Wegener’s granulomatosis presenting as multiple bilateral renal masses

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Introduction

Wegener’s granulomatosis (WG) is a systemic disease characterized pathologically by necrotizing granulomatous inflammation of the respiratory tract and generalized vasculitis involving medium- and small-sized vessels. Kidney involvement is usually manifested as a focal segmental necrotizing glomerulonephritis, with crescents [1]. Anti-neutrophil cytoplasm antibody (ANCA) testing has provided a very useful diagnostic aid. The majority of patients with WG have antibodies towards proteinase 3 (PR3-ANCA) (>70%), but antibodies towards myeloperoxidase (MPO-ANCA) is seen in 20% of cases. A few patients (<10% of cases) are ANCA negative. Occasionally, the disease may present as a single renal mass [2,3]. However, WG presenting as bilateral renal masses in a patient who is ANCA negative is unusual and illustrates the diagnostic dilemma presented by such a case. Recognition of these limited forms of WG is crucial in order to ensure early diagnosis and treatment.

Case

A 66-year-old male presented in March 2001 with a 2 month history of fever, night sweats, lower extremity weakness and pain. He had been well until September 2000 when, following a skiing accident, he was found to be hypertensive and was started on a combination of atenolol and hydrochlorothiazide. In January 2001 he began to notice increased fatigue, lower extremity pain and weakness. He also developed upper respiratory tract symptoms with a dry cough. He was placed on a sequential course of amoxicillin, cephalaxin and doxycycline with no improvement. In addition to these symptoms, a month prior to the clinic visit, the patient began experiencing nightly fevers with drenching night sweats. Blood tests showed anaemia, leukocytosis, thrombocytosis and elevated sedimentation rate (76 mm/1 h). He was admitted to his local hospital for work-up of fever of unknown origin. An ENT evaluation showed no polyps or ulceration in the nasal cavity and posterior rhinoscopy was normal. A head computerized tomography (CT) scan showed opacity of the left sphenoid sinus as well as the left ethmoid and maxillary sinus, together with marked thickening of the mucosa of the sphenoid and maxillary sinus. He was started on a course of azithromycin. Blood tests showed that his ANA was negative, serum creatinine was 1.0 mg/dl and urinalysis was normal. Bone marrow biopsy examination showed normal cellularity with a M:E ratio of 3:1. Tests for ANCA showed that he had a positive p-ANCA. Anti-myeloperoxidase (MPO) and anti-proteinase 3 (PR3) antibody titres were unavailable. Because of a concern for systemic vasculitis, he was referred to the Mayo Clinic for further evaluation. When seen at our institution, he complained of weight loss of >20 lbs over the last 6 months, increasing headaches and abdominal pain mainly over the left flank for the previous 10 days. On physical exam his temperature was 36.1°C, blood pressure was 145/80 mmHg and pulse rate was 89. Apart from some punctuate lesions on his back, which resembled the start of a vesicular rash, the remainder of the physical examination, including a complete ENT exam, was unremarkable. Laboratory evaluation showed haemoglobin 12.6 g/dl, white cell count 11.2 × 10⁹/l, platelets 184 × 10⁹/l, sedimentation rate 54 mm/1 h, serum creatinine 1.2 mg/dl and a normal urinalysis. Also normal were the...
results of bilateral temporal artery biopsies, renal ultrasound and an abdominal angiogram that included the renal arteries, performed to evaluate the abdominal pain. ANCA serology was positive with a p-ANCA pattern and an anti-MPO of 60.3 EU/ml, together with an elevated C-reactive protein of 10.9 mg/dl. A diagnosis of systemic vasculitis was entertained and he was started on oral prednisone 60 mg daily, which resulted in prompt relief of his symptoms. Prednisone was gradually tapered and completely discontinued at the end of October 2001. In January 2003, 22 months after the initial presentation, the patient returned complaining that his night sweats had returned and he was experiencing progressive fatigue, but no return of the abdominal pain. His sinus symptoms had improved, but he had, however, developed peripheral oedema and leg pain, mostly in the calves, without a clear relationship with exercise. Laboratory evaluation again showed a normal serum creatinine and an entirely normal urinalysis. He had a mildly elevated C-reactive protein, but with a normal sedimentation rate and negative assays for MPO and PR3-ANCA. Chest X-ray, Doppler studies of the legs as well as an echocardiogram were all reported as normal. In the process of evaluating the cause of his oedema, a CT scan of the abdomen and pelvis was performed, which showed multiple bilateral renal masses, 2–3 cm in size (Figure 1). To further characterize these masses, the patient underwent renal ultrasound and excretory urogram, which showed the masses to be solid. Fine needle aspiration of the renal masses was suspicious for lymphoma, but this was not confirmed on the tissue specimen, which was reported as fibrotic with a mixed reactive inflammatory cell infiltrate. The patient then underwent bilateral surgical exploration of the renal masses. Pathological examination of the surgical specimens submitted from both kidneys showed similar morphological alterations. Much of the renal parenchyma was replaced by numerous, confluent small necrotizing granulomas with central collections of neutrophils and cellular debris (Figure 2). There was also an associated mixed interstitial inflammatory cell infiltrate. No infectious organisms, including acid-fast bacilli, were detected on Gomori–methenamine silver (GMS) or auramine–rodamine stains. The glomeruli appeared normal and no necrotizing glomerular lesions were identified. No arteritis was observed. These pathological findings were consistent with the diagnosis of WG. Based on these results, the patient was started on a combination of prednisone 60 mg daily and oral methotrexate 25 mg weekly, together with single-strength trimethoprim–sulphamethoxazole daily. This resulted in prompt symptomatic improvement. Prednisone dose was tapered to 10 mg daily at 6 months while methotrexate was continued at the same dose. Six months after the beginning of treatment, a repeat CT of the abdomen showed that the renal masses had decreased in size with no evidence of new masses (Figure 2). During the same period, several MPO and PR3 assays remained negative.

Discussion

WG is a systemic disease characterized pathologically by the presence of necrotizing granulomatous lesions of the upper and lower respiratory tracts and a generalized vasculitis of small to medium-sized vessels, often associated with a glomerulonephritis [4]. Kidney involvement is common, but extrarenal manifestations usually precede renal disease by many months [5,6]. Renal pathology usually reveals a focal segmental necrotizing glomerulonephritis, with or without crescents, and rarely accompanied by necrotizing
granulomas [1]. However, the overall clinical picture varies considerably, with forms of the disease limited to the lungs not being uncommon [7]. A few cases of WG presenting as crescentic glomerulonephritis, without respiratory tract involvement, have also been recognized [8]. Rarely, a solitary renal mass, which pathological examination reveals to be WG, has been described [2,3,9–12]. However, in only two of these cases was a renal mass the sole initial manifestation of the disease [2,3]. Even rarer, WG can present as multiple renal masses. We found only one previously reported case in which multiple renal masses were the initial manifestation of WG [13]. This case was similar to ours in the fact that renal function was not affected and needle biopsies of the masses were non-diagnostic. In contrast to our case, however, the previously described patient was ANCA positive, which helped in making a presumptive diagnosis of WG. The discovery of serum IgG antibodies against cytoplasmic components of neutrophils and monocytes (ANCA) and of its association with WG has provided a useful diagnostic tool for the patient with this disease. ANCA are present in >90% of patients with active systemic

WG and are highly specific [14]. However, ANCA sensitivity is lower in patients with active localized disease, as demonstrated by our case. Therefore, a negative c-ANCA test result does not exclude a diagnosis of WG. Treatment with prednisone and cyclophosphamide has significantly improved survival of WG, although relapse rates remain high and side effects of treatment are not trivial [6]. In patients with normal renal function, an alternative treatment using prednisone combined with low-dose weekly methotrexate has been shown to be equally effective in
inducing remission, while reducing the number of side effects [15]. Although urogenital tuberculosis may show a similar presentation on CT, multiple renal biopsy sections failed to be stained for acid-fast bacilli. In addition, the fact that the patient improved while on high-dose prednisone and methotrexate argues against this diagnosis.

In summary, we present a case of WG in which multiple bilateral renal masses were the major clinical findings. This form of presentation is rare, but emphasizes the importance of considering WG in the differential diagnosis when dealing with tumour-like lesions of the kidney.

Conflict of interest statement. None declared.

References