Oncology

Primary ureteral lymphoma presenting as bilateral obstructive uropathy

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A B S T R A C T

Primary ureteral lymphomas are rare. We present a case of extranodal B-cell lymphoma of the ureter presenting as asymptomatic bilateral ureteral obstruction. A 34-year-old male was incidentally found to have obstructive uropathy. Imaging showed severe bilateral hydronephrosis and percutaneous nephroureteral stents were placed. Diagnostic work up did not uncover any apparent etiology to the obstruction. Histopathological analysis of the ureter excised during ureteral reimplantation revealed CD20$^+$, CD5$^-$, CD10$^-$ B-cell lymphoma with areas of aggressive disease. The patient received six cycles of R-CHOP chemotherapy and is currently disease free.

Introduction

Extranodal presentations of non-Hodgkin lymphomas (NHLs) are relatively common, usually occurring in the gastrointestinal tract.[1] If the ureters are involved, it is typically due to extrinsic compression from bulky lymphadenopathy.[2] Primary involvement of the ureter is rare, with few cases reported.[3,4] Furthermore, the typical presentation of primary ureteral lymphomas (UL) involves localized genitourinary (GU) symptoms in a unilateral nature.[5] Here, we present a unique case of primary UL presenting with asymptomatic bilateral obstructive uropathy (OU), treated with ureteral re-implantation and chemotherapy.

Case presentation

A 34-year-old male with a past medical history of seizure disorder and recurrent prostatitis with no known renal dysfunction was found to have acute kidney injury (AKI) discovered on routine labs. He was sent to the emergency department, where serum creatinine was 4.6 mg/dL and renal ultrasound demonstrated bilateral severe hydronephrosis with moderate prostatomegaly, and a 74 mL post void residual. For concern of OU secondary to lower urinary tract obstruction (UTO), a urinary catheter was placed for maximal decompression. Of note, catheter insertion was difficult, and required multiple attempts. He was discharged home three days later with the catheter and a creatinine of 3.7 mg/dL.

On subsequent follow up at our institution two weeks later, the patient denied any voiding issues at baseline. Repeat ultrasound revealed unchanged severe bilateral hydroureteronephrosis, with a creatinine of

5.1 mg/dL despite adequate catheter drainage. The patient was admitted for further evaluation and management of his asymptomatic AKI.

A mercaptuacetyltriglycine-3 (MAG3) diuretic renogram revealed bilateral obstruction (Fig. 1A–B). Following insertion of bilateral percutaneous nephroureteral (PCNU) stents, his creatinine trended to 2.9 mg/dL over the next five days, and catheter was removed. A trial of PCNU clamping was not tolerated due to severe right flank pain.

Diagnostic cystoscopy and ureteroscopy with bilateral retrograde and anterograde pyelograms were performed. The retrograde studies revealed marked stenosis of distal ureters bilateral with proximal dilatation (Fig. 1C–D). Random biopsies of bladder trigone, right distal ureter, and prostatic urethra were notable only for inflammatory changes and negative IGG4 immunohistochemical staining. PSA was 0.5 ng/mL. C-reactive protein and erythrocyte sedimentation rate were within normal limits and urine acid fast testing was negative for GU tuberculosis. Videourodynamic studies demonstrated safe bladder pressures during filling, slightly obstructive voiding pressures (60 cm H$_2$O) with complete emptying, and severe bilateral vesicoureteral reflux during voiding.

At this point, the working diagnosis was idiopathic retroperitoneal fibrosis (RPF), and the patient underwent robotic bilateral ureteral reimplantation with psoas hitch. Intraoperatively, severe fibrotic reaction of the inferior portion of the bladder and distal ureters was noted. Right ureteral biopsy revealed CD20$^+$, CD5$^-$, CD10$^-$ B-cell lymphoma with mostly small cells. However, there were some large atypical cells with Ki67 of 50% concerning for a component of aggressive B-cell lymphoma (Fig. 2). Both right periureteral tissue and left ureteral biopsies were benign with atypical lymphoid infiltrate. Staging position

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emission tomography-computed tomography (PET-CT) during hospitalization for left-sided pyelonephritis demonstrated moderate fluorodeoxyglucose (FDG)-avid fibrosis (SUV 4.7, Deauville score 4) at the right distal ureter (Fig. 3A) and indeterminate left-sided retroperitoneal lymphadenopathy (Fig. 3B) consistent with Lugano stage IV disease. An ensuing bone marrow biopsy was unremarkable. The patient underwent six cycles of R-CHOP (Rituximab, Cyclophosphamide, Doxorubicin, Prednisone) for curative intent. He tolerated therapy well with only mild paresthesias of the distal fingertips. His creatinine remains stable at 1.6 mg/dL and he is voiding without difficulty. Post-chemotherapy PET-CT demonstrated no new hypermetabolic lymphadenopathy, consistent with disease remission (Fig. 3C and D).

Discussion

The differential diagnosis of OU is extensive and must be considered in the context of clinical signs and symptoms. In this case, the etiology of the patient's OU was difficult to discern, and required thorough endoscopic, radiographic, and urodynamic evaluation. Ultimately, the primary location of obstruction was narrowed down to bilateral distal ureters. Given the unremarkable workup and high suspicion for extrinsic upper UTO, the working diagnosis of exclusion was RPF. Therefore, we proceeded to definitive treatment with surgical reimplantation, which excluded RPF and revealed GU lymphoma as the cause. Malignant ureteral involvement is often secondary to metastatic invasion or external compression from bulky lymphadenopathy.[2] However, primary
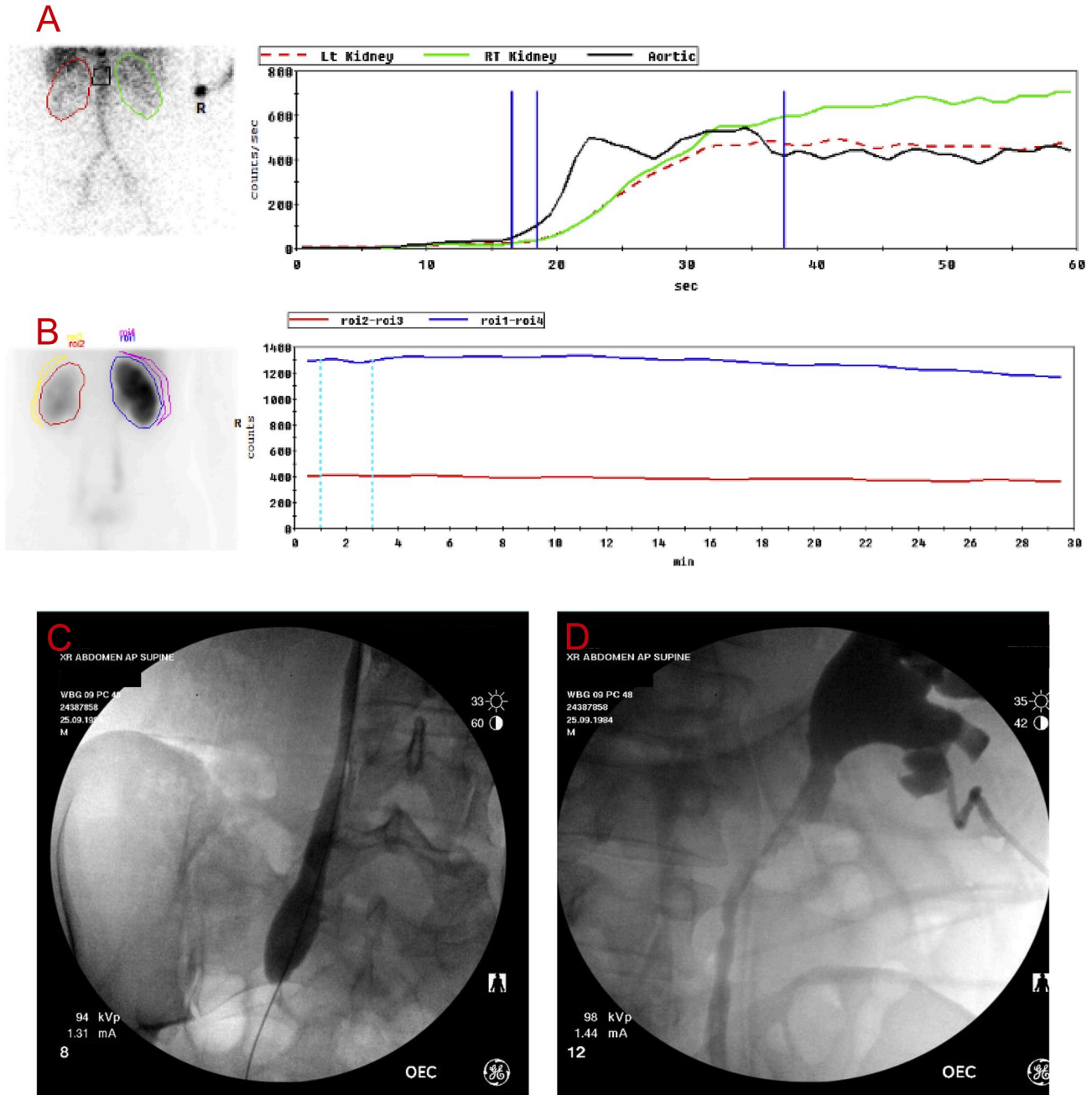
Fig. 1. MAG3 renogram demonstrating (A) minimal uptake by the left kidney in the perfusion phase with a differential function of 51% on the left and 49% on the right. (B) Both kidneys failed to clear radiotracer following diuretic administration ($t_{1/2}$ was not reached), consistent with bilateral obstruction. (C) Retrograde pyelograms revealed bilateral distal ureteral strictures with blind ending ureters (right ureter shown) and (D) dilated pelvicalyceal systems (left shown). Abbreviations: MAG3 = mercaptuacetyltriglycine-3.
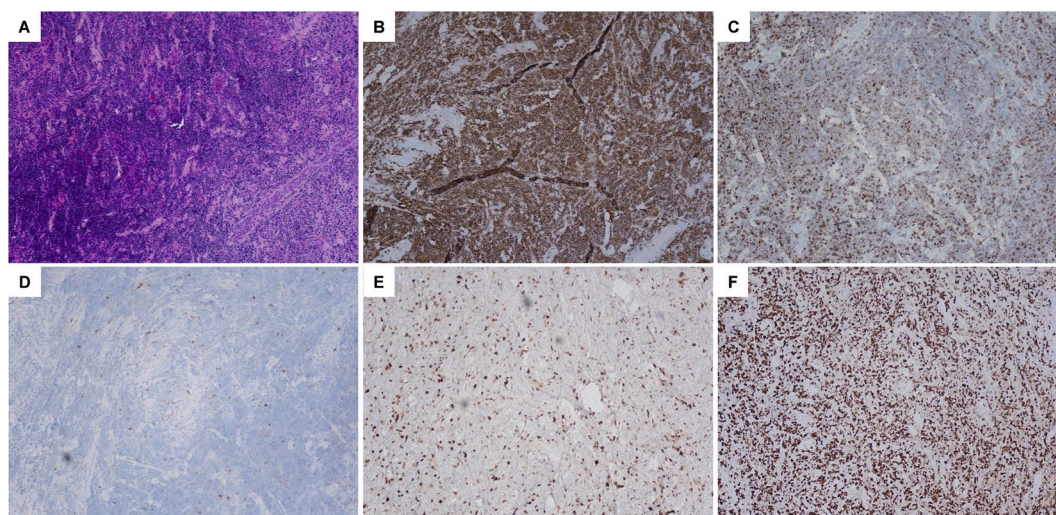
Fig. 2. Histologic sections demonstrate an atypical lymphoid infiltrate that infiltrates into skeletal muscle and adipose tissue. (A) The infiltrate is composed of a mixture of small lymphocytes with mature chromatin and other medium-sized lymphocytes with irregular nuclear shapes. (B) There is a dense predominance of CD20 positive-B cells. CD5 (C) and CD10 (D) are negative. (E) Cyclin D1 appears negative but stains numerous endothelial cells in the neoplastic area. (F) The Ki67 proliferation index is low in most areas but is about 50% in the area of larger atypical B cells.
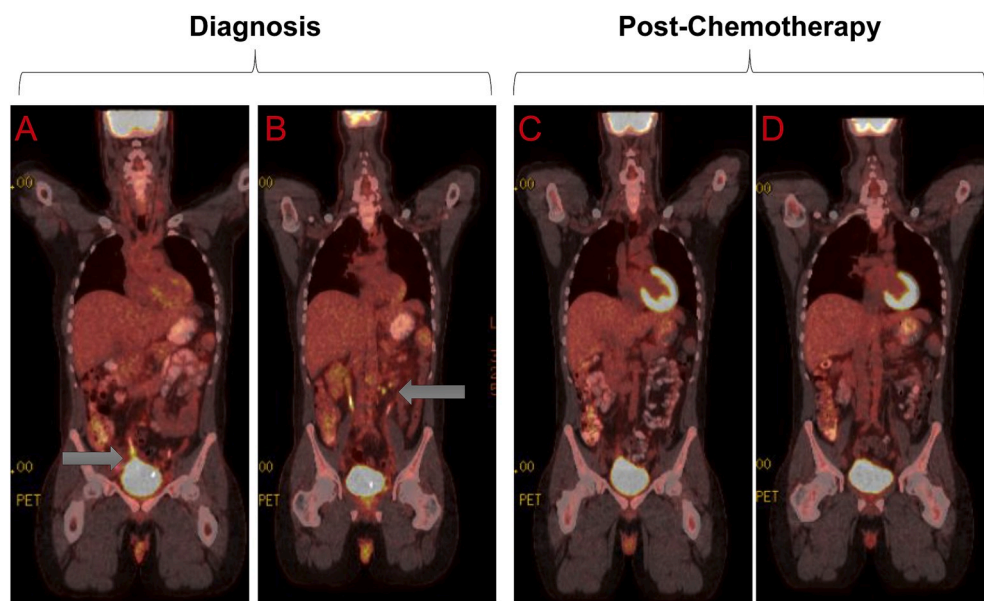
Fig. 3. PET-CT pre and post-chemotherapy. PET scan revealed (A) FDG avid fibrosis of the distal right ureter corresponding with biopsy-proven Lugano stage IV B-cell lymphoma and (B) indeterminate retroperitoneal para-aortic lymphadenopathy. (C) Post-chemotherapy response of distal right ureter and (D) retroperitoneal lymphadenopathy. Abbreviations: PET-CT = positron emission tomography-computed tomography; FDG = fluorodeoxyglucose.

UL is exceedingly rare, with approximately 20 cases ever reported in the literature.[4,5] This unique presentation suggests that UL should be considered in the OU differential diagnosis, particularly when diagnostic work-up is otherwise unrevealing.

This case presents many unique features and diagnostic challenges. For one, most cases of reported UL present with flank pain localized to the affected ureter.[3–5] Asymptomatic hydronephrosis has been reported in only 10–20% of cases. Here, the patient reported no symptoms of obstruction and elevated creatinine was found on routine labs. Other elements including bilateral hydronephrosis, pain with PCNU clamping, high voiding pressures, and severe ureteral reflux with voiding on uro-dynamics mimicked lower UTO and delayed the eventual diagnosis of NHL. Furthermore, only two other cases have been associated with bilateral hydronephrosis, both from direct invasion into bilateral ureters. In this case, biopsy proven NHL was seen in the distal right ureter and it is presumed that the distal left ureter was also involved based on the lymphoid invasion of the intraoperative biopsy specimen, which was

likely proximal to the bulk of the disease.

Due to its rarity, the optimal management of ureteral lymphoma is undetermined. PET-CT scans are recommended, but findings may be equivocal, with difficulty in determining the primary source of disease. In this case, PET-CT allowed for monitoring of disease response after chemotherapy but prompted questions about the initial extent of disease due to the left-sided lymphadenopathy in the setting of an active kidney infection. Regardless, final diagnosis should be made with histopathological examination, suggesting the importance of procedural intervention in diagnosis and management of this malignancy. Often a combination of surgery and chemotherapy is implemented for treatment, and favorable outcomes have been demonstrated with both techniques.[3–5]

Conclusion

We report a rare case of primary ureteral NHL resulting in

asymptomatic bilateral hydronephrosis and OU. UL should be considered in the setting of unexplained OU and diagnosis should be made with histopathological examination.

Funding

Declaration of competing interest

None.

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