



Case Report

Two cases of immunoglobulin G4-related disease diagnosed by transvaginal urethral needle biopsy

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Abbreviations & Acronyms

CRP = C-reactive protein
HPF = high power field
IgG4-RD = immunoglobulin G4-related disease
MRI = magnetic resonance imaging
PET-CT = positron emission tomography-computed tomography

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Introduction: Immunoglobulin G4-related disease is a systemic disease characterized by multifocal systemic involvement. We report two cases of women diagnosed with immunoglobulin G4-related disease in the urethra.

Case presentation: Case 1: A 67-year-old woman presented with discomfort around her perineum. Magnetic resonance imaging revealed a well-defined mass around the urethra. She underwent an ultrasound-guided core needle biopsy of the mass. The pathologic specimen showed immunoglobulin G4 positive cells. Steroid therapy was initiated, causing improvement of symptoms, decreased serum immunoglobulin G4 levels, and shrinking of the mass. Case 2: An 89-year-old woman was accidentally diagnosed with renal pelvic wall thickening on computed tomography. The pathologic specimen captured by ultrasound-guided needle biopsy showed immunoglobulin G4 positive cells. She had no symptoms and received no medical treatment.

Conclusion: The frequency of urethral mass formation in female patients with immunoglobulin G4-related disease may also be high, and an echo-guided transvaginal urethral biopsy may be performed as a definitive diagnostic tool for immunoglobulin G4-related disease.

Key words: IgG4-RD, urethra.

Keynote message

To diagnose IgG4-RD, biopsy of some mass, nodule, or hypertrophic lesion is needed. Women with or without discomfort around her perineum may be able to avoid unnecessary invasive procedures and surgery by ultrasound-guided core needle biopsy. When PET-CT is performed, it may be a good idea to pay attention to the urethra as well.

Introduction

IgG4-RD is a systemic disease characterized by multifocal systemic involvement. There have been only a few cases report describing the involvement of the urethra in a female patient. We report two cases of women diagnosed with IgG4-RD in the urethra.

Case presentation

Case 1

A 67-year-old woman presented with discomfort around her perineum and difficulty in voiding. She had no allergies or history of malignancies. A firm but movable mass in the anterior wall of the vagina was detected on pelvic examination. Laboratory studies, including the serum levels of IgG, and CRP and eosinophil count, uroflowmetry, and cystoscopy findings were unremarkable. MRI revealed a well-defined mass around the urethra. PET-CT showed urethral uptake only. Urethral carcinoma was suspected and the patient underwent an ultrasound-guided core needle biopsy of the mass. The pathologic specimen showed fibrous granulation tissue with lymphocyte and plasma cell infiltration. Immunohistochemical staining revealed IgG4 (more than 50/HPF, IgG4/IgG \geq 50%) positive cells. Laboratory studies showed a serum IgG4 level of 572 mg/dL. These results were concordant with IgG4-RD

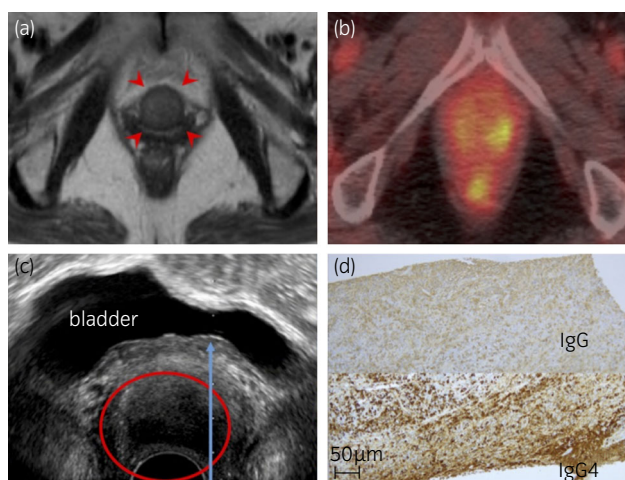


Fig. 1 (a) T2-weighted magnetic resonance imaging showed a well-defined mass around the urethra. (b) Positron emission tomography-computed tomography showed urethral uptake. (c) The patient underwent ultrasound-guided core needle biopsy of the mass. (d) The pathologic specimen showed fibrous granulation tissue with lymphocyte and plasma cell infiltration.

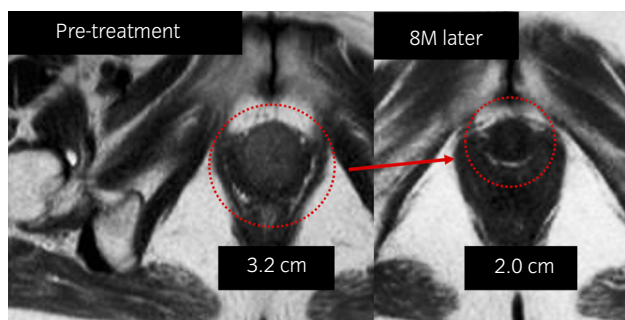


Fig. 2 The urethral mass on follow-up magnetic resonance imaging shrank.

(Fig. 1). Steroid therapy was initiated at 0.6 mg/kg, and the steroid dose was reduced by 5 mg every 2 weeks. At 8 months after the start of treatment, the dose of oral steroids was 8 mg/day, and the serum IgG4 level at that time was 112 mg/dL, which was below the standard value of 135 mg/dL. In addition, her symptoms of discomfort around her perineum and difficulty in voiding improved, and the mass on follow-up MRI shrank (Fig. 2). Since the serum IgG4 level increased when the steroid dose was further reduced, the patient has been taking 8 mg/day of steroids as maintenance therapy for about 2 years.

Case 2

An 89-year-old woman was accidentally diagnosed with renal pelvic wall thickening on CT. She had no allergies or history of malignancies. Abdominal US showed a mass around her urethra protruding into the bladder, mimicking median lobe protrusion of the prostate. On CT, thickened regions were seen in other organs aside from the renal pelvis. Laboratory

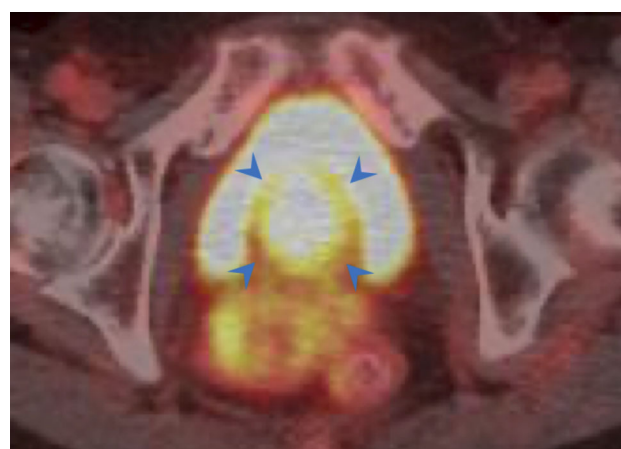


Fig. 3 Positron emission tomography-computed tomography showed uptakes in urethra.

studies showed serum IgG4 levels of 895 mg/dL, but no remarkable findings on the serum levels of IgG, and CRP and eosinophil count. PET-CT showed uptakes in salivary glands, pericardium, both renal pelvis, pelvic lymph nodes, and urethra (Fig. 3). The pathologic specimen captured by ultrasound-guided needle biopsy showed more than 10/HPF IgG4 positive cells and IgG4/IgG \geq 70%. Thus, she was diagnosed with IgG4-RD. She had no symptoms and received no medical treatment.

Discussion

IgG4-RD is a newly established systemic disease, occurring in around 0.28–1.08 per 100 000 people. The average age of occurrence is 58.8 years and it is approximately 1.6–4 times more common in males than in females. IgG4-RD occurs in multiple organs, mainly the salivary glands, lacrimal glands, and bile ducts. Urologic diseases are most commonly found in the retroperitoneal cavity, kidney, and prostate.

The clinical manifestations of the disease are rare (about a quarter of cases), and IgG4-RD is suspected if there is an enlargement, mass, nodule, or hypertrophic lesion in single or multiple organs on imaging. PET-CT imaging is recommended for the diagnosis of other lesions.

IgG4-RD is diagnosed when the following criteria are met: (i) clinically enlarged mass, nodule, or hypertrophic lesion in single or multiple organs; (ii) serum IgG4 level of at least 135 mg/dL; and (iii) cell infiltration, IgG4/IgG-positive cell ratio $>$ 40% on high-power field.¹

The female urethra has not been described as a preferred site for IgG4-RD, and there has only been one case, reported by Choi *et al.*,² and Sangsoad *et al.*³ Patients may either present with symptoms, as in Case 1, or be asymptomatic with multiple organ involvement, as in Case 2.

Aside from these two cases, there have been eight female patients diagnosed with IgG4-RD in the last 5 years at our institution. Not all of them have had CT, but we retrospectively reviewed the images of these cases and found one case with a urethral mass positive on CT and PET-CT (Fig. 4).

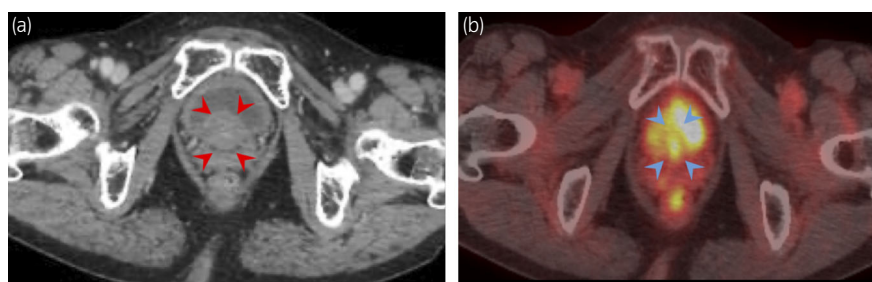


Fig. 4 (a) CT showed a well-defined mass around the urethra. (b) Positron emission tomography-CT showed urethral uptake.

The patient was asymptomatic and was observed to be treatment-free. Including our two cases, the total number of female patients diagnosed with IgG4-RD was 3 out of 10 (30%), suggesting that accumulations in the female urethra may have been missed due to the physiological accumulation in the bladder on PET-CT. Ultrasound-guided transvaginal urethral biopsy is a safe and well-established tissue sampling method and is a diagnostic procedure that should be considered if a mass is found in the urethra.

Conclusion

We encountered two cases of IgG4-RD, wherein the diagnosis was confirmed by ultrasound-guided transvaginal urethral biopsy. The frequency of urethral mass formation in female patients with IgG4-RD may also be high, and an ultrasound-guided transvaginal urethral biopsy may be performed as a definitive diagnostic tool for IgG4-RD to avoid unnecessary invasive procedures and surgery.

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Conflict of interest

The authors declare no conflict of interest.

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