African Journal of Urology

CASE REPORTS

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IgG4-related retroperitoneal fibrosis mimicking renal pelvis tumor: a case report and literature review

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Abstract

Background Retroperitoneal fibrosis (RPF) is a rare disease characterized by the development of a fibroinflammatory mass in the retroperitoneum. Immunoglobulin-G4 related RPF was suggested as a secondary form of RPF and thought to be part of the spectrum of Immunoglobulin-G4 related diseases (IgG4-RD). Patients often present to the clinic because of flank pain. Ranging from mild to end-stage renal failure can be observed. The main purpose of treatment is to preserve renal function. As it is a rare condition, there is no definite treatment strategy. We report a case of 39-year-old man with left flank pain and diagnosis of IgG4-related RPF mimicking a renal pelvis tumor.

Case presentation A 39-year-old male patient presented with left flank pain. MRI suggested solid retroperitoneal mass associated with hydronephrosis in the left kidney collecting system. Upon identifying the retroperitoneal origin of the mass during nephroureterectomy, the procedure was concluded following the acquisition of frozen section and routine pathological samples from the lesion. In the histopathological examination, inflammatory cells were observed and specific immunohistochemistry for IgG-4 was detected focally positive. Following the placement of a DJ stent, immunosuppressive therapy was initiated with Prednol and Azathioprine. After a one-year follow-up period, during which the patient received immunosuppressive treatment and underwent tri-monthly DJ stent replacements, the DJ stent was subsequently removed, revealing complete regression of hydronephrosis.

Conclusions With the correct diagnosis and treatment of IgG4-related RPF, it is possible to prevent irreversible complications of the disease. Because it is a rare disease, case reports in the literature will be useful for treatment.

Keywords Retroperitoneal fibrosis, Immunoglobulin-G4 related disease, Hydronephrosis, Retroperitoneal mass

1 Background

Retroperitoneal fibrosis (RPF) is a relatively rare condition, often underdiagnosed and underreported. It is characterized by the development of fibroinflammatory lesions in the retroperitoneum, particularly in the periaortic and periiliac areas. The etiology of RPF has not been fully elucidated. While secondary retroperitoneal fibrosis can be seen due to conditions such as malignancy, drugs, radiation exposure and infection, the majority of cases are in the idiopathic RPF class, which is thought to be of immunological origin [1]. In recent years, studies on Immunoglobulin-G4-related diseases (IgG4-RD) revealed intense IgG4 plasma cell infiltration in biopsy samples of some idiopathic RPF cases. These results suggested the definition of IgG4-related RPF, which is part of the IgG4-RD spectrum [2]. Clinical findings are usually insidious and of slow onset. Clinical symptoms include flank pain and uremia, which develops with involvement of the ureters. After radiological imaging, biopsy can be taken from the lesion to confirm the diagnosis. Since RPF is a rare disease and there are not enough randomized

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controlled trials, there is no definitive treatment strategy for RPF. However, corticosteroids (CS) or other immunosuppressant agents are frequently used together with KS. Despite high success rates, relapse rates of up to 72% have been demonstrated [3].

2 Case presentation

2.1 Patient information

A 39-year-old male patient presented to our clinic with left flank pain of 2 months durations. He did not have any other disease.

2.2 Clinical findings

No specific findings were observed during the physical examination.

2.3 Diagnostic approach

The patient underwent abdominal magnetic resonance imaging (MRI) which showed grade 2 hydronephrosis in the left renal collecting system and a 4.5×3.5 cm solid mass in the left renal pelvis (Fig. 1). His creatinine value was 1.28 mg/dl and he had leukocytosis (19.500/μL). CRP value were within normal limits.

2.4 Therapeutic intervention

The pre-operative diagnosis was renal pelvis transitional cell carcinoma (TCC) and nephroureterectomy was planned for the patient. During the surgical procedure, a firm fibroinflammatory soft tissue lesion originating from the retroperitoneal region and encircling the renal hilum was identified. The procedure was concluded following the acquisition of frozen section and routine pathological samples from the lesion. In the frozen section examination, the preliminary diagnosis was lymphoma. But in the histopathological examination, inflammatory cells were observed on the fibrous background. Immunohistochemical staining of inflammatory cells with CD20, CD5 and CD3 was positive. IgG-4 was detected focally positive (Fig. 2). In a subsequent surgical intervention, a double J (DJ) stent was placed in the left collecting system, and a retrograde pyelography (RGP) procedure was performed. The left collecting system displayed hydronephrosis, with no discernible filling defect. Rheumatology consultation was requested in terms of IgG4-RD. In the evaluation, the patient's CRP, erythrocyte sedimentation rate, serum IGG and autoantibody values were normal range. For a duration of one year, the patient commenced an oral regimen consisting of 50 mg of azathioprine twice daily and

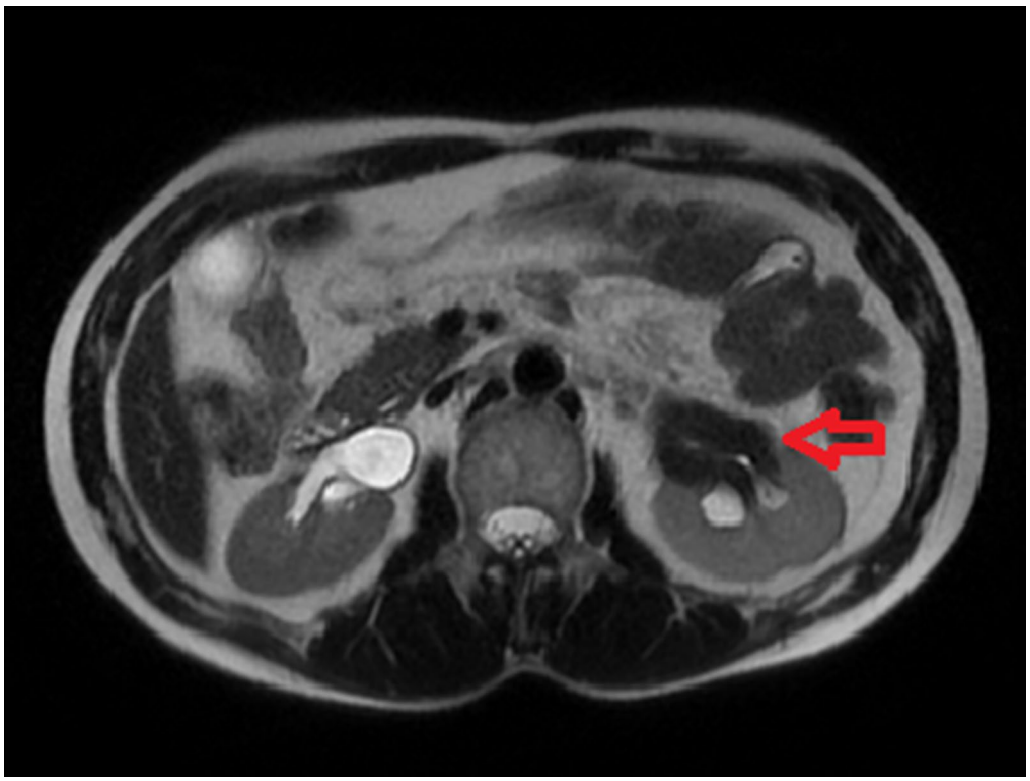

Fig. 1 Abdominal MR image of our patient during the initial diagnosis

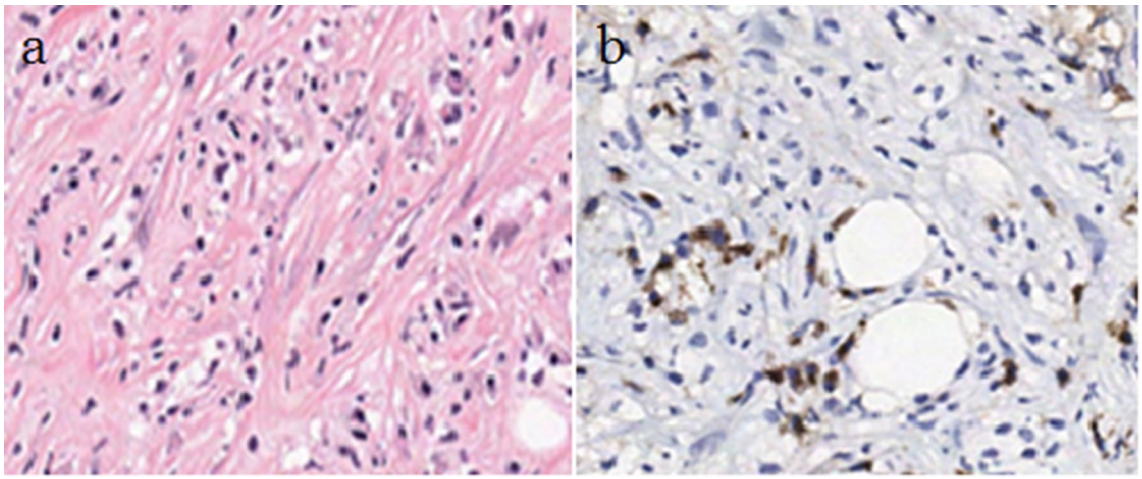

Fig. 2 **a** Chronic inflammation accompanied by fibrosis, **b** IgG-4+ plasma cells

4 mg of prednol once daily. No treatment-related side effects were observed.

2.5 Follow-up and outcome

Upon the patient's initial consultation, the pulmonary computed tomography revealed no abnormalities. The third-month follow-up was performed using abdominal tomography, the lesion shrank to 3.5×2.5 cm and hydronephrosis regressed with DJ stent. After a one-year follow-up period, during which the patient received immunosuppressive treatment and underwent tri-monthly DJ stent replacements, the mass regressed to 26×17 mm and the DJ stent was subsequently removed, revealing complete regression of hydronephrosis. The patient is still being followed up by our clinic without any problem.

3 Discussion

IgG4-related disease is a rare fibroinflammatory condition that can be seen in almost all organs and tissues. In the affected tissues, IgG4 is characterized by plasma cell infiltration, lymphoplasmocytic inflammation, fibrosis, and generally high serum IgG4 levels [4]. Previous studies have shown that IgG4-related disease can affect all organ systems, and the most commonly affected area is the retroperitoneum [5]. Other frequently affected areas; pancreas, biliary tract, submandibular, major glands such as parotid and lymph nodes [6]. In our patient, who were thought as IgG4-related RPF, the localization of the lesion was observed to be in the retroperitoneum and around the left renal pelvis. In 2021, Mizushima et al. showed that 32% of inflammatory lesion localization in 28 patients with RPF was around the renal pelvis or ureteropelvic junction [7].

RPF is a rare disease manifested by fibroinflammatory lesions in the retroperitoneal space. It is usually characterized by fibroinflammatory lesions in the aorta and iliac artery adventitia and surrounding retroperitoneal tissues. RPF, which has a tendency to spread to the retroperitoneal surrounding tissues, often affects adjacent organs such as the ureter [8]. Clinical findings occur as a result of obstructive uropathy caused by pressure on the ureters. The clinical manifestation of the disease can be seen from acute and chronic renal failure to end-stage renal failure [9]. RPF is divided into 2 subgroups as secondary and idiopathic. The idiopathic form accounts for the majority of cases, while secondary RPF accounts for about one third of cases. Secondary RPF is usually caused by infection, drug use, radiotherapy and malignancies. In recent years, RPF has been considered to be part of the IgG4 RD spectrum [10]. In studies conducted with large patient groups, the prevalence of RPF has been shown to be approximately 15–30% among patients with IgG4 RD [5, 11]. While it is known that the epidemiology of RPF is not fully elucidated, its incidence has been shown to be 0.1–1.3/100000 person/year in some studies [9, 12]. While the male/female ratio is approximately 3/1, the mean age of onset has been reported to be 40–60 [12, 13]. In some studies, idiopathic RPF has been shown to be associated with systemic (small vessel vasculitis, rheumatoid arthritis) and organ-specific (hashimoto's thyroiditis) autoimmune diseases [8].

The pathogenesis of RPF is thought to be multifactorial with a combination of genetic and environmental factors. Goldoni et al. have shown that combined exposure to asbestos and cigarettes is a risk factor for the development of RPF [14]. Although its relationship with infection has not been fully clarified, it has been shown

that mycobacterium tuberculosis has a disease-initiating effect [15]. Genetic studies on RPF have shown its relationship with HLA-DR1B*03, which is a well-known risk factor for autoimmune diseases, and this relationship has been confirmed in a case–control study conducted in recent years [16, 17]. These results showed that RPF may be of autoimmune origin.

The main clinical findings of RPF often occur due to ureteral obstruction. Patients may present to the clinic with variable symptoms such as mild fever, nausea and weight loss due to systemic inflammation [12, 18]. The most common symptom is pain. The localization of pain is usually in the abdomen, back or flank region [13, 19]. The most common complication of the disease is hydroureteronephrosis due to ureteral involvement and is seen in approximately 60–70% of cases. Renal failure may occur due to bilateral involvement of the ureters, while unilateral ureteral involvement may be asymptomatic and cause renal atrophy/hypoplasia [9]. About one fourth of the patients have lower extremity edema as a result of retroperitoneal venous and lymphatic vessel compression. Rarely, thrombophlebitis and deep vein thrombosis can be observed [12].

In laboratory findings, an increase in acute phase reactants such as CRP and erythrocyte sedimentation rate is observed in 80–100% of patients. Mild to moderate anemia is a common finding [20]. Serum creatinine elevation and azotemia may be seen due to bilateral ureteral obstruction [7]. In IgG4-related RPF cases, increased serum IgG4 level, eosinophilia and hypocomplementemia may be observed [4]. Studies have shown that 3–30% serum IgG4 level can be within normal limits [21].

Computed abdominal CT, MRI and positron emission tomography (PET-CT) are commonly used for diagnosis. Because it is non-invasive and easy to apply, the first evaluation can be done with abdominal ultrasonography (USG) [2]. However, USG is insufficient to define a retroperitoneal mass. Abdominal CT is valuable for the diagnosis and follow-up of hydronephrosis and retroperitoneal mass. Abdominal MRI is a suitable method for soft tissue evaluation in patients with impaired renal function. Fluorodeoxyglucose (FDG)-PET is a useful method for the evaluation of active inflammation and activity of the retroperitoneal mass, the distribution width of the mass, and the response to treatment [2]. Abdominal MRI was preferred for imaging because the serum creatinine value of our patient was borderline high at the time of admission.

The most valuable method in diagnosis is histological evaluation and immunohistochemical IgG4 staining with a pathological sample. In pathological examination, lymphocyte and plasmocyte infiltration accompanied by fibrosis, lymphoid follicles and immunohistochemical IgG4 positivity are observed [22]. In our patient, the diagnosis of IgG4-related RPF was confirmed after fibroinflammatory lesions were observed in the pathology sample and IgG4 positive detection.

The main aim of treatment is to protect renal functions and to provide urinary drainage. Urinary drainage can be provided with a DJ stent or percutaneous nephrostomy catheter [23, 24]. First-line medical treatment includes glucocorticoids. Although there is no standard treatment protocol, prednisolone treatment is started at a dose of 0.6–1 mg/kg/day for 2–4 weeks. Maintenance therapy is 2.5-5 mg daily for at least 6 months. Immunosuppressive agents such as mycophenolate mofetil, azathioprine, cyclophosphamide, methotrexate and tacrolimus have been shown to be effective in glucocorticoid resistant disease [3, 25, 26]. In selected patients who do not respond to medical treatment, surgical treatment methods such as ureterolysis are beneficial for the treatment of ureteral obstruction [27]. In order to prevent renal damage, a left DJ stent was first applied to our patient, and a successful response was obtained to the combined medical treatment of corticosteroid and azathioprine, as previously practiced in the literature [1].

4 Conclusions

RPF, a rare disease, should also be kept in mind in patients with abdominal pain, retroperitoneal soft tissue lesion and hydronephrosis. Promising results are obtained with immunosuppressive therapy. With the increasing awareness of IgG4-related RPF, which has been defined in recent years, it is possible to prevent its irreversible complications with early diagnosis.

Abbreviations

RPF	Retroperitoneal fibrosis
IgG4-RD	Immunglobulin G-4 related disease
CS	Corticosteroids
MRI	Magnetic resonans imaging
TCC	Transitional cell carcinoma
DJ	Double J
RGP	Retrograde pyelography
CT	Computerized tomography
PET-CT	Positron emission tomography
USG	Ultrasonography

Acknowledgements
Not applicable.

Author contributions
GS was a major contributor to the conception of the study and responsible for drafting, writing, revision, and approval of final version of manuscript. TS contributed to drafting and writing. MD senior author contributed to editing and final submission composition. All authors read and approved the final manuscript.

Funding
Not applicable.

Availability of data and materials
Not applicable.

Declarations

Ethics approval and consent to participate
Not applicable.

Consent for publication
Written informed consent for publication has been acquired from the patient.

Competing interests
The authors declare that they have no competing interests.

Received: 2 October 2023 Accepted: 21 December 2023
Published online: 13 February 2024

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