

Acute uric acid nephropathy during DA-EPOCH-R therapy in primary mediastinal large B-cell lymphoma

✉ Murat Bekir Özyurt^{*1}, ✉ Uğur Çalış², ✉ Serhat Çelik², ✉ Alparslan Güneş³, ✉ Meltem Kurt Yüksel²

¹Department of Internal Medicine, Faculty of Medicine, Ankara University, Ankara, Türkiye

²Division of Hematology, Department of Internal Medicine, Faculty of Medicine, Ankara University, Ankara, Türkiye

³Division of Nephrology, Department of Internal Medicine, Faculty of Medicine, Ankara University, Ankara, Türkiye

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Dear Editor,

Primary mediastinal large B-cell lymphoma (PMBCL) is an aggressive lymphoma subtype that predominantly affects young adults and is commonly treated with dose-adjusted EPOCH-R (DA-EPOCH-R), which provides high response and cure rates.^{1,2} Despite its efficacy, intensive chemotherapy regimens may lead to rare but clinically significant metabolic and renal complications. Here, we report a case of acute kidney injury (AKI) developing during DA-EPOCH-R therapy, suggestive of acute uric acid nephropathy, with concomitant acyclovir-associated nephrotoxicity remaining a possible contributing factor, in the absence of classical tumor lysis syndrome (TLS).

A 32-year-old male patient with PMBCL developed AKI on day +17 following initiation of the fourth cycle of DA-EPOCH-R (dose level 4, initiated on October 27, 2025). On November 13, 2025, serum creatinine increased to 5.79 mg/dl (KDIGO stage 3), accompanied by an elevated serum uric acid level of 9.4 mg/dl. The patient was hemodynamically stable, non-oliguric, and did not exhibit electrolyte abnormalities typically associated with TLS. Renal ultrasonography and Doppler studies excluded obstructive or vascular causes. Urine sediment analysis performed on November 14, 2025, revealed amorphous urate crystals, while acyclovir crystals were not detected despite being specifically sought. Notably, allopurinol prophylaxis had been discontinued prior to this episode due to previously normal uric acid levels and low perceived TLS risk. During follow-up, the patient had also been receiving intravenous acyclovir at therapeutic doses.

Based on clinical and laboratory findings, acute uric acid nephropathy was considered a possible cause of AKI, although concomitant acyclovir-associated nephrotoxicity could not be excluded. Intravenous hydration was intensified, and potentially nephrotoxic agents, particularly acyclovir, were discontinued on November 13, 2025, immediately after AKI was identified. Renal function gradually improved, with serum creatinine and uric acid levels returning near baseline

(Figure). However, the simultaneous initiation of hydration and discontinuation of acyclovir prevented definitive attribution of AKI to a single mechanism.

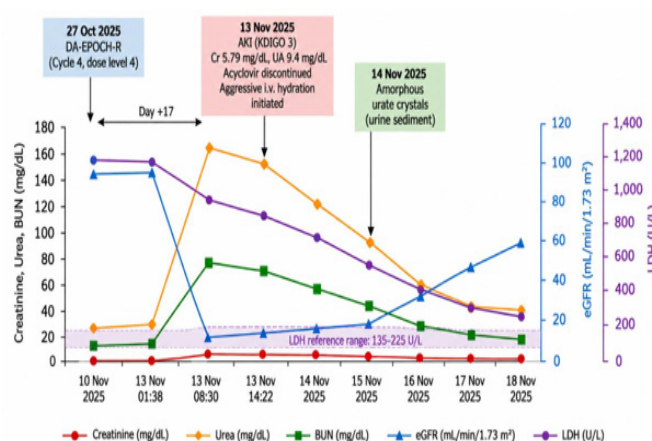


Figure. This figure shows the temporal changes in the patient's serum creatinine, urea, blood urea nitrogen (BUN), estimated glomerular filtration rate (eGFR), and lactate dehydrogenase (LDH) levels between November 10 and November 18, 2025. The fourth cycle of DA-EPOCH-R was initiated on October 27, 2025. Acute kidney injury and hyperuricemia were identified on November 13, 2025 (creatinine, 5.79 mg/dl; uric acid, 9.4 mg/dl), when intravenous acyclovir was discontinued and intensified hydration was initiated. Urine sediment examination on November 14, 2025, revealed amorphous urate crystals, while specifically sought acyclovir crystals were not detected. Renal parameters and LDH values are displayed on the same time axis, with separate axes used for eGFR and LDH. Reference range limits for LDH are indicated with dashed lines

Although TLS is a well-recognized cause of AKI in lymphoma patients receiving intensive chemotherapy, isolated acute uric acid nephropathy without classical TLS criteria has been reported, particularly in highly proliferative malignancies.^{3,4} According to the Cairo-Bishop classification, laboratory TLS requires at least two characteristic metabolic abnormalities within the defined period surrounding chemotherapy.⁴ Uric acid crystal precipitation in renal tubules may lead to intrarenal obstruction and subsequent AKI. In the present

*Corresponding Author: Murat Bekir Özyurt, muratbekirr@gmail.com



case, hyperuricemia and amorphous urate crystals supported the possibility of uric acid-associated nephropathy, although these findings were not diagnostic. Moreover, AKI developed outside the conventional Cairo–Bishop laboratory TLS time window. In addition, acyclovir-associated nephrotoxicity should be considered in the differential diagnosis, especially in the setting of intravenous administration and high doses.⁵⁻⁷ The absence of acyclovir crystals in urine sediment does not exclude this diagnosis, as crystal detection may be inconsistent. Acyclovir may also cause renal injury through mechanisms other than crystal precipitation. In the absence of renal biopsy, the relative contributions of uric acid-associated nephropathy and acyclovir-related nephrotoxicity could not be determined conclusively.

This case highlights that AKI during DA-EPOCH-R therapy may be multifactorial. Even in the absence of classical TLS findings, uric acid-associated nephropathy and drug-related nephrotoxicity should be considered. Early recognition, prompt discontinuation of nephrotoxic agents, and aggressive supportive management are critical to prevent irreversible renal damage.

In patients with PMBCL receiving intensive chemotherapy, AKI may develop independently of classical TLS criteria. Uric acid-associated nephropathy and concomitant drug-induced nephrotoxicity should be considered as potentially overlapping mechanisms, and early intervention may significantly improve outcomes.

ETHICAL DECLARATIONS

Informed Consent

Written informed consent was obtained from the patient for the publication of this correspondence and any related clinical details.

Peer Review Process

This letter was externally peer-reviewed.

Conflict of Interest

The authors declare no conflicts of interest.

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Editor Note

Serhat Çelik is a member of the Editorial Board of this journal. He was not involved in the editor assignment, reviewer selection, peer review process, or editorial decision for this manuscript. The peer review process was managed independently by another editor.

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