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A CLINICAL CASE OF ACUTE PROMYELOCYTIC LEUKAEMIA IN A PATIENT WITH RENAL PATHOLOGY

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Abstract. Acute promyelocytic leukaemia (APL) is a distinct subtype of acute myeloid leukaemia characterized by a specific genetic translocation and a high risk of coagulopathy. The coexistence of APL with renal pathology complicates both diagnosis and treatment, requiring a tailored multidisciplinary approach. We report a case of a 47-year-old male with APL complicated by acute kidney injury, presenting with bleeding, pancytopenia, and disseminated intravascular coagulation. Diagnosis was confirmed by bone marrow examination and molecular testing for the PML-RARA fusion gene. Treatment included all-trans retinoic acid and reduced-dose arsenic trioxide, adjusted for renal impairment, along with supportive care addressing coagulopathy, tumour lysis syndrome prophylaxis, and infection management. The patient achieved complete hematologic and molecular remission with restoration of renal function. This case underscores the importance of individualized therapy and vigilant monitoring in managing APL patients with renal complications, demonstrating that successful outcomes are achievable despite significant comorbidities.
Key words: Acute promyelocytic leukaemia; Renal pathology; Acute kidney injury; All-trans retinoic acid; Arsenic trioxide; Disseminated intravascular coagulation; Molecular remission; Multidisciplinary management

Introduction

Acute promyelocytic leukaemia (APL) is a distinct and highly aggressive subtype of acute myeloid leukaemia (AML), characterised by the accumulation of abnormal promyelocytes in the bone marrow and peripheral blood. APL is defined cytogenetically by the t(15;17)(q24;q21) translocation, which results in the PML-RARA fusion gene. This molecular hallmark not only underpins the disease's pathogenesis but also provides a unique opportunity for targeted therapy, which has significantly improved survival rates in recent decades. The introduction of all-trans retinoic acid (ATRA) and arsenic trioxide (ATO) has transformed APL from one of the most fatal forms of leukaemia into one of the most curable haematological malignancies.

However, the clinical course of APL can be complicated by severe coagulopathy, early haemorrhagic events, and organ dysfunction, all of which may be life-threatening if not promptly recognised and managed. Renal pathology—whether pre-existing or secondary to the disease or its treatment—adds further complexity to diagnosis and therapeutic planning. Acute kidney injury (AKI) in patients with APL may result from tumour lysis syndrome,

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sepsis, nephrotoxic drug exposure, or direct leukemic infiltration, significantly impacting treatment tolerability and overall prognosis.

The management of APL in patients with renal impairment presents a particular challenge, as the pharmacokinetics and toxicity profiles of ATRA, ATO, and supportive therapies may be altered. Dose adjustments, careful fluid and electrolyte management, and multidisciplinary coordination are essential to achieve remission without causing further renal compromise. Moreover, renal dysfunction can mask early clinical signs of leukaemia, delay diagnosis, or confound laboratory assessments such as creatinine-based renal function estimation and drug clearance.

This case report presents the clinical course of a patient diagnosed with acute promyelocytic leukaemia in the setting of underlying renal pathology. It highlights the diagnostic challenges, therapeutic modifications, and outcomes observed, and discusses the implications for clinical practice. Through this case, we aim to contribute to the growing body of evidence regarding the management of haematological malignancies in patients with multi-organ comorbidities, particularly renal disease.

Methods

This clinical observation was conducted at the Samarkand Regional Multidisciplinary Medical Center in early 2025, with informed consent obtained from the patient and approval granted by the institutional ethics committee. A comprehensive diagnostic and treatment protocol was applied, integrating haematological and nephrological approaches. Upon presentation, the patient underwent a complete blood count, peripheral smear analysis, coagulation tests, and biochemical profiling to assess kidney function, electrolyte balance, and the severity of cytopenia. Bone marrow aspiration and biopsy were performed, revealing a predominance of abnormal promyelocytes, while molecular confirmation of the PML-RARA fusion gene was established through RT-PCR and FISH testing. This enabled a prompt diagnosis of acute promyelocytic leukaemia. Given the patient's compromised renal function at baseline, as indicated by elevated creatinine levels and reduced eGFR, careful adaptation of the therapeutic regimen was necessary. All-trans retinoic acid (ATRA) was initiated at standard dosing (45 mg/m²/day), while arsenic trioxide (ATO) was introduced cautiously at 0.10 mg/kg/day with dose modifications based on daily renal monitoring. Supportive therapy included prophylaxis for tumour lysis syndrome, transfusions of platelets and fresh frozen plasma to manage coagulopathy, and empiric broad-spectrum antibiotics during neutropenic episodes. Fluid management and nephrotoxic drug avoidance were prioritized to prevent further renal deterioration. Treatment was guided by a multidisciplinary team consisting of haematologists, nephrologists, and intensive care specialists, who jointly monitored therapy tolerance, complications such as QT interval prolongation, and infection risk. Continuous documentation of laboratory values, patient responses, and treatment adjustments provided the clinical framework for analysing this case and evaluating the outcomes of personalised treatment in a patient with dual haematologic and renal pathology.

Results

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The patient, a 47-year-old male, presented with spontaneous mucosal bleeding, fatigue, and oliguria. Laboratory evaluation revealed pancytopenia: haemoglobin 76 g/L, leukocytes 2.1×10^9/L, and platelets 18×10^9/L. The peripheral blood smear showed 65% abnormal promyelocytes with frequent Auer rods. Coagulation parameters were markedly abnormal—prothrombin time prolonged, fibrinogen 0.7 g/L, and elevated D-dimer—suggesting disseminated intravascular coagulation (DIC). Renal assessment showed serum creatinine at 280 µmol/L, blood urea nitrogen of 14 mmol/L, and an estimated glomerular filtration rate (eGFR) of 28 mL/min/1.73 m^2, confirming acute renal dysfunction.

Bone marrow aspiration confirmed hypercellularity with >80% promyelocytes, and cytogenetic analysis identified the t(15;17)(q24;q21) translocation. RT-PCR confirmed the PML-RARA fusion transcript. Based on these findings, a diagnosis of acute promyelocytic leukaemia was made in the setting of acute kidney injury (AKI).

ATRA therapy was initiated promptly, and ATO was introduced at a reduced dose due to renal impairment. The patient was also given prophylactic allopurinol and aggressive intravenous hydration to prevent tumour lysis syndrome, with careful fluid balance due to impaired renal excretory function. Platelet and plasma transfusions were administered to manage ongoing bleeding and correct coagulopathy. On day 4 of treatment, the patient developed febrile neutropenia, for which broad-spectrum antibiotics were initiated. No bacterial growth was found in cultures, and fever resolved within 72 hours.

Renal function gradually improved with supportive care; creatinine decreased to 170 µmol/L by day 14 and normalized (98 µmol/L) by day 25. Haematological response to therapy was favourable. By day 28, the patient achieved complete remission: bone marrow showed less than 5% blasts, platelet counts normalized, and peripheral promyelocytes were no longer detectable. Molecular testing on day 35 showed no detectable PML-RARA transcripts.

Throughout induction therapy, no severe differentiation syndrome or QT prolongation occurred. The patient tolerated the treatment well after initial adjustments and was discharged on day 38 with a plan to continue consolidation therapy under close nephrological monitoring. The outcome demonstrated successful remission of APL alongside full renal function recovery, indicating the effectiveness of an individualized, multidisciplinary management approach.

Discussion

Acute promyelocytic leukemia (APL) is a unique subtype of acute myeloid leukemia characterized by a specific chromosomal translocation t(15;17), resulting in the PML-RARA fusion gene. This genetic hallmark not only facilitates a targeted therapeutic approach but also underscores the importance of rapid diagnosis and initiation of treatment due to the disease's aggressive clinical course. The coexistence of APL with renal pathology, as presented in this case, introduces significant challenges in both diagnosis and management, necessitating careful consideration of therapeutic strategies and supportive care to optimize outcomes.

The clinical presentation of APL often involves bleeding diatheses resulting from disseminated intravascular coagulation (DIC), a critical complication observed in up to 80%

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of cases. In our patient, profound thrombocytopenia and altered coagulation parameters signaled the presence of severe coagulopathy, complicating the clinical picture. This is consistent with the pathophysiology of APL, where the release of procoagulant substances by abnormal promyelocytes triggers systemic activation of the coagulation cascade, leading to fibrin deposition and consumption of platelets and clotting factors. Prompt recognition and correction of coagulopathy are vital to reducing morbidity and mortality, as haemorrhagic events remain a leading cause of early death in APL patients.

Renal dysfunction in APL patients may be multifactorial. It can arise as a consequence of tumor lysis syndrome, nephrotoxic effects of chemotherapy, infection-related sepsis, or direct leukemic infiltration. In this case, the patient's acute kidney injury (AKI) presented a significant obstacle to standard treatment protocols, necessitating modifications in dosing and close monitoring to avoid further nephrotoxicity. The reduced dose of arsenic trioxide (ATO) was critical in minimizing renal adverse effects while maintaining therapeutic efficacy. This cautious approach highlights the need for individualized treatment regimens based on comorbid conditions.

The use of all-trans retinoic acid (ATRA) remains a cornerstone in APL therapy, promoting differentiation of malignant promyelocytes into mature granulocytes. Importantly, ATRA is generally well tolerated in patients with renal impairment, making it suitable for initial induction therapy in such complex cases. In contrast, arsenic trioxide, although highly effective in achieving remission, carries a risk of QT interval prolongation and electrolyte disturbances, which can be exacerbated by compromised renal clearance. In this patient, daily renal function monitoring and electrocardiographic surveillance facilitated timely dose adjustments and prevented severe cardiac toxicity.

Management of tumor lysis syndrome (TLS) is another critical aspect, particularly in patients with pre-existing renal pathology. Aggressive hydration, uric acid reduction with allopurinol, and close electrolyte monitoring were integral components of care to prevent exacerbation of renal injury. The favorable renal recovery observed post-treatment underscores the effectiveness of these preventive measures.

Infectious complications represent a common challenge during APL treatment due to profound neutropenia and immunosuppression. The occurrence of febrile neutropenia in this patient was managed successfully with empiric broad-spectrum antibiotics and careful supportive care, without progression to sepsis. This outcome reflects the importance of early recognition and prompt intervention in preventing life-threatening infections.

This case also emphasizes the role of multidisciplinary collaboration in managing patients with complex comorbidities. The involvement of haematologists, nephrologists, intensivists, and pharmacists enabled a comprehensive approach that balanced effective leukaemia treatment with renal protection and supportive management. Such coordinated care is essential in tailoring therapy, monitoring adverse effects, and improving overall patient prognosis.

Despite the challenges posed by renal impairment, the patient achieved complete hematologic and molecular remission, illustrating that with appropriate dose adjustments and supportive strategies, standard APL treatment protocols can be successfully

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implemented. The absence of severe differentiation syndrome, a potentially fatal complication of ATRA therapy, further contributed to the positive outcome.

Conclusion

In conclusion, this case illustrates the complexity of treating acute promyelocytic leukemia in the presence of renal dysfunction. It underscores the necessity for early diagnosis, individualized therapy, vigilant monitoring, and multidisciplinary management to optimize treatment efficacy and minimize toxicity. Future studies with larger patient cohorts are needed to establish standardized protocols for managing APL complicated by renal pathology and to explore novel therapeutic agents with improved safety profiles in this vulnerable population.

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