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Case report

An atypical cause of retroperitoneal fibrosis: Case report and literature review

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Abstract
Introduction: Retroperitoneal fibrosis (RPF) is a rare inflammatory disease resulting in the development of a retroperitoneal mass, which may encase the aorta and its branches, as well as the ureters.
Observation: The systemic inflammatory response causes constitutional symptoms. The mass itself leads to symptoms of non-specific back pain and abdominal pain, as well as ureteric obstruction and subsequent renal insufficiency. Immunoglobulin 4 (IgG4) has recently been found to be involved in the pathogenesis of multiple autoimmune and inflammatory disorders, including RPF. Blood work-up, imaging and biopsy of the mass remain the mainstay of diagnosis.
Conclusion: RPF remains a diagnosis of exclusion. Treatment hinges on corticosteroids, but other immunosuppressants and disease-modifying agents are also being used more commonly. Surgical intervention is only carried out when conservative measures have failed or are contraindicated, and in order to preserve renal function.

Introduction

Retroperitoneal fibrosis (RPF) is a systemic inflammatory disease resulting in retroperitoneal plaque formation. This mass is initially inflammatory in nature, and later evolves into a fibrotic mass [1]. The estimated incidence varies between 0.1 in 100 000 and 1 per 200 000 in different studies, but little epidemiological data exists to confirm or refute this [1]. Much controversy surrounds the diagnosis and treatment of this disease. With this case report, we wish to highlight a patient with immunoglobulin-mediated RPF confirmed on histology.

Case report

A 56-year-old male, with no known comorbidities, presented with right flank pain. The patient was found to have microscopic

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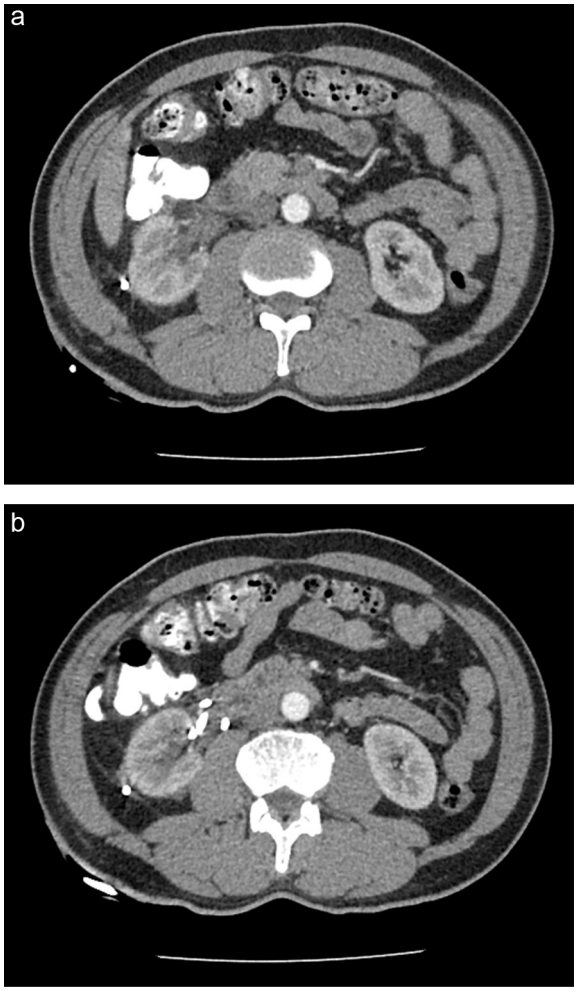

Fig. 1 (a) Mass at the level of the renal hilum. (b) Mass at the level of the renal hilum – nephrostomy visible in proximal ureter.

haematuria on urine dipsticks on admission, as well as abnormal renal function, with a creatinine of 134 μmol/L. The erythrocyte sedimentation rate (ESR) was 60, with a white cell count (WCC) of 7.2×10^9.

On renal ultrasound, the patient was found to have right-sided hydronephrosis and proximal hyroureter. The patient then underwent an uncontrasted computer-tomography (CT) scan of his abdomen and pelvis in order to assess for a cause for the unilateral hydronephrosis. The CT scan revealed a mass extending from the level of the renal hilum on the right and encasing the right ureter as noted in Fig. 1.

A right percutaneous nephrostomy tube was inserted as an emergency, and the patient's renal function subsequently decreased to 109 μmol/L. A double-J (DJ) ureteric stent was placed (antegrade) while pending further work-up. The patient was also started on high-dose oral glucocorticoid therapy due to the CT features and raised ESR suggesting RPF. Despite ureteric stenting and glucocorticoid therapy, it was not possible to remove the percutaneous nephrostomy tube. During attempted clamping of the nephrostomy tube, the patient experienced pain relieved only by unclamping of the tube. The cause was thought to be related to extrinsic compression by the mass.

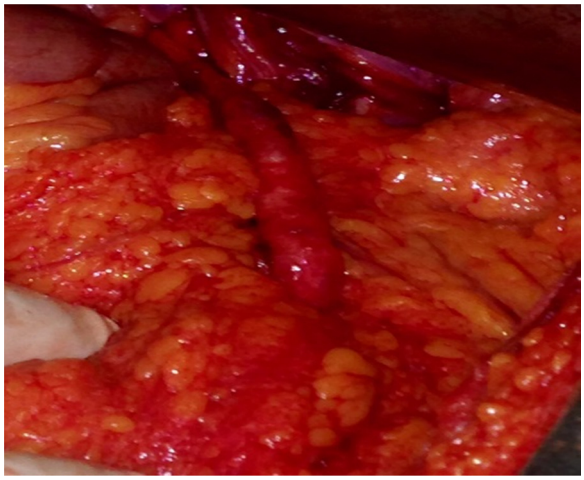

Fig. 2 Right ureter mobilised with omentum to be used for wrapping ureter.

Diagnostic and therapeutic laparoscopy was performed in view of the ongoing obstructive uropathy despite ureteral stenting and glucocorticoid therapy. The mass was noted to resemble an inflammatory plaque, and frozen section specimens were sent intra-operatively. The results of frozen section revealed inflammatory tissue, with no features of malignancy. Ureterolysis was performed, whereby the ureter was released from the inflammatory plaque and wrapped in omentum, as seen in Fig. 2. Unfortunately, it was necessary to convert to laparotomy due to challenges with tissue planes and the proximity of vital structures to the obstructed portion of the ureter.

The percutaneous nephrostomy tube, as well as the DJ stent were both removed within 6 weeks of the ureterolysis procedure. The patient has normal renal function and is currently asymptomatic. Formal histology confirmed the diagnosis of IgG4-related retroperitoneal fibrosis with extensive collagenous fibrosis, dense lymphoplasmacytic chronic inflammation, obliterative phlebitis (Fig. 3a), and >30 $IgG4^+$ plasma cells per high power field (Fig. 3b).

Discussion

RPF was first described by Ormond in 1948 [2]. The classical description is that of a retroperitoneal plaque encasing the great vessels and the ureters from the level of the renal hilum up to the pelvis [1]. Seventy percent of these cases are idiopathic in nature, with the other 30% having an underlying precipitating cause [1,3]. The most important of these underlying causes that a treating physician must rule out is a malignant process. Malignancy has been found in 8–10% of cases of patients with RPF [1]. Other precipitants are documented in Table 1 [1,4].

Other disease processes that may be associated with RPF, but not necessarily precipitating causes, include [1,3]:

- Sclerosing cholangitis
- Pancreatitis
- Riedel's thyroiditis
- Ankylosing spondylitis
- Uveitis
- Systemic lupus erythematosis

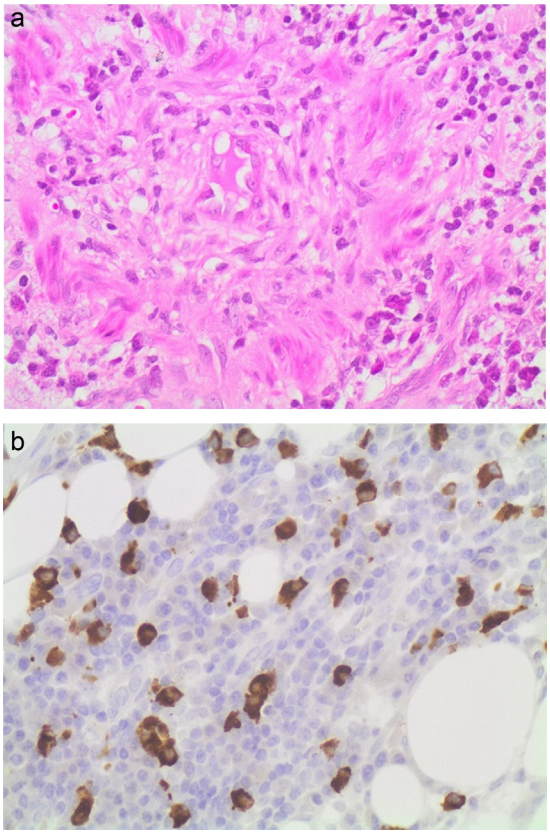

Fig. 3 (a) Fibrous obliteration of the lumen of a small vein, the wall of which is infiltrated by lymphocytes and plasma cells (haematoxylin and eosin stain, high power magnification). (b) Numerous IgG4$^+$ plasma cells (immunohistochemical stain for IgG4, high power magnification).

Table 1 Precipitating causes of RPF.

- Drugs
  - Methysergide
  - Amphetamines
  - Beta-blockers
- Irradiation
- Chemicals
  - Talcum powder
  - Methyl methacrolate
- Inflammatory processes
  - Amyloidosis
  - Ascending lymphangitis
  - Inflammatory bowel disease
- Retroperitoneal haemorrhage
  - Abdominal and pelvic surgery
  - Ruptured viscera (Trauma)
  - Henoch-Schonlein Purpura
- Peri-arteritis (release of ceroid)
  - Atherosclerosis
- Infection
  - Gonorrhoea
  - Recurrent UTI
  - Tuberculosis
  - Syphilis
- Endometriosis

Patients present with a variety of non-specific symptoms. These include abdominal or back pain, fever, malaise, loss of weight, and may develop new-onset hypertension, as well as obstructive uropathy [1,4].

Investigations include blood work-up, with a serum creatinine, a WCC and an ESR as the initial tests to be performed [1,3]. These are non-specific tests, but RPF tends to be associated with raised inflammatory markers, including a high ESR, as well as a raised C-reactive protein (CRP) level [1,5]. Other blood tests that may be considered include those for autoimmunity work-up, such as anti-double-stranded DNA, anti-nuclear antibody, anti-neutrophil cytoplasmic antibodies, and recently, raised IgG4 levels. IgG4 levels have been found to be increased with RPF, and a IgG4:total IgG has also been proved to be useful in that a higher ratio confirms the diagnosis [6]. Serum IgG4 levels may or may not be raised. These patients also tend to present with features of autoimmune disease as opposed to the classical symptoms associated with RPF, including constitutional symptoms alone, generalised painless lymphadenopathy, autoimmune pancreatitis and sialadenitis [7,8]. Renal dysfunction in these patients may also be caused by IgG4-related tubulo-interstitial nephritis, as opposed to the obstruction from RPF itself [9].

It is becoming apparent that more cases that were previously labelled idiopathic RPF are actually IgG4-related RPF [9,10]. The true importance of this finding is yet to be confirmed. However, given that many patients with IgG4-related RPF have associated autoimmune symptoms, it is important to specifically look for these symptoms in order to optimise overall patient care. Treatment is currently still glucocorticoid-based, but with further investigations it may be found that it may be more useful to use B-cell depletion therapy (e.g. Rituximab) for these cases [8].

On imaging, CT scan and magnetic resonance imaging (MRI) are considered to be the most sensitive and specific for RPF [3,6]. The classical appearance of RPF on a CT scan is a centrally situated retroperitoneal plaque from the level of the renal hilum and extending distally until the aortic bifurcation at the level of the sacral promontory [1,6]. A patient with the afore-mentioned clinical presentation, a raised ESR on blood work-up, and a CT scan suggestive of the diagnosis may be treated empirically as RPF without biopsy. However, any atypia in the presentation or work-up should alert one to the possibility of a retroperitoneal malignant process. This warrants biopsy by either percutaneous or opens means [1].

Medical management includes the use of high-dose steroids initially, and then tapering to chronic low-dose continuation therapy [1,11]. However, much controversy exists regarding the optimal dosage and dosing schedule. One regimen that has been suggested involves using 60 mg of prednisolone on alternate days for 2 months, and then tapering down to 5 mg on alternate days over the following 2 months [11]. There are many options that have been tried, each with varying levels of success. A successful treatment regimen is regarded as improved symptoms, as well as regression of the mass and normalisation of the ESR [1,11]. Other methods of medical management have been used, including: azathriprine, mycophenolate mofetil, tamoxifen, and pulses of methylprednisolone [3,4,6,12]. Rituximab has been used for IgG4-related disease in an off-label capacity [8]. Due to the rare nature of the disease, and the variability in patient response to treatment, it is difficult to truly assess

which treatment regimen is optimal. Follow-up routines also vary, but include symptom assessment and ESR monitoring every 3–6 months, and possibly CT scan follow-up to assess for regression of the mass [11].

Surgical management plays a role in medically refractory cases, as well as in cases where medical therapy is not tolerated or contra-indicated [1]. Surgical management involves biopsy of the mass, as well as ureterolysis (release of the ureters from the plaque) with intra-peritonealisation and wrapping in omentum [1,13]. This prevents further entrapment of the ureters should the process progress or recur. One criticism of surgical management is that it does not manage the systemic symptoms of the disease process [12].

Conclusion

RPF is an uncommon disease process that is difficult to diagnose and requires a high index of suspicion in order to facilitate expeditious diagnosis and management. Atypical presenting features such as a unilateral mass, as seen with our patient, must raise the question of malignancy requiring full work-up to exclude this possibility. This case also highlights autoimmune entities, such as IgG4-related disease, that may be a part of the pathogenesis of the disease process. These entities should be sought as they may influence management protocols in the future. Medical management is currently regarded as first-line treatment of choice, but surgical management may be necessary in selected patients. Further studies with regards to the aetiology of RPF are needed so as to optimise patient care.

Conflict of interest

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Authors' contributions

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Sunil Sinha: Co-author; assisted with ensuring facts of the case were correct (as he was the surgeon involved). Also provided intra-operative images used. (Email address: sinhasj@hotmail.com).

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