Case Report

Immunoglobulin G4-related renal disease masquerading as renal pelvic tumor

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ABSTRACT

The recently recognized immunoglobulin G4 (IgG4)-related disease presenting as renal pelvic pseudotumor is rare. A definitive diagnosis is often difficult to obtain preoperatively, with patients being subjected to radical surgery due to suspicion of malignancy. We present a 64-year-old male with lower urinary tract symptoms, who, on evaluation had a right renal pelvic tumor on imaging and ureteroscopy. The patient underwent laparoscopic radical nephroureterectomy on clinical suspicion of upper tract urothelial carcinoma. The final histopathology revealed IgG4-related disease.

INTRODUCTION

Immunoglobulin G4-related disease (IgG4-RD) is a recently recognized disease involving almost every anatomic site. Among the genitourinary organs, the kidney is most commonly affected, usually presenting as tubulointerstitial nephritis (TIN).[1] IgG4-RD presenting as isolated renal pelvic pseudotumor is rare, and contemporary imaging modalities are unable to differentiate it from pelvic urothelial carcinoma, Eventually patients have to undergo radical surgery, as malignancy cannot be ruled out.

CASE REPORT

A 64-year-old male presented with complaints of poor flow and frequency without hematuria. Ultrasonography (USG) and computed tomography scan (CT scan) revealed a 6.4 cm × 4.2 cm × 4.2 cm right renal pelvic mass [Figure 1a]. Urine cytology did not show any malignant cells. With a diagnosis of renal pelvic urothelial carcinoma, the patient underwent right retrograde pyelogram (RGP) and ureteroscopy (URS). RGP showed a filling defect, and URS revealed a solid-looking growth in the pelvis. Based on the CT image and ureteroscopic visualization of the tumor, the patient underwent endoscopic disconnection of the right lower ureter and laparoscopic radical nephroureterectomy (RNU). The gross specimen showed a yellowish-white solid-looking lesion filling the pelvis [Figure 1b]. The final histopathology showed inflammatory lesion with storiform fibrosis and infiltration with IgG4-positive plasma cells [Figure 1c and d]. Postoperatively, serum IgG4 and complement C3, C4 levels were obtained, which were normal. At 4-month follow-up, the patient is asymptomatic, and a repeat serum IgG4 level was within normal limits. The USG showed a normal left kidney and no other mass in the abdomen.

DISCUSSION

IgG4-RD is a rare systemic disease affecting mainly middle-aged men involving every site in the body, with the most common manifestation being autoimmune pancreatitis (AIP). Kawano *et al.*, in their study of AIP patients, reported the renal involvement to be up to 35%. More than 90% of

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patients with renal involvement have a history of extrarenal lesions.[1] In the kidneys, the most common lesion is TIN followed by membranoproliferative glomerulonephritis. Isolated renal pelvic pseudotumor is rare, with only a few cases reported in the literature [Table 1]. Hyper-IgG-emia is an important finding in these patients, but up to 20%–30% of patients have normal IgG levels. Over 50% of patients with IgG4-related kidney disease have hypocomplementemia.[2]

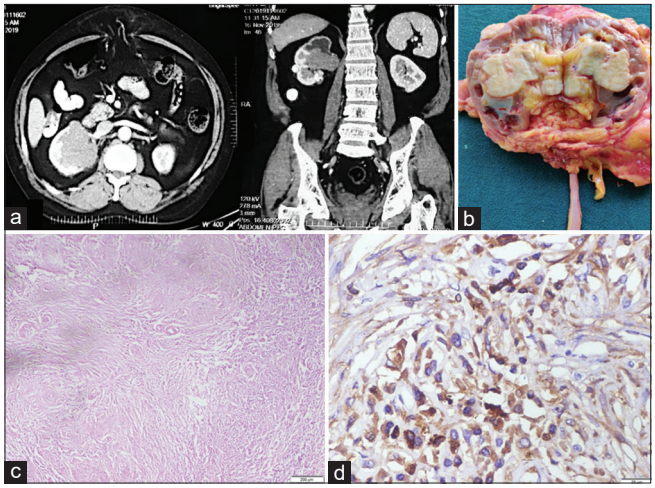

Figure 1: (a) Computed tomography picture showing the right renal pelvic mass. (b) Gross specimen showing a yellowish-white tumorinvolving the pelvicalyceal system (PCS). (c) Microscopic image from the kidney section shows storiform fibrosis along with dense lymphoplasmacytic infiltrate (H and E, ×200). (d) Immunohistochemistry showing immunoglobulin G4-positive plasma cells (>30 per high-power field)

USG, CT, and magnetic resonance imaging give a picture of the renal mass. The characteristic pathological feature noted in the IgG4-associated renal pseudotumor is storiform fibrosis along with infiltration by lymphocytes, IgG4-positive plasma cells, and eosinophils.

Two different diagnostic criteria exist in the literature for IgG4-RD. The diagnostic criteria by Kawano *et al*. are based on the presence of some kidney damage, abnormal radiologic findings, elevated serum IgG4 levels, and histologic findings in the kidney and other extrarenal organs.[2] The diagnostic criteria by Raissian *et al*. consider the deposition of IgG4-rich plasma cells on histology as a mandatory criteria and imaging, serology, and extrarenal involvement as supportive.[1] Diagnosing IgG4-related kidney disease presenting as a renal pelvic pseudotumor is difficult preoperatively, with the final diagnosis resting on the histopathology obtained either from the biopsy or surgically removed specimens.

Patients with IgG4-RD mimicking a renal pelvic cancer are often managed surgically because of the limitations in making a definite diagnosis preoperatively. Our case raises the question of whether a preoperative biopsy should be mandatory in all suspected cases of upper tract urothelial carcinoma (UTUC), where upfront RNU is performed in the presence of high-risk features. In the recent European Association of Urology guidelines on UTUC, the presence of upper tract urothelial tumor size >2 cm on CT scan

Table 1: Published reports of immunoglobulin G4-related disease mimicking renal pelvic tumor

Author	Age/ sex	Location	Presentation	Extrarenal manifestations	Serum IgG	Serum IgG4	Diagnosis	Treatment	Follow-up
Kuroda *et al*.[6]	49/ female	Left	Incidental	Salivary, lacrimal glands	Elevated	Elevated	NUTx	NUTx	-
Takata *et al*.[7]	80/ male	Right	Incidental	None	-	Elevated	NUTx	NUTx	36 months, in remission
Mehta *et al*.[8]	71/male	Right	Incidental	-	-	-	RGP+Nx	Nx	-
Yoshino *et al*.[9]	71/male	Left	Hematuria, flank pain	None	Elevated	Elevated	Diagnostic prednisolone therapy	Steroids	14 months, in remission
Tsuzaka *et al*,[10]	69/ male	Left	Incidental	Pancreas, salivary glands	Elevated	Elevated	NUTx	NUTx + steroids	11 years, in remission
Wang *et al*.[4]	54/ female	Left	Flank pain	Sicca Complex	-	Elevated	NUTx	NUTx + steroids	12 months, in remission
Zhang *et al*.[11]	53/ female	Right	Incidental	None	-	Elevated	NUTx	NUTx	-
Park *et al*.[12]	75/ male	Right	Incidental	None	-	Normal	NUTx	NUTx	10 months, in remission
Bianchi *et al*.[13]	56/ male	Right	Incidental	None	Elevated	Elevated	NUTx	NUTx	18 months, in remission
Savov *et al*.[14]	61/male	Right	Flank pain	None	Normal	Elevated	NUTx	NUTx	-
Surintrspanont *et al*.[15]	52/ male	Right	Hematuria	Pulmonary, hepatic	Elevated	Elevated	Biopsy	Steroids	3 months, in remission
Zhang *et al*.[16]	60/ female	Bilateral	Incidental	None	Elevated	-	Biopsy	Steroids	-
Jiang *et al*.[17]	70/ female	Left	Incidental	Salivary glands	-	Elevated	Diagnostic prednisolone therapy	Steroids	-
Our Case	64/ male	Right	Incidental	None	-	Normal	NUTx	NUTx	4 months, in remission

NUTx=Nephroureterectomy, Nx=Nephrectomy, IgG=Immunoglobulin G4

itself meets the criteria for high-risk tumors, and RNU is strongly recommended.[3] At our tertiary care center, besides the CT scan, we also consider urine cytology and tumor visualization on flexible URS for decision-making. RNU is performed if two of the three are positive. Moreover, in addition to extra cost and delay in definitive treatment awaiting biopsy report, URS biopsy is limited by inadequate sampling of tissues, 15% false-negative rate, 11% incomplete report without grade information, and significant grade discordance with the final histopathology, making the role of routine preoperative biopsy uncertain.[4]

IgG4-RD responds rapidly to steroid therapy, which is considered as first-line treatment. Although no data exist specifically for IgG4-RD mimicking renal pelvic tumor, a response rate of 90% with steroids was reported in a French cohort of 25 patients with IgG4-related systemic disease, including 16% IgG4-related pseudotumors (orbit, liver, and meningeal).[5] Second-line therapies for resistant or refractory cases include azathioprine, methotrexate, rituximab, and cyclophosphamide.[5] Patients with evidence of systemic disease in the form of multiple organ involvement or elevated serum IgG4 levels should receive steroid therapy. These patients should be followed with imaging and renal function, although no clear consensus exists regarding the follow-up protocol.

CONCLUSION

IgG4 disease presenting as a renal pelvic mass is rare, and the diagnosis is difficult to establish preoperatively. A definite diagnosis preoperatively may spare the patients unnecessary surgery. Larger, prospective studies are required to establish strategies for diagnosis, management, and follow-up of IgG4-RD presenting as a renal pelvic pseudotumor.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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