poses clinical complications that create a need to intervene, with urgent treatment directed at each condition. Managing overlapping DIC and STLS poses unique challenges because of their opposing pathophysiology and treatment goals. DIC requires anticoagulation and clotting factor replacement to address bleeding and thrombosis, whereas STLS requires aggressive hydration, rasburicase, and electrolyte correction to prevent renal failure and arrhythmias. The therapeutic balance is delicate, as interventions for one condition may worsen the other-e.g., fluid resuscitation for STLS can exacerbate bleeding in thrombocytopenic DIC patients. Overlapping laboratory abnormalities (e.g., hypocalcemia, elevated lactate dehydrogenase) further complicate monitoring, necessitating frequent reassessment of coagulation profiles, electrolytes, and renal function. The absence of consensus guidelines for this overlap underscores the need for individualized, multidisciplinary management to mitigate risks and optimize outcomes.[9,10] Other important supportive care methods include transfusions of platelets and clotting factors. Prompt initiation of ATRA and ATO, as per current guidelines, significantly reduces early mortality.[11] However, aggressive

Table 1. Laboratory parameters of the patient

Parameter	Patient value	Reference range[7]
White blood cell count	15,000/µL	4,500-11,000/µL
Promyelocytes	80%	0%
Hemoglobin	7 g/dL	13.5-17.5 g/dL (males)
Platelet count	20,000/µL	150,000-450,000/µL
Prothrombin time	18 seconds	11-13 seconds
Activated partial thromboplastin time	60 seconds	25-40 seconds
D-dimer	2.0 µg/mL	<0.5 µg/mL
Electrolyte abnormalities:		
Potassium	6.5 mmol/L	3.5-5.0 mmol/L
Phosphorus	6.0 mg/dL	2.3-4.7 mg/dL
Uric acid	10.0 mg/dL	4.0-8.5 mg/dL (males)

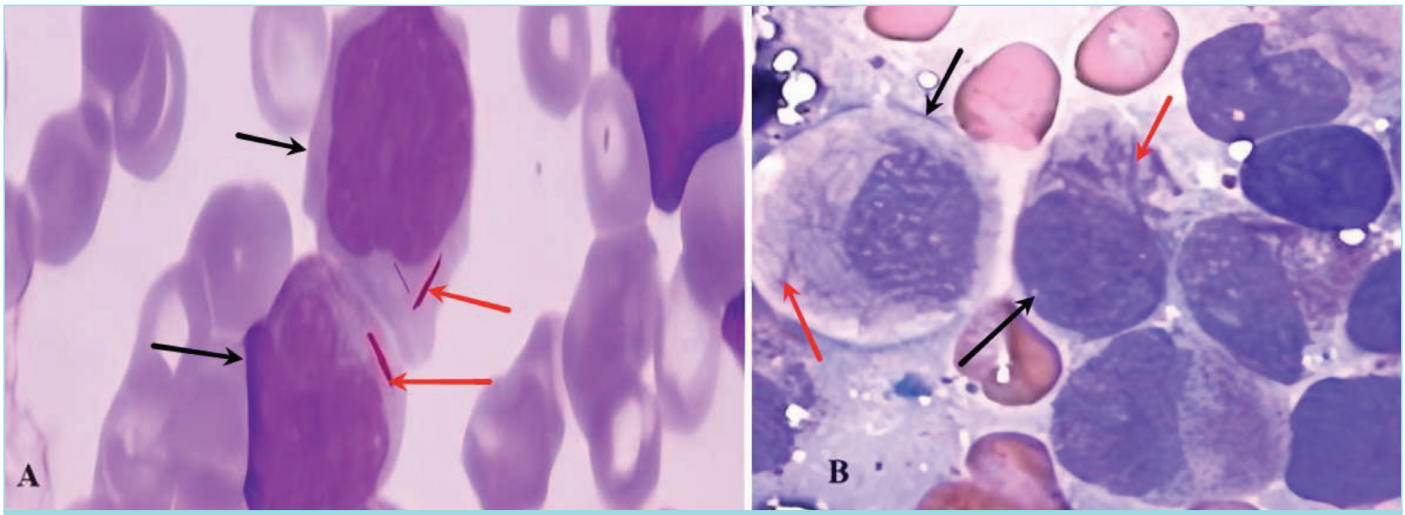

Figure 1. Peripheral blood smear and bone marrow aspiration.

Peripheral blood smear and bone marrow aspiration: (A) blood film showing blasts with auer rods (red arrow). (B) bone marrow aspirate showing a high number of abnormal promyelocytes (black arrow) with auer rods (black arrow) (original magnification 1000x).

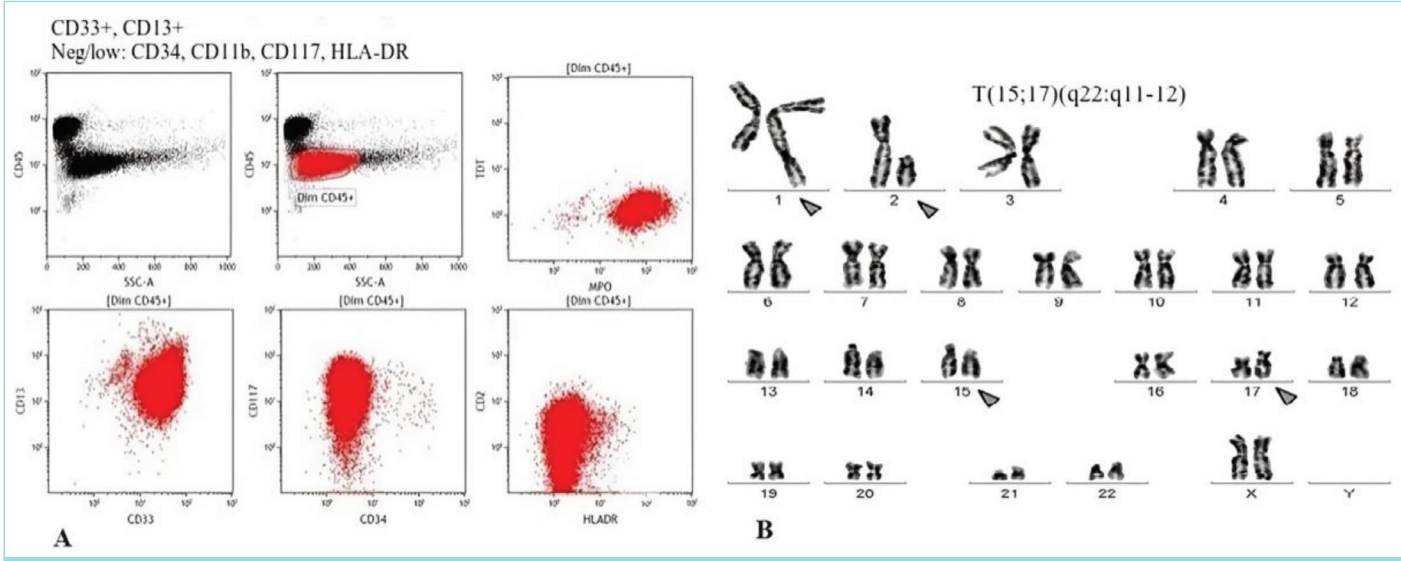

Figure 2. Flow cytometry analysis and chromosomal study.

Flow cytometry analysis and chromosomal study: (A) flow cytometry analysis demonstrating the immunophenotypic profile of abnormal promyelocytes, which is consistent with APL. (B) the chromosomal study revealed the characteristic translocation t (15;17) (q24;q21) associated with APL. APL: Acute promyelocytic leukemia.

hydration, electrolyte correction, and urate lowering measures, which are required for the management of TLS, using urinary drugs such as rasburicase, have the potential to precipitate and worsen AKI.[6] However, the patient's condition did not improve but rather worsened, leading to the development of multiorgan failure and illustrating how severe the condition of overlapping DIC and STLS was. This case highlights the need for early recognition of DIC and STLS in APL patients followed by aggressive management. The initiation of ATRA and ATO should be carried out rapidly to avoid DIC, and metabolic derangements related to STLS must be corrected promptly. When both complications are present, the mortality risk remains high and represents an indication for vigilant monitoring and rapid therapeutic adjustments. Cases of STLS in APL patients are extremely rare, with few reported in the literature.[7,12] In this case, additional knowledge about STLS in APL patients is provided, and further research is needed to improve the management strategy of patients with both complications. We report here an uncommon case of concomitant life-threatening events of DIC and STLS in an APL patient with newly diagnosed APL. Although the existence of DIC as a complication in APLs is well known, spontaneous TLS prior to starting therapy is incredibly rare. These severe complications can be recognized and treated early with ATRA, ATO, and supportive care. Consequently, the risk decreases. Proper management of these conditions is possible, but the high mortality naturally associated with the overlap underscores the need for operator

surveillance and prompt initiation of treatment. Further studies are needed to clarify the pathophysiology of STLS in patients with APL and to change the treatment strategy for this high-risk patient group.

CONCLUSION

This case highlights the fatal cytotoxicity of the simultaneous flows of DIC and STLS in untreated APL. Even when diagnosed and treated with ATRA, ATO and intense supportive care, the patient still inevitably progressed to multiorgan failure. The occurrence of refractory coagulopathy in connection with hyperkalemia, hyperuricemia, and hyperphosphatemia at the same time points to the need of increased clinical awareness, early biochemical screening, and interdisciplinary management at the point of presentation. Seeing that such presence of contradictory complications is much more of a therapeutic gauntlet, it is necessary to conduct more studies regarding the mechanism of this setup and how evidence-based tailored treatment guidelines could be created to deal with this issue.

MAIN POINTS

- Acute promyelocytic leukemia (APL) commonly presents with disseminated intravascular coagulation (DIC), which significantly contributes to early mortality, and the rare occurrence of spontaneous tumor lysis syndrome (STLS) in untreated APL patients is a diagnostic challenge.
- A 25-year-old male with newly diagnosed APL developed both DIC and STLS before treatment and presented with metabolic abnormalities, including hyperkalemia, hyperphosphatemia, and hyperuricemia, along with coagulopathy.
- Despite the administration of all-trans retinoic acid and arsenic trioxide, combined with supportive care for electrolyte imbalances and coagulopathy, the patient's condition rapidly deteriorated, leading to multiorgan failure and death within one week.
- The coexistence of DIC and STLS in APL patients necessitates urgent and contrasting treatment strategies for both conditions, emphasizing the importance of early recognition and aggressive management.
- This case underscores the need for further research into the pathophysiology and management of STLS in APL patients to improve treatment outcomes and survival in high-risk patients.

ETHICS

Informed Consent: Written informed consent was obtained from the patient for the publication of clinical details and images.

Footnotes

Authorship Contributions

Surgical and Medical Practices: A.A.A., Concept: A.A.A., A.F.B., I.A.M., Design: A.A.A., A.F.B., Data Collection and/or Processing: A.A.A., I.A.M., Analysis and/or Interpretation: A.A.A., A.F.B., Literature Search: A.A.A., I.A.M., Writing: AA.A.A., A.F.B., I.A.M.

DISCLOSURES

Conflict of Interest: No conflict of interest was declared by the authors.

Financial Disclosure: The authors declared that this study had received no financial support.

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