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Case Report

Unusual presentation in a case of diffuse large B-cell lymphoma ☆

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ABSTRACT

Non-Hodgkin's lymphoma are neoplasms derived from T cells and B cells and their precursors in the lymphoid system with higher susceptibility in involvement of extra-nodal sites. Predominant ureteric involvement is an unusual presentation. We present a case of diffuse large B-cell lymphoma with secondary involvement of ureter who had symptoms of urinary tract infection in absence of positive urine culture, non-responsive to broad spectrum antibiotics and masquerading pyogenic infection leading to pyelonephritis with ureteritis. Radiological examination revealed mass like soft tissue thickening of ureter extending from renal pelvis throughout the length of ureter. FNAC as well as biopsy from the periureteric thickening revealed lymphomatous involvement of ureter. The following case report provides insight on differentials and varied symptoms of lymphomatous involvement of ureter.

Introduction

NHLs are a heterogeneous group of malignancies in the lymphoid system. As compared to Hodgkin's lymphoma, non-Hodgkin's lymphoma has greater propensity in involvement of extra-nodal sites [1]. Non-Hodgkin's lymphoma (NHL) most frequently occurs in the gastrointestinal tract (GIT), accounting for 10%-15% of NHL cases and 30%-40% of all extra-nodal lymphomas [2]. The urinary system is involved in less than 5% of lymphomas overall, with the kidneys and bladder accounting for the majority of these cases [3]. There is exceptional rarity of ureteral involvement in non-Hodgkin's lymphoma as evident by few very case studies. When consider-

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ing the nodal counterpart, extra-nodal DLBCL frequently has a worse prognosis [4]. Ureteral lymphoma may have varied spectrum of presentations and in addition to absence of definite ideal course of its treatment [5], it becomes important to include it in our differential diagnosis so as to ensure prompt management and improve prognosis.

In the following case report, we present an unusual presentation of ureteric involvement in a 70-year-old patient of diffuse large B cell lymphoma with insight on varying presentation and review of literature.

Case presentation

A 70-year-old female with diffuse large B cell lymphoma on remission presented with symptoms of urinary tract infection like burning micturition and high-grade fever. She was being treated with broad spectrum antibiotics for over 1 month but symptoms did not improve satisfactorily. Blood reports revealed kidney function tests within normal limits with decreased hemoglobin (5.2 gm/dL) and TLC count (2.99×10^3/microliter). However, HSCRP level were raised (195 mg/L). Urine examination showed microscopic hematuria with negative aerobic as well as anerobic culture examination.

Initially, the patient presented with abdominal pain in January 2023, for which CECT abdomen was performed and revealed sclerosing mesenteritis. On further work up, diffuse large B-cell lymphoma was diagnosed on immunophenotyping by flow cytometry. Initial PET-CT was performed and it revealed hypermetabolic changes of skeleton with abdominal and axillary lymphadenopathy. Patient received 6 cycles of chemotherapy on R-CVP regimen (rituximab, cyclophosphamide, vincristine, and prednisolone). Follow up PET-CT scan was performed after completion of chemotherapy and it showed near complete resolution of the hypermetabolic lesions and was considered to be on remission. However, after 3 months, she presented with urinary tract symptoms which eventually revealed recurrence of lymphoma with ureteric involvement.

On NCCT KUB, there is diffuse soft tissue thickening involving right renal hilum and entire right ureter. (Figs. 1A and 2A) On CECT KUB, right kidney was enlarged in size (~ 112×64 mm) with ill-defined mass like soft tissue enhancing thickening was seen circumferentially encasing the renal hilar structures extending to ureter. The renal vessels were seen normally without luminal compromise. The renal pelvis was mildly prominent and compressed by the thickening with mild hydroureteronephrosis with proximal dilated ureter. Rest of the ureter is not visualized separately from the mass like thickening with maximum transverse diameter measuring approximately 60 mm at upper border of L5 vertebral body. The thickening was seen extending throughout the length of ureter till the right vesico-ureteral junction. Even on delayed scans, there was no opacification of kidney or ureter. There were significant periureteric fat stranding and inflammatory changes. The soft tissue thickening showed loss of fat plane with IVC wall, surrounding bowel walls and right psoas muscle (Figs. 1B-D and 2B, C).

USG guided FNAC as well as linear core biopsy from the periureteric thickening was done. On FNAC, it demonstrated large atypical cells dispersed singly and in small groups associated with fibrin. The cells showed large nuclei with small nucleoli and granular coarse chromatin with variable amount of cytoplasm, therefore diagnosis of large round cell malignancy/ large cell lymphoma of the periureteric deposits was made (Fig. 3).

On biopsy, confirmation of diagnosis was done. It showed areas of tumor necrosis with tumor cells disposed in sheets which were markedly pleomorphic, large sized with round to irregular contour, vesicular chromatin and moderate amount of cytoplasm. On immunohistochemistry, LCA, PAX-5, CD3 markers were positive with Ki67 index of 90 %. However, CD 20 marker was negative due to probable post-chemotherapy effect (Fig. 4).

Thereafter, patient was planned for re-initiation of chemotherapy regimen as she was a poor surgical candidate. However, her fever remained uncontrolled with medications and she gradually developed klebsiella pneumonia. Due to compromised immunity and marrow suppression, pneumonia got worsened and she developed respiratory discomfort. After admission to intensive care unit, she gradually developed sepsis and multiorgan dysfunction syndrome before she passed away.

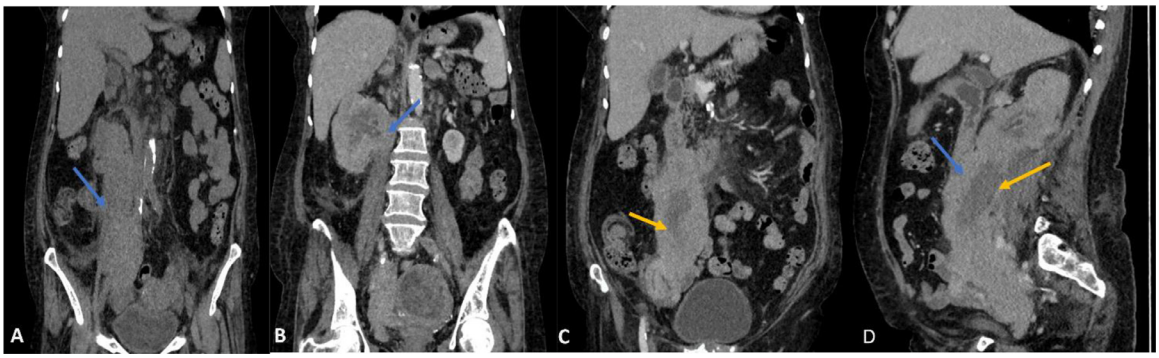

Fig. 1 – NCCT KUB Coronal (A) image showing diffuse circumferential ureteric thickening. CECT KUB Coronal (B, C) and Sagittal (C) images showing ill-defined soft tissue enhancing thickening (blue arrows) involving right renal hilum and extending to ureter. Images (C, D) showing nonvisualization of right ureter from the enhancing thickening with hypodense areas (yellow arrows) within the thickening suggestive of necrosis.

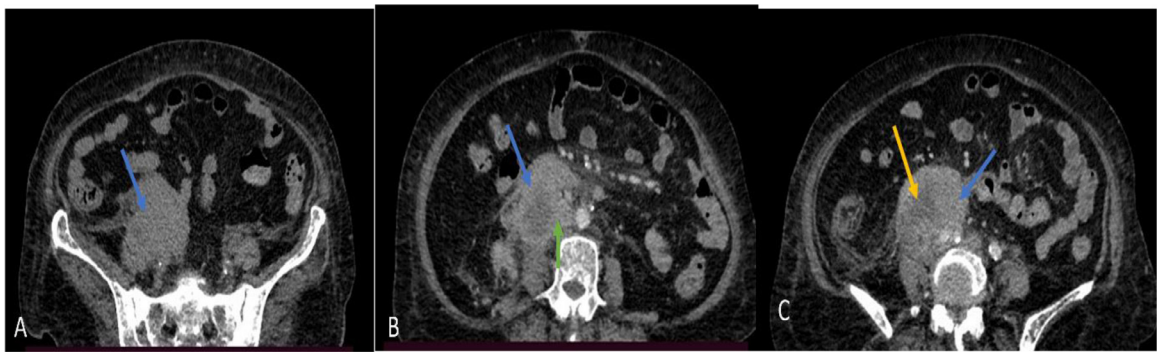

Fig. 2 – NCCT KUB Axial section (A) showing circumferential thickening of right ureteric wall(blue arrows) CECT KUB Axial section (B,C) showing circumferential enhancing thickening (blue arrows) of right ureter with central necrotic areas (yellow arrow). (B)The thickening is seen closely abutting IVC (green arrow).

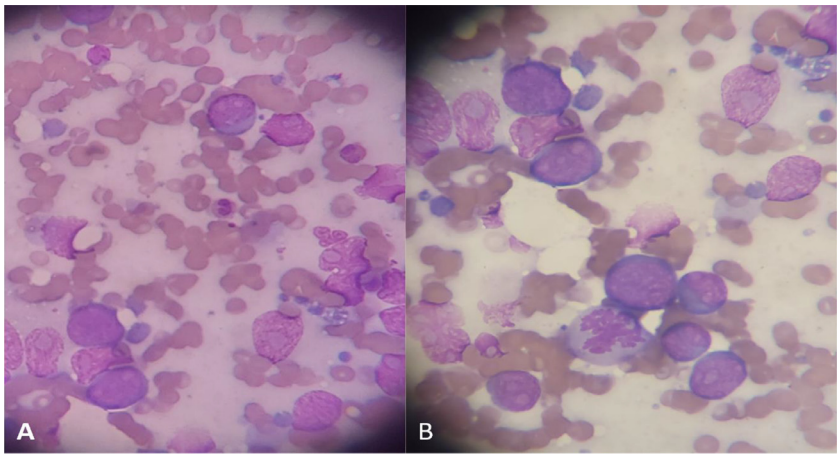

Fig. 3 – A & B : Fine needle aspirate from periureteric deposits showing atypically proliferated large atypical cells (arrows) showing large nuclei with small nucleoli and granular coarse chromatin with variable amount of cytoplasm suggestive of round cell malignancy (deposits of large cell lymphoma).

Discussion

Non-Hodgkin's lymphoma includes diverse range of neoplasms derived from T cells and B cells and their precursors in the lymphoid system. It shows a greater intent to involve the extra nodal sites as compared to Hodgkin's lymphoma. Genitourinary tract involvement is present in less than 5% of incidents of extra nodal non- Hodgkin's lymphoma [6]. There is lack of specific clinical and radiologic features, thus making its diagnosis difficult. Among cases of non-Hodgkin's lymphoma involving genitourinary tract, highest incidence was found to be of diffuse large B-cell lymphoma in study done by Schiederian et al. [7]. Kidney is most common genitourinary site of extra nodal involvement of NHL [6]. Ureteric involvement can occur by displacement due to retroperitoneal lymphadenopathy or lymphomatous mass or by direct involvement of ureteric tissues [8]. In an autopsy series by Scharifker, Ureteric involvement was noted in 16% of patients with 8 of 21 patients having ureteral infiltration by lymphomatous tissue [9].

Lymphomatous involvement of ureter may have varying presentations. A 45-year-old man, complained of 2 months of dull, excruciating flank discomfort that was unaccompanied by lower urinary tract symptoms, dysuria, or hematuria showed right moderate right hydroureteronephrosis (HUN) to the lower ureter on noncontrast CT abdomen and was diagnosed with lower ureteric non-Hodgkin lymphoma causing ureteric stricture after undergoing open ureterectomy [10]. Another case report by Caesar Khairul Wallad [11], a 30-year-old woman presented with right flank and right upper quadrant abdominal pain for 6 months with no hematuria or urinary tract symptoms or peripheral lymphadenopathy. The laboratory findings showed no signs of myelosuppression or leukemia blood image, and they were all within normal ranges while cytology of urine also revealed no evidence of malignant cells. Based on Positron Emission Tomographic (PET) examination with Multi Slice CT scan, diagnosis of upper tract transitional carcinoma was made before she underwent radical nephron-uretrectomy with bladder cuff excision with final histopathological confirmation of non-Hodgkin ma-

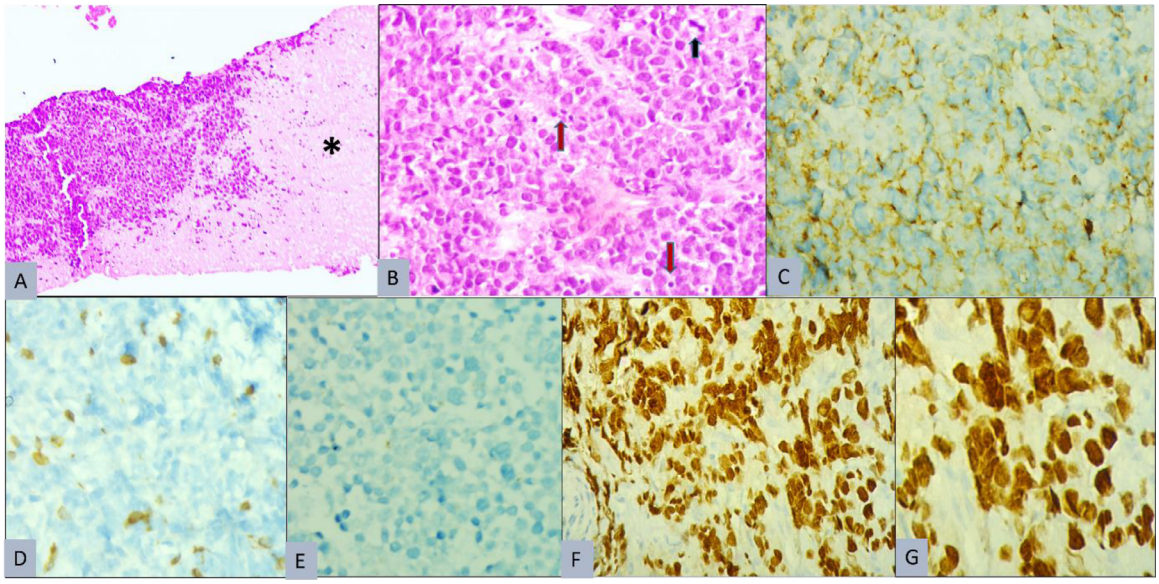

Fig. 4 – (A) Tumor with adjacent areas of tumor necrosis (black asterisk) (H and E, 10× magnification). (B) Tumor cells are moderately pleomorphic and having vesicular chromatin, prominent nucleoli and moderate amount of cytoplasm. Few mitotic figures (black arrow) and apoptotic bodies (red arrows) are also evident. (H and E, 40× magnification). (C) Tumor cells show positivity for leukocyte common antigen (LCA) immunohistochemistry (40× magnification). (D) Tumor cells show focal positivity for CD20 immunohistochemistry (40× magnification). (E) Tumor cells are negative for CD3 immunohistochemistry (40× magnification). (F) Tumor cells show positivity for PAX-5 immunohistochemistry (40× magnification). (G) Tumor cells show high Ki-67 proliferation index (40× magnification).

lignant lymphoma. In a comparable case of Nida Zahid et al., [12] a 37-year-old man had right flank pain and symptoms related to the lower urinary system with gradual development of obstructive uropathy due to distal ureteric stricture whose CT KUB revealed presacral soft tissue infiltration, a severely thick-walled urinary bladder and bilateral extensive hydroureteronephrosis. He underwent bladder biopsy and a double J stent insertion followed by stent removal and bilateral ureteric reimplantation with ultimate histological diagnosis of DLBCL according to WHO classification of lymphoid neoplasm. Our patient presented with symptoms of urinary tract infection like fever and burning urination with no gross hematuria. Possibility of transitional cell ureteral carcinoma (TCC) was kept in view, however there was absence of features of TCC on CT scan like fine encrusted calcification, small filling defects and mass lesion. Also, with absence of gross hematuria and flank pain in our patient, our differentials narrowed to pyelonephritis and lymphomatous involvement of ureter as both them can show diffuse enhancing urothelial wall thickening with periureteric and perinephric fat stranding. Variable imaging characteristics of lymphomatous ureteric involvement can be identified [10–12] as in our case there was right sided hydroureteronephrosis with gross soft tissue enhancing thickening of ureter throughout its entire length with central areas of necrosis and surrounding inflammatory changes. However, there was absence of cytological evidence of pyelonephritis with lack of malignant cells on urine examination. On CECT scan, the soft tissue thickening showed loss of fat plane with surrounding IVC, bowel walls and right psoas muscle, which was consistent with its malignant nature Corresponding to our case, there is mostly unilateral involvement of ureter, however bilateral ureteral involvement is also identified [13]. Ureteroscopy with biopsy imparted more conclusive findings in comparison to radiography for differentiating primary neoplasms from metastasis to ureter [14]. So, in our case, where USG guided biopsy from the ureteric thickening as well as fine needle aspiration from the hypodense areas within the thickening was done which yielded the conclusive results of ureteric involvement of lymphoma.

There is variation in terms of treatment strategy in the management of patients with NHL of ureter in the reported cases and include radiation after partial urethrectomy or chemotherapy. Ruth et al. [15] reported a case of ureteric DLBCL in a 50-year-old patient with HIV who received R-CHOP chemotherapy and remained alive at 6 months. In study done by Huang et al. [16] demonstrated DLBCL patients treated with R-CHOP-like regimens or with GCB subtype exhibited better clinical outcomes. Our patient was initially planned for nephroureterectomy however deemed unsuitable due to age and therefore, she was started on R- CHOP regime of Chemotherapy. But regrettably, the patient did not survive 1 month after the diagnosis was made.

Conclusion

Patients with ureteric involvement in lymphoma may have varied presentations. In absence of supportive biochemical

and lab parameters in suggesting urinary tract infection, ureteric involvement should be included in the differential diagnosis as it is generally associated with poorer prognosis and earlier diagnosis may impart better and improved management strategy.

Patient consent

Our patient didn't survive 1 month after the diagnosis was made. Consent was taken from concerned family members.

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