Case report

Bilateral calcified ureteral stenosis in eosinophilic granulomatosis with polyangitis

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SUMMARY

Ureteral calcification is a rare complication of systemic vasculitis. Bilateral ureteral calcification in a patient with eosinophilic granulomatosis with polyangitis led to obstructive uropathy. A combination of immunosuppressive therapy and ureteral reconstruction successfully restored kidney function.

BACKGROUND

Renal involvement is present in one quarter of patients with eosinophilic granulomatosis with polyangitis (EGPA), usually manifesting as glomerulonephritis.¹ Acute kidney injury due to calcified ureteral obstruction is a rare complication of vasculitis, and few cases of EGPA have been published in the literature.

CASE PRESENTATION

A 39-year-old previously healthy man presented to an outside hospital with progressive leg weakness, necrotic skin lesions and acute lower abdominal pain. Three months prior to this presentation, right foot numbness and weakness of both lower extremities developed, causing him to drag his right leg as he walked. Discoloration of his fingertips and both plantar surfaces developed, and he developed anterior ulcerations on both shins. He had significant eosinophilia (10 998 cells/ μ L), but myeloperoxidase (MPO) and proteinase 3 (PR-3) antineutrophil cytoplasmic antibodies (ANCA) were negative. A skin biopsy of the sole of the right foot revealed eosinophilic vasculitis (figure 1), and the nerve conduction tests showed mononeuritis multiplex, resulting in a diagnosis of EGPA. Prednisolone 40 mg per day was started, then tapered to 25 mg over 2 weeks.

Two days prior to presentation, acute right lower abdominal pain developed and the patient presented to the emergency department of the outside hospital. The patient had had a similar right groin pain 2 months prior, and renal function and a CT scan were unremarkable at that time. There were no fevers, chills, cough, sputum, nausea, vomiting, diarrhoea, haematochezia, dysuria, or haematuria.

His medical history was unremarkable, aside from the recent diagnosis of EGPA. His prescription medications included prednisolone 25 mg/day, sulfamethoxazole-trimethoprim 400 mg/80 mg/day, loxoprofen 180 mg/day, lansoprazole 15 mg/day, cilostazol 200 mg/day and duloxetine 300 mg/day. The patient was a professional chrysanthemum

grower and lived with his wife and two children. He smoked tobacco one pack per day for 19 years and drank minimal alcohol. He did not use illicit drugs, had no recent travel, and no known exposure to animals.

On physical examination at the other hospital, the temperature was 36.9°C, blood pressure was 141/86 mm Hg, the pulse 94 beats per minute, the respiratory rate 18 breaths per minute, and oxygen saturation on ambient air was 97%. Patient was alert, but in moderate distress due to abdominal pain. The heart and lung examinations were normal. There was tenderness at right lower abdomen but no rebound. Multiple skin ulcers with necrotic changes were found on fingertips and legs (figure 2A, B). Neurological examination showed intact cranial nerves. Strength was five out of five in all muscle groups, except for right quadriceps, anterior tibial muscle and gastrocnemius muscle being four out of five. Sensation to light touch and pinprick was reduced in dorsum of bilateral feet. Deep tendon reflexes were symmetrical.

The patient was transferred to this hospital for further evaluation.

INVESTIGATIONS

Laboratory studies at the other hospital (2 days prior to the transfer) showed a serum sodium of 138 mmol/L, a potassium of 4.2 mmol/L, a chloride of 100 mmol/L, a calcium of 9.2 mg/dL, a phosphate of 2.9 mg/dL, blood urea nitrogen level of 15.9 mg/dL and serum creatinine (Cr) of 1.24 mg/dL (compared with Cr 0.74 mg/dL, 2 months ago). Liver function tests, lipase and amylase were all normal. Total protein was 6.7 g/dL and albumin was 3.8 g/dL. C reactive protein (CRP) was 3.3 mg/dL and erythrocyte sedimentation rate was 31 mm

Figure 1 Skin biopsy of the sole of the right foot revealed eosinophilic vasculitis.

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Figure 2 Multiple skin ulcers with necrotic changes. (A) Right fingertips. (B) Left lower leg.

per hour. The complete blood counts showed a leucocyte count of 5780/ μ L, and neutrophils were 53.7% and eosinophils had fallen to 0.3% (17 cells/ μ L). Haemoglobin was 136 g/L, haematocrit was 41.2%, and mean corpuscular volume (MCV) was 87 fL, with a platelet count of 316 000/ μ L. Urinalysis showed no haematuria, proteinuria or casts. Additional studies at our hospital showed normal C3 and C4 levels, and negative monoclonal pattern on immunoglobulin panel. Parathyroid hormone—intact level was 34 pg/mL (normal range: 10–60 pg/mL). Chest radiography and ECG findings were unremarkable. CT scan of abdomen with contrast material showed bilateral ureteral stenosis, hydronephrosis and leakage of urine into the right retroperitoneum (figure 3A, B). Cytology of the urine was negative and urine cultures did not grow any organisms,

Figure 3 (A) Coronal view. (B) Axial view. CT scan of abdomen with contrast material showed bilateral ureteral stenosis (long arrows), in which the length of calcified lesion was 7.5 cm on right side and 3 cm on left side. There was hydronephrosis and leakage of urine into the right retroperitoneum (short arrow) before nephrostomy.

including mycobacterium tuberculosis. Postrenal acute kidney injury due to bilateral ureteral stenosis was diagnosed.

DIFFERENTIAL DIAGNOSIS

The differential diagnosis of bilateral calcified ureteral stenoses with acute kidney injury in a patient with EGPA on corticosteroids includes ureteral carcinoma, ureteral tuberculosis, schistosomiasis, normocalcemic hypercalciuria, sarcoidosis and vasculitis.

Antinuclear antibodies, rheumatoid factor, MPO and PR3 ANCA remained negative. Interferon-gamma releasing assays testing and a urine culture for tuberculosis were also negative.

TREATMENT

Acute kidney injury (Cr 1.48 mg/dL) and anuria developed on hospital day 14. With unresolving skin lesions and vasculitic neuropathy as well as rapidly progressive calcified ureteral stenosis in 2 months, oral prednisolone was increased to 60 mg/day, and intravenous cyclophosphamide was begun. Bilateral percutaneous nephrostomies were placed, and kidney function promptly recovered.

OUTCOME AND FOLLOW-UP

Six cycles of intravenous cyclophosphamide were given, and prednisolone was gradually tapered. His skin ulcers and neurological manifestations responded rapidly. Eosinophilia recurred when prednisolone was 11 mg/day, and mepolizumab was added. Despite therapy, he continued to be anuric whenever his percutaneous nephrostomies were occluded and an antegrade pyelogram showed long calcified stenoses of both ureters without detectable forward flow (figure 3).

Surgical reconstruction was elected in order to eliminate the need for permanent external drainage. The left ureter was amenable to ureteropyelostomy, but the repair of the right ureter required interposition of intestinal tissue.

Pathology of left ureteral surgical specimen showed obstruction of ureter by calcification and granulomatous changes without signs of eosinophilic vasculitis (figure 4). Two months after surgery, prednisolone was tapered to 8 mg/day. His kidney function has remained normal, and he is free of vasculitic symptoms.

Figure 4 Pathology of left ureteral surgical specimen showed obstruction of ureter by calcification and granulomatous changes without signs of eosinophilic vasculitis.

Table 1 Characteristics of ureteral stenosis in patients with eosinophilic granulomatosis with polyangiitis

Reference	Age, sex	Presentation	Associated conditions	Presentation of ureteral stenosis	Nephrostomy	Treatment	Outcome
Symes <i>et al</i> ⁷	19 M	Abdominal pain	Multiple perforation of small bowel	In remission	+	Steroid Immunosuppression	Need operation
Cortellini <i>et al</i> ⁸	22 M	Anuria	Asthma mononeuritis multiplex	Initial presentation	+	Prednisolone, cyclophosphamide	Need operation
Watanabe <i>et al</i> ⁹	43 M	Abdominal pain	Asthma mononeuritis multiplex perforation of small bowel	When tapering prednisolone 60 mg–45 mg	+	Prednisolone, cyclophosphamide	Improved
Kawai <i>et al</i> ¹⁰	55 F	Abdominal pain Anuria	Asthma mononeuritis multiplex	Initial presentation	+	Prednisolone 40 mg	Improved
Current case	39 M	Abdominal pain	Mononeuritis multiplex Legs and fingertips ulcer	When tapering prednisolone 40 mg–25 mg	+	Prednisolone, cyclophosphamide	Need operation

DISCUSSION

A 39-year-old man with EPGA presented with acute kidney injury due to bilateral calcific ureteral obstruction. His vasculitis and eosinophilia both responded to immunosuppressive therapy, but ureteral reconstruction was necessary to maintain renal function. Histology showed calcified ureters with granulomatous changes.

EGPA is characterised by chronic rhinosinusitis, asthma and prominent peripheral blood eosinophilia, but can affect any organ including lung, skin, kidney, gastrointestinal tract, and the cardiovascular and nervous systems. EGPA is classified as a vasculitis affecting small and medium sized arteries. Only 40–60% of patients with EGPA have detectable ANCA. Abrupt onset mononeuritis multiplex, severe eosinophilia and eosinophilic vasculitis of the skin all were features suggestive of EGPA.

The unusual feature of this case was acute kidney injury due to rapidly developing calcified stenoses of both ureters with pathological findings of granulomata in the ureters. Ureteral involvement has been reported in other types of systemic vasculitis, such as polyarteritis nodosa, systemic lupus erythematosus (SLE), granulomatosis with polyangiitis (GPA) and Henoch-Schönlein purpura.^{2–6} Calcific ureteral obstruction coincided with vasculitis of high disease activity. Histology of rapidly progressive calcified

ureteral stenoses showed necrotising vasculitis with granulomatous inflammation and fibrinoid changes among cases of GPA and SLE.^{3,4} Vasculitic involvement of periureteral vessels was a likely trigger for ischaemia and necrosis, ultimately resulting in calcification and fibrosis.³

Four cases of ureteral stenosis have been reported in patients with EGPA, all of which have been bilateral.^{7–10} Steroids and cyclophosphamide were frequently used for treatment, followed by surgical intervention with favourable outcomes (table 1).

In summary, a patient with active EGPA developed abdominal pain and acute kidney injury. Bilateral calcified ureteral stenosis and renal function responded to immunosuppressive therapy and surgical intervention. This case illustrated EGPA with complicated by ureteral involvement, a rare mechanism by which acute kidney injury may result from active vasculitis.

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Patient's perspective

Once I was diagnosed with EGPA, it was a relief to know what had been responsible for the agonizing pain in my fingers and the weakness in my legs. However, I suffered from emotional instability while being treated with steroids, which deepened into depression when I developed groin pain and anuria. I was able to return to work and to a normal life after successful surgery and reduction of my steroid dose.

Learning points

- Acute kidney injury in a patient with eosinophilic granulomatosis with polyangiitis (EGPA) could result from ureteral involvement as well as glomerulonephritis.
- Many types of vasculitis, including EGPA, may present with calcified ureteral stenosis.
- Both immunosuppressive therapy and surgical intervention may be necessary to improve renal outcomes due to ureteral pathology in EGPA.

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