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Wegener's granulomatosis masquerading as a renal cancer: a case report and review of the literature

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ABSTRACT

A 32 year-old man presented with sinusitis, proteinuria, mononeuritis multiplex, very increased acute phase proteins. Anti-PR3 ANCA were detected and Wegener's granulomatosis (WG) was diagnosed. As abdominal tomodensitometry detected a tumoral process of the left kidney, a paraneoplastic vasculitis associated with a renal cancer was suspected. Biopsy of the mass showed fibrosis, inflammatory infiltrates and necrotizing granulomas. No malignant cells were detected. The outcome was favourable after administration of methylprednisolone and cyclophosphamide. Characteristics of the nine previously reported renal inflammatory pseudotumors associated with WG are discussed.

Introduction

Wegener's granulomatosis (WG) is a small vessel necrotizing vasculitis associated with anti-neutrophil cytoplasmic antibodies (ANCA), involving – in its classical form – the upper and lower airways. Renal involvement defines the generalized form of the disease and strongly influences the mortality (1). Clinical presentation of renal involvement is highly variable and ranges from asymptomatic forms to rapidly progressive renal failure which leads to end-stage renal failure (2). Renal inflammatory pseudotumor is a very unusual form of renal involvement, less than ten cases have been reported in the literature.

Case report

A 32 year-old man presented with left lower quadrant pain, polyarthralgias, temperature, hypoesthesia of fingers and toes. Colic biopsy only showed a mild aspecific colitis. Elevation of inflammatory parameters and positivity of rheumatoid factor were noted. The clinical condition did not improve despite treatment with corticosteroids. The patient was admitted to our hospital because of worsening of symptoms. Physical exam revealed left lower quadrant pain and hypoesthesia of fingers and toes. Biological abnormalities consisted of: ESR 78 mm/h, CRP 33.5 mg/dl, WBC 11 500 / mm^3. Haemoglobin, platelet count, creatinine were within the normal range. Urinanalysis showed proteinuria (0.7 g per day) but no microscopic hematuria. Mononeuropathy multiplex was diagnosed on the basis of electromyography findings (reduction in amplitude of action potentials in different muscles), and presence of conduction blocks, nervous conduction velocity being relatively preserved. Because of abdominal pain, abdominal tomodensitometry was performed and showed a mass of left kidney with infiltration of perirenal fat, suggestive of renal cancer, adenocarcinoma or lymphoma (Fig. 1). Left kidney ultra-sound-guided needle biopsy was performed: no malignant cells were found, the tissue sample showed fibrosis, inflammatory infiltrates and focal necrosis. Presence of anti-proteinase 3 ANCA strongly suggested the

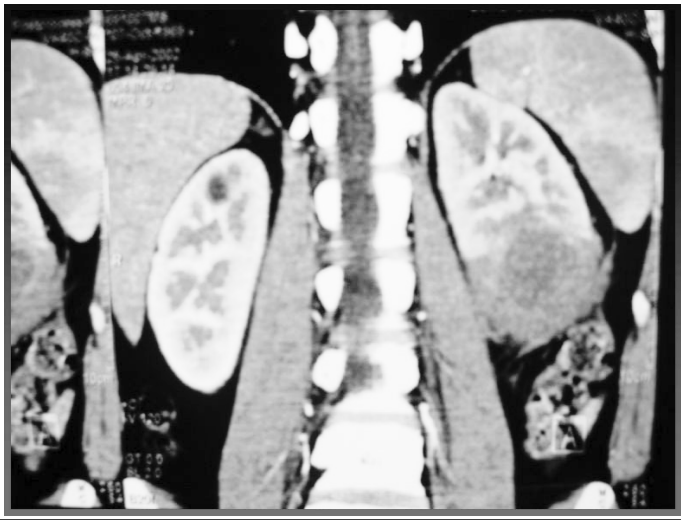

Fig. 1. Abdominal tomodensitometry showing a mass of left kidney with infiltration of perirenal fat, suggestive of renal cancer.

Table I. Main characteristics of published case report.

Author (year)	Patient	E.N.T. involvement	Pulmonary Involvement	Urinanalysis	Renal histology			Nephrectomy
					Glomerulo-nephritis	Granulomas	Fibrosis	
Maguire (1978)	27 y / f	+	+	N.M.	+	+	-	Partial
Schapira (1986)	45 y / m	+	+	Proteinuria	+	+	-	Partial
Schydlowsky (1992)	47 y / m	-	+	N.M.	+	+	-	Total
Boubenider (1994)	45 y / f	-	-	Proteinuria Hematuria Cylindruria	+	+	+	
Smith (1993)	52 y / f	+	-	N.M.	+	+	-	Total
Verswijvel (2000)	24 y / m	+	-	Microscopic hematuria	+	N.M.	N.M.	No
Fairbanks (2000)	68 y / m	+	-	N.M.	+	+	-	Total
Leung (2004)	66 y / m	+	-	Normal	-	+	+	No (involvement of both kidneys)
Krambeck (2005)	61 y / m	+	-	Normal	-	+	+	Partial
Present case	32 y / m	+	-	Proteinuria	+	+	+	Partial

Y: year old; f: female; m: male; E.N.T.: ear, nose and throat;N.M.: not mentionned.

diagnosis of Wegener's granulomatosis (3). The patient received high-dose methylprednisolone (1 g per day for 3 consecutive days) and cyclophosphamide (0.7 g/m^2). A rapid improvement was noted from clinical and biological points of view. A left kidney biopsy was performed under laparoscopy. Main histological changes consisted of: fibrosis and inflammatory infiltrates in the interstitium, necrotizing granulomas involving renal parenchyma and perirenal fat which also contained inflammatory infiltrates. About fifty percent of the glomeruli showed fibrosis and sclerosis. A renal inflammatory pseudotumor associated with Wegener's granulomatosis was diagnosed.

Discussion

Renal inflammatory pseudotumor is an exceptional manifestation of Wegener' s granulomatosis. Nine cases have been reported in the literature (Table I). One case presenting with multiple bilateral renal masses has been described (4).

The main differential diagnosis is renal cell carcinoma associated with WG.

Villa-Forte reported a case of WG presenting with a renal mass. Needle biopsy of the kidney revealed the characteristic features of WG (glomerulonephritis with capillaritis and fibrosis). Because renal function has not improved and renal mass showed no change in size under treatment, nephrectomy was performed. The pathology revealed renal cell carcinoma (5). In this case, immunosuppressive treatment (in particular cyclophosphamide) did not appear to play a role in malignancy, since the patient had not received the treatment prior to recognition of the renal mass.

Tatsis found a close temporal association between renal cell carcinoma and WG (6). In his retrospective study, he analysed the frequency and the type of malignant neoplasms occuring before or simultaneously with the diagnosis of WG, compared with a control group of patients with rheumatoid arthritis (RA). The most frequent neoplasm found in the WG group was renal cell carcinoma, the prevalence of this neoplasm was significantly higher in the WG group compared with the RA group, with an odds ratio of 8.73 (p = 0.0464, 95% CI 1.04-73.69). Hypothetically, ANCA may bind to proteinase 3 (PR3) - the target antigen of ANCA in WG - expressed on the surface of renal epithelial cells, which induces signaling events leading to proliferation (6). Thus, PR3 may be the missing link between autoimmunity and uncontrolled cell proliferation in patients with WG and renal cell carcinoma and other types of cancer (e.g. bladder) (8). However, studies of the presence of PR3 on renal epihitelial cells have given conflicting results: PR3 could not be detected in any of the malignant tissue samples from WG patients with renal cell carcinoma in Tatsis' study. Nevertheless, Mayet found expression of proteinase 3 on renal tubular epithelial cells (7) and on a human renal cancer line (9).

Except in the case described by Verswijvel (10), in which six months of medical treatment allowed disparition of the renal mass, nephrectomy (at least partial) was performed in every patient. Main histological changes described in renal inflammatory pseudotumors are mentioned in Table I. Presence of granulomas is reported in all the described cases of renal inflammatory pseudotumor. As a comparison, in a meta-analysis about 349 cases of WG, granulomas in kidney biopsy is only reported in 7 of 134 cases (5.2 %) (2) .

Radiological features of renal inflammatory pseudotumor are similar to those observed in renal carcinoma, so that differential diagnosis cannot be made on the basis of imaging findings.

Other inflammatory pseudotumors have

been reported in association with WG: mainly orbit - which has been noted in up to 15% of the patients (1) - but also as isolated case reports - breast (11), retro-peritoneal space, bladder, infra-temporal fossa (12). In total, there are at least 28 reports of 79 patients with pseudotumors in WG. In particular, the lesions are characterized by a high proportion of fibrosis not seen to the same extent in other granulomatous manifestations in WG. This might explain the fact that immunosuppressive therapy is probably less effective than in other manifestations. In a recent small pilot study, rituximab - often showed as effective in refractory cases of WG - was not associated with obvious clinical improvement of refractory retro-orbital pseudotumors (13).

In conclusion, WG should be considered in the differential diagnosis of renal mass, in particular when general signs are present. In addition, when a renal mass is found in a patient having WG, renal cell carcinoma should be ruled out by at least fine needle biopsy and perhaps by renal biopsy or partial nephrectomy.

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