

Back pain and acute kidney injury

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Case presentation

A 45-year-old Somali man with a background of type 2 diabetes mellitus was referred to the acute medical take with lethargy, anorexia and an acute deterioration in his renal function. He had been seen in hospital several weeks earlier for a dull lower back pain without 'red flag' features (such as symptoms and signs that might suggest a radiculopathy or cauda equina syndrome). He had undergone a CT of the kidneys, ureters and bladder (KUB) that showed no renal tract abnormalities but detected incidental sclerotic foci in his iliac bones, possibly representing bone islands. An outpatient radionuclide bone scan and MRI of the lumbar spine and pelvis were performed for clarification, both of which were reported as normal. The patient's pain was therefore attributed to muscular strain and treated with simple analgesia (paracetamol and diclofenac).

The patient presented with a worsening in his back pain, associated with lethargy and anorexia, and new onset left testicular swelling. His blood creatinine had risen from 57 to 591 $\mu\text{mol/l}$ and urea from 5 to 25.2 mmol/l . Other bloods were unremarkable, although the C-reactive protein was 53 mg/l . There was no clinical evidence of severe dehydration or fluid overload, the serum potassium was 6.1 mmol/l and there was no severe metabolic acidosis.

What is the differential diagnosis and the most likely diagnosis?

The analgesia (diclofenac) might have provoked acute kidney injury through a combination of gastritis with decreased oral intake and a direct nephrotoxic effect. The admitting team was concerned, however, about the new testicular swelling and wanted to exclude aggressive testicular malignancy with retroperitoneal metastasis causing ureteric obstruction. Alternatively, left-sided varicocele can be encountered in the context of retroperitoneal masses (such as renal cell carcinoma) as the result of obstruction of the left internal spermatic or renal vein.¹

What is the initial management?

The patient was admitted for close observation of his renal function and fluid balance by hourly urine output measurement and repeated biochemistry. All potentially nephrotoxic drugs (such as the diclofenac) were discontinued, as was metformin.

An out-of-hours repeat CT KUB was requested to further investigate the possibility of post-renal obstruction. This revealed bilateral ureteric obstruction and hydronephroses caused by a para-aortic soft tissue mass (measuring 175 mm long axis, 57 mm width and 30 mm depth), which had not been visible on previous imaging (Fig 1a, b). This extended from the level of the left renal artery to that of the common iliac arteries, enveloping the origin and primary branches of the inferior mesenteric artery as well as both ureters. The patient underwent emergency nephrostomy insertion (Fig 1c, d), which resulted in rapid normalisation of his renal function.

Testicular ultrasound showed a moderate hydrocoele but no primary tumour, and contrast CT of the chest, abdomen and pelvis did not reveal other primary or satellite lesions. The patient's erythrocyte sedimentation rate and his serum prostate specific antigen, lactate dehydrogenase, immunoglobulins, α -fetoprotein and β -human chorionic gonadotrophin concentrations were normal.

Case progression

As the nature of the retroperitoneal mass remained uncertain, a CT-guided biopsy was performed. Histology showed marked fibrosis and a mixed inflammatory cell infiltrate, which was rich in plasma cells and with a few eosinophils (Fig 2). There were no granulomata or acid/alcohol fast bacilli. Immunohistochemistry indicated a mixture of B and T lymphocytes, without evidence of lymphoma or metastatic germ cell tumour. A specific request for IgG4 immunohistochemistry demonstrated numerous aggregates of IgG4+ plasma cells (>20/high power field). The IgG4/IgG ratio in the plasma cells was more than 70%, corroborating

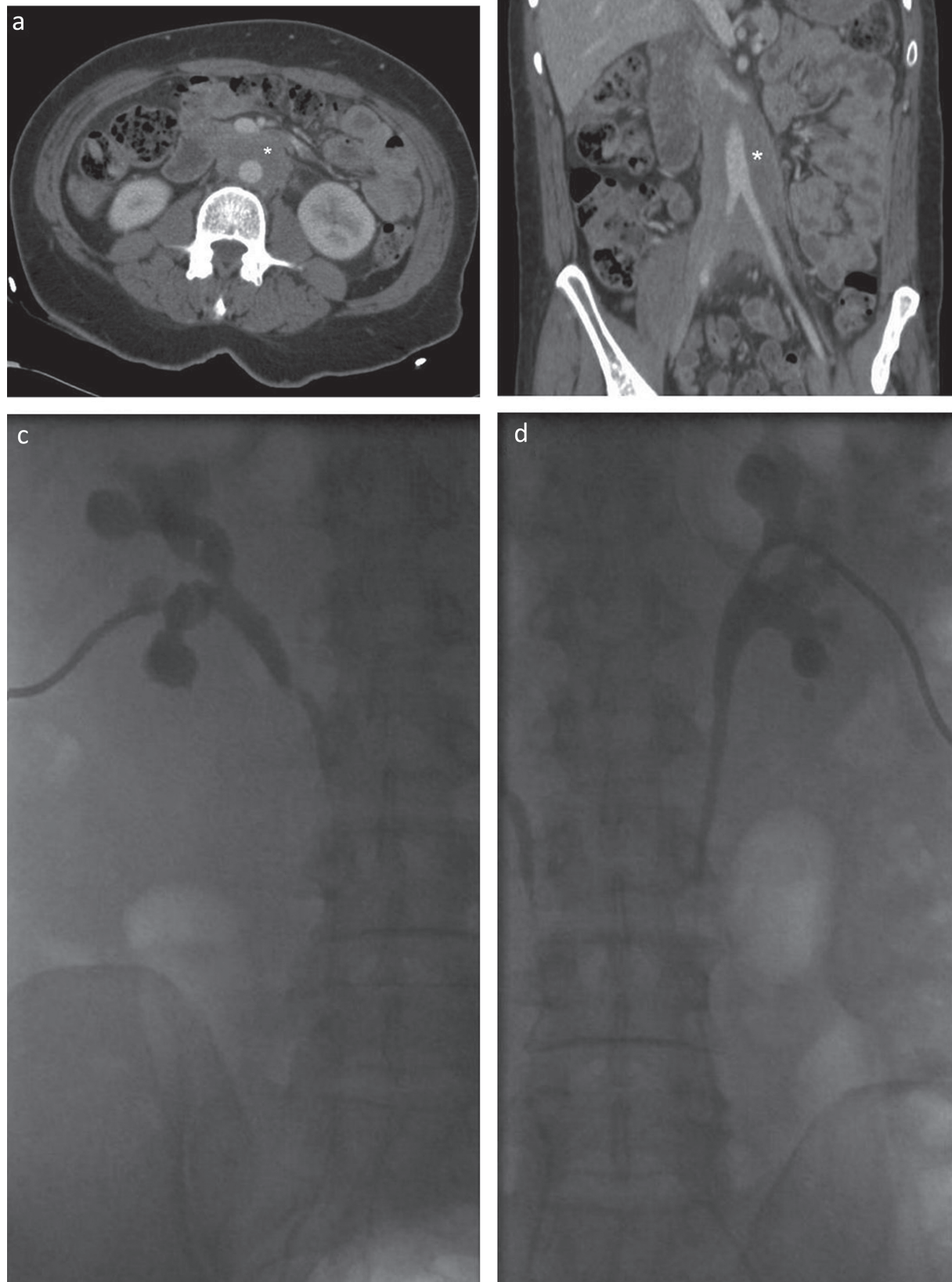
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Key learning points

- 1 If acute kidney injury is thought to be caused by obstructive uropathy on clinical grounds, prompt imaging is essential for subsequent management.
- 2 Retroperitoneal masses of unestablished aetiology require tissue diagnosis to determine prognosis and treatment.
- 3 Retroperitoneal fibrosis is a rare but highly treatable cause of retroperitoneal masses causing obstructive uropathy.
- 4 IgG4-related systemic disease is a recently recognised entity that encompasses a number of previously described conditions that feature fibrotic inflammation, including retroperitoneal fibrosis.

Fig 1. CT of the kidneys, ureters and bladder (KUB). (a) Transverse and (b) coronal sections demonstrating an extensive inflammatory mass (*) enveloping the aorta and both ureters. Nephrostograms demonstrate dilatation of the (c) left and (d) right renal pelvicalyceal systems, and obstruction to flow of contrast through both ureters.



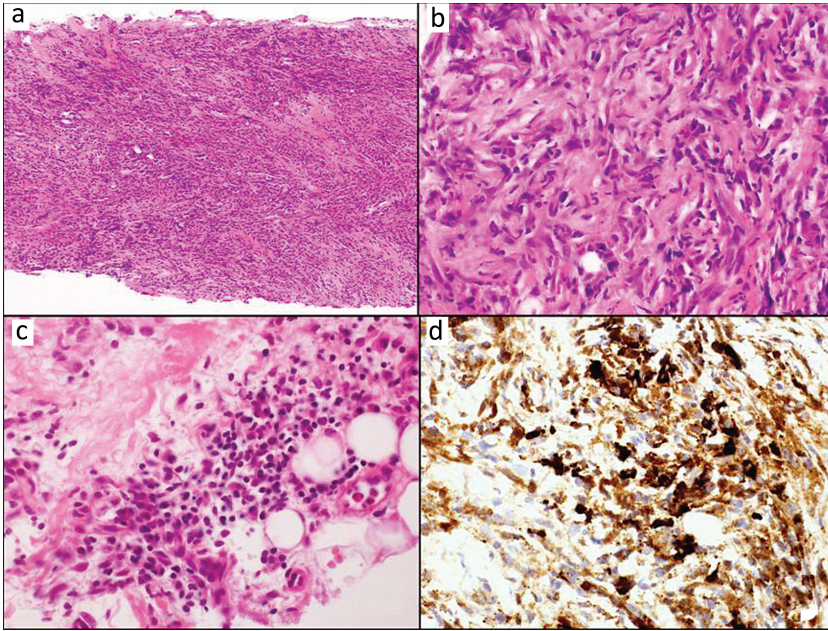


Fig 2. Histological analysis of the retroperitoneal mass biopsy. (a) Low-power images (haematoxylin and eosin stain, magnification x100) demonstrate fibrosis with a rich inflammatory cell infiltrate. (b, c) High-power views (x400) show fibroblasts, eosinophils and plasma cells. (d) Specific immunostaining for IgG4 reveals an abundance of positive cells.

a diagnosis of an IgG4-related systemic disease causing retroperitoneal fibrosis (RPF). Plasma levels of IgG4 were within normal reference limits.

Treatment with 40 mg prednisolone daily was initiated, and then slowly tapered to 5 mg daily over 2 months. Interval CT scanning confirmed substantial regression of the inflammatory mass, with consequent resolution of ureteric compression on nephrostogram allowing placement of bilateral ureteric stents and removal of the nephrostomies.

At last review, the patient had tapered his prednisolone dose to 5 mg once a day. A MAG3 renogram showed kidneys of equal size with a differential function of 52% left kidney and 48% right kidney, good uptake of the tracer and a brisk outflow pattern with no evidence of retention.

Discussion

Retroperitoneal fibrosis is a rare disorder that can present to acute medical services. Insidious onset back pain, although non-specific, is the most common symptom. Constitutional features including lethargy, anorexia, weight loss and low-grade pyrexia should be actively sought. Despite early investigation of our patient with imaging, the diagnosis was not made until a strikingly rapid evolution of disease volume resulted in ureteric and probably venous obstruction, and histology was obtained.

The incidence of RPF is 0.1 per 100,000 annually, with a 2–3:1 male predominance. It principally affects patients between the ages of 50 and 60 years.² It is idiopathic in two-thirds of cases, although several secondary causes are recognised, including

abdominal aortic aneurysms, drugs (most notably the synthetic ergot derivative methysergide), radiotherapy, mycobacterial infection and carcinoid tumours.² The pathogenesis of idiopathic RPF has been further delineated in recent years by the increasing recognition of IgG4-related systemic disease.^{2–4} First described in the early 2000s, IgG4-related inflammatory disease was originally identified in the pancreas (autoimmune pancreatitis) and subsequently in other organs, such as the salivary, lachrymal and thyroid glands. In many cases, elevated levels of serum IgG4 are detectable.⁴ The exact role of IgG4 is not yet entirely clear, but its detection in serum and tissues implies a modified Th2 response.⁴ Possible aetiological factors are human leukocyte (HLA) haplotype, molecular mimicry of pathogens such as *Helicobacter pylori*, and autoimmunity.⁴

In retroperitoneal fibrosis that is associated with IgG4-related disease, imaging typically reveals inflammatory masses rather than diffuse involvement. Such masses often involve the abdominal aorta, the kidneys or the ureters, and commonly cause ureteric obstruction. The abdominal aorta can also be aneurysmal and

peri-aortitis can be a dominant feature, so its imaging is essential.⁵ These radiological findings along with an appropriate clinical presentation can be sufficient for diagnosis and trial of treatment. Biopsy remains important when there is any uncertainty, given the wide-ranging differential. Histology is usually diagnostic and shows characteristic lymphoplasmocytic inflammation, 'storiform' (matted and irregularly whorled) fibrosis, obliterative phlebitis with numerous eosinophils, and a substantial number of plasma cells expressing IgG4.^{3–5} The microscopic features are more important for diagnosis than the detection of IgG4 in serum or the finding of IgG4-positive plasma cells.⁴

Although urological intervention is often required in the acute management of RPF for emergency relief of ureteric obstruction, corticosteroids remain the mainstay of treatment. They both improve symptoms and reduce disease volume. Monitoring of therapeutic response (and relapse) is not straightforward as serum IgG4 levels correlate poorly, and therefore sequential imaging is usually required.⁴ There might be a role for 18F-fluorodeoxyglucose position emission tomography (FDG-PET) to quantify inflammatory activity, particularly with regards to the vasculature.⁴

In some patients, long-term maintenance on steroids can be necessary, and steroid-sparing agents including cyclophosphamide, methotrexate, azathioprine and mycophenolate mofetil often need to be considered.⁴ B-cell depletion with rituximab can give rapid improvement,⁴ and the selective oestrogen receptor modulator tamoxifen has been shown to be beneficial in some cases.²

In summary, this case highlights the emergency presentation of a rare disease. There are several key learning points, including

the importance of early recognition and assessment of acute kidney injury, the role of early imaging to identify obstructive uropathy, the significance of acute scrotal swelling in suggesting this pathology, and the importance of tissue diagnosis for retroperitoneal masses of unestablished aetiology. Consideration of the diagnosis of retroperitoneal fibrosis will expedite appropriate histological analysis and institution of disease-modifying therapy, minimising long-term risks to renal function.

References

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