



Inflammation and infection

Peri-ureteric mass an unusual case of immunoglobulin G4-related disease (IgG4-RD)

Isabella S.C. Williams^{a,b,*}, Nelson Wang^{a,b}, Paul Bergamin^{a,b}, Christopher W. Toon^c,
Jeremy N. Pulvers^c, Matthew Winter^{a,b}

^a Department of Urology, Royal North Shore Hospital, Sydney, Australia

^b North Shore Urology Research Group, Sydney, Australia

^c Department of Anatomical Pathology, NSW Health Pathology, Royal North Shore Hospital, Sydney, Australia

ARTICLE INFO

Keywords:

Ureter
IgG4
Peri-ureteric mass

ABSTRACT

Immunoglobulin G4-related disease (IgG4-RD) of the ureter is a rarely reported disease, often mimicking urothelial carcinoma. This paper describes a case of an otherwise healthy patient with a lesion involving the ureter revealed on Computed tomography (CT), avid on fludeoxyglucose positron emission tomography (FDG PET), that prior to surgery was suspicious for urothelial carcinoma, until intra-op frozen section revealed otherwise. Diagnosis of ureteral IgG4-RD should be considered as a differential diagnosis, with serum IgG4 levels obtained.

Introduction

IgG4-RD is a fibro-inflammatory disease, with elevated IgG4 plasma cells forming mass forming lesions with specific histopathological appearance. It poses a diagnostic challenge for urologists, due to its vague, often non-specific clinical symptoms, and is often misdiagnosed as urothelial carcinoma on radiological appearance, with surgery performed to avoid missed diagnosis of carcinoma. Whilst IgG4-RD has been frequently reported in other organs, there are few cases of ureteric disease.

Case presentation

A 40-year-old male patient presented with a 4-day history of right lower quadrant abdominal pain, no significant past medical history, with a 20-year smoking history.

Serum creatinine was elevated at 160, with corresponding estimated glomerular filtration rate of 46 ml/min/1.73m². Ca 19-9 normal (2.1 kU/L), normal CEA (1.0 µg/l). Urine cytology negative for malignant urothelial cells.

CT showed mild hydronephrosis and hydroureter secondary to partial obstruction of the distal right ureter within the pelvis. A transition point noted marked by an irregular, lobulated soft tissue mass 39 × 20 mm. Ureteroscopy revealed no intraluminal masses. A stent was inserted due to extrinsic compression from the periureteric mass. A percutaneous

biopsy was not performed due to concerns for sarcoma and seeding of the biopsy tract. Laparoscopic operation was planned.

Repeat CT Intravenous Pyelogram prior to surgery showed the mass had grown 1.6x in 6 weeks (65 × 20 × 66 mm), enhancing on the portal phase (Fig. 1a). FDG PET showed an avid lesion in the right pelvis corresponding with the CT, with probable avid nodal involvement in the left common iliac region, with less specific uptake in the pre carinal and right hilar nodes (Fig. 1b).

At the time of surgery, the mass found was 'concrete like', fibrotic with infiltration throughout the right pelvic side wall. It was approximately 60 × 30 mm in size (Fig. 1c). An intraoperative frozen section showed no malignant cells hence a distal ureterectomy was performed and re-anastomosed to the bladder in combination with a psoas hitch and boari flap.

Final immunohistochemistry (Fig. 2 a,b) and histopathology (Fig. 3 a-c) confirmed Immunoglobulin G4 (IgG4)-related peri-ureteric fibrosis (idiopathic retroperitoneal fibrosis) with 50–60% IgG4+ plasma cells per, up to 180 IgG4+ plasma cells per high power field (hpf). Ki67 positive 1–5%. Post-operative serum IgG4 was not elevated.

After 12 months of follow-up, the patient had not developed relapse or any other IgG4-related disease.

Discussion

Immunoglobulin G4-related disease is a fibro-inflammatory disease

* Corresponding author. Royal North Shore Hospital, Reserve Rd, St Leonards, 2065, Australia.

E-mail address: isabella.williams@health.nsw.gov.au (I.S.C. Williams).

<https://doi.org/10.1016/j.eucr.2021.101666>

Received 24 February 2021; Received in revised form 23 March 2021; Accepted 25 March 2021

Available online 31 March 2021

2214-4420/© 2021 Published by Elsevier Inc. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

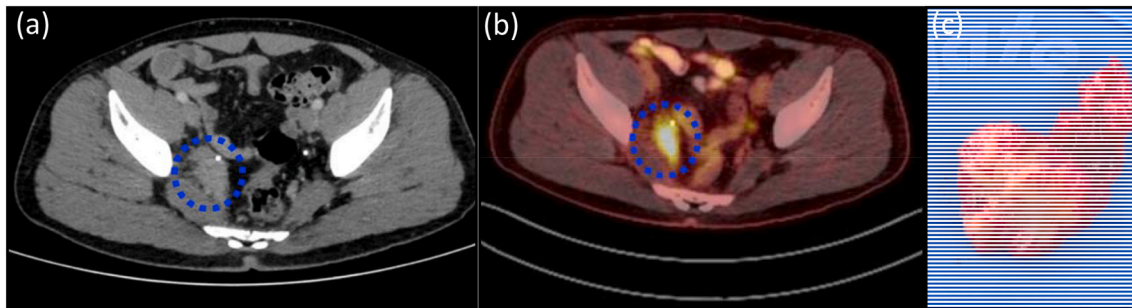


Fig. 1. Radiological images pre-operatively and macroscopic tumour. (a) CT Intravenous pyelogram showing ureteric mass 65 × 20 × 66 mm. (b) FDG-PET showing avid lesion in the right pelvis corresponding with the CT. (c) macroscopic image of ‘concrete like’, fibrotic tumour approximately 60 × 30 mm in size.

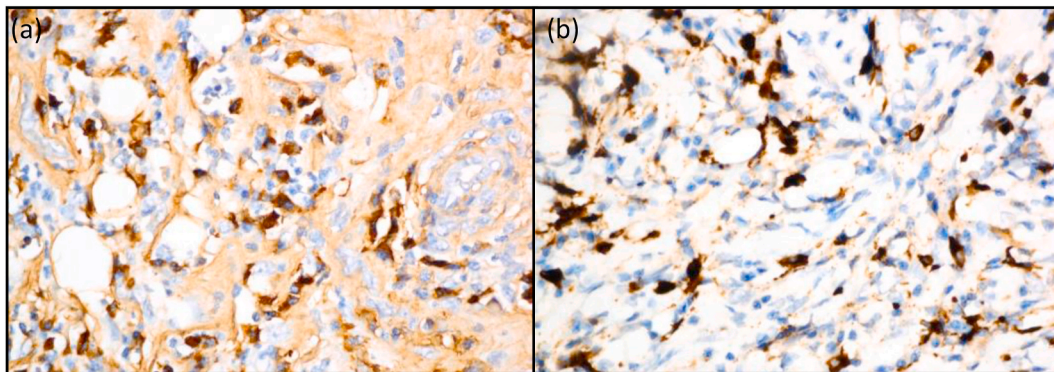


Fig. 2. Immunohistochemistry (a) IgG total immunohistochemistry (IHC). (b) IgG4 IHC 50–60% IgG4+ plasma cells per, up to 180 IgG4+ plasma cells per high power field. (a) and (b) shows increased IgG4:IgG total.

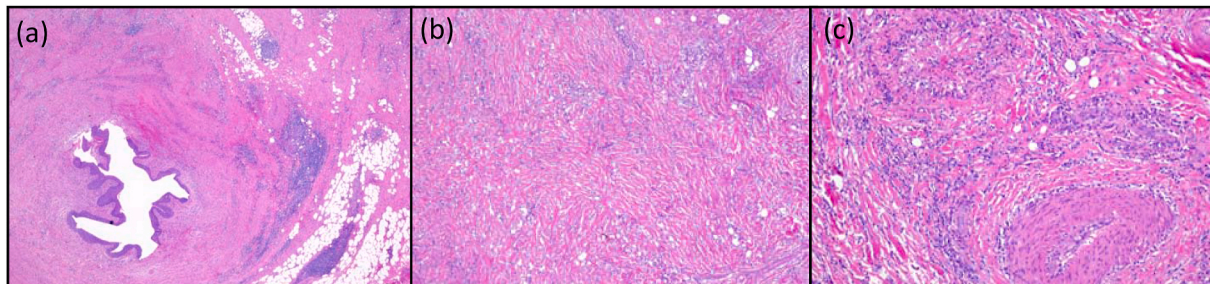


Fig. 3. Histology (a) periureteric – H&E low magnification, showing luminal compression of the ureter due to fibrosis with lymphoplasmacytic inflammation. (b) Storiform fibrosis – H&E high magnification, the fibrosis shows striking storiform architecture. (c) obliterative phlebitis – H&E high magnification, showing obliterative phlebitis.

that may involve different organs and is characterised by specific histopathological appearance and elevated IgG4 plasma cells in mass forming lesions. There is often associated elevation in serum IgG4 levels.¹ It is difficult to diagnose pre-operatively and frequently misdiagnosed as malignancy following radiological imaging. IgG4-RD commonly resolves without treatment, however, can be treated with steroids or other immunomodulators if it does not resolve, or it recurs.²

First described in the pancreas, IgG4-RD has been frequently reported in the lungs, breast, prostate, thyroid, skin, lymph nodes, salivary glands and periorbital tissue.^{1,3} IgG4-RD in the urinary tract has less commonly been reported, mainly involving the kidney and bladder. IgG4-related ureteric disease is an uncommon clinical condition.^{1,3} Examining the literature, only 15 case reports (pertaining to 23 cases) have immunohistochemical evidence of IgG4-related ureteric disease globally.^{2–5}

The three major histopathological appearance features are (1) dense lymphoplasmacytic infiltrate, (2) storiform pattern of fibrosis and (3)

obliterative phlebitis, with two other possible histopathological features – phlebitis without lumen obliteration and increased eosinophils.¹ Cases should ideally have IgG4 immunostaining with 2 or more characteristic histological features.¹

IgG4 immunostaining is essential for pathological diagnosis of IgG4-RD, particularly applying to cases without elevated serum IgG4. Some researchers have suggested a 40% IgG4/IgG plasma cells per hpf cut-off, with most documented IgG4-RD showing >40%, however >30 hpf has been reported to have acceptable specificity in any organ, with >30 hpf in retroperitoneum being histologically highly suggestive of IgG4-RD.¹ Of note, whilst elevated IgG4 serum levels may help diagnose IgG4-RD, serum levels can be elevated as a result of other diseases including parasitic diseases, atopic dermatitis, pemphigus vulgaris, pemphigus foliaceus and even pancreatic cancer.^{1,3}

Before 2010, it was rare for a mass to be tested for IgG4. Cases of inflammatory pathology were characterised as “inflammatory pseudotumour”, “idiopathic segmental ureteritis”, and “retroperitoneal

fibrosis".³ If tested according to diagnostic criteria now, some of these cases may well be IgG4-RD. It has been estimated that up to 60% of all retroperitoneal fibrosis cases are IgG4 related, with ureteric obstruction found in 60%–80% of patients with IgG4 related retroperitoneal fibrosis.⁵

Preoperative diagnosis of IgG4-related ureteric disease is extremely challenging as radiological investigation is often suggestive of urothelial carcinoma, serum markers may or may not be elevated, and requires biopsy. Typical clinical presentations include dull vague abdominal pain, backache, along with nonspecific constitutional symptoms of fever, myalgia, anorexia and weight loss. However, many patients remain asymptomatic.² Ureterectomy/nephroureterectomy is commonly performed to avoid missed diagnosis of urothelial carcinoma.^{3,4}

Conclusion

This case report illustrates a patient presenting with mild hydronephrosis due to a ureteric mass secondary to IgG4-RD. When CT reveals a lesion involving the ureter, and FDG PET shows an avid lesion localised to an unusual region, clinicians should consider IgG4-RD as a differential diagnosis and obtain serum IgG4 levels.

Consent was obtained from the patient. This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Acknowledgements

Dr Justin Vass, Consultant Urologist, who also performed the operation.

References

1. Deshpande V, Zen Y, Chan JK, et al. Consensus statement on the pathology of IgG4-related disease. *Mod Pathol*. 2012 Sep;(9):1181–1192.
2. Ueki T, Miyake T, Narita M, et al. IgG4-related focal retroperitoneal fibrosis in ureter suggestive of colon cancer recurrence and resected laparoscopically: a case report. *Surg Case Rep*. 2020;6:197.
3. Marando A, D'Ambrosio G, Catanzaro F, La Rosa S, Sessa F. IgG4-related disease of the ureter: report of two cases and review of the literature. *Virchows Arch*. 2013;462(6):673–678.
4. Zhong W, Kam J, Beattie K, Yuminaga Ym, Ferguson R, Ko R. A rare case of ureteral IgG4 disease masquerading as Urothelial Carcinoma. *Urology*. 2018;118:e1–e2.
5. Niaz A, Ahmad AH, Rahman K, Saeed MA, Sabir O, Tariff N. IgG4-related retroperitoneal fibrosis: a case report and review of the literature. *J Pakistan Med Assoc*. 2016;66(2):220–222.