An Unusual Renal Presentation of Wegener’s Granulomatosis#

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SUMMARY
A 63-year-old woman was admitted to our clinic with arthralgia, microhematuria and a pleural based solid mass in lower lobe basal segment of right lung seen in computerised tomogram of thorax. She was diagnosed as Wegener’s granulomatosis by histopathological findings of right thoracotomy, wedge resection and decortication. The patient had positive antineutrophil cytoplasmic antibodies (c-ANCA) in serum and tissue specimens. Histopathologic examination of the renal biopsy specimen revealed the diagnosis of tubulointerstitial nephritis. We report this case because of the unusual histologic type of renal involvement by reviewing the literature.

Key Words: Wegener’s granulomatosis, tubulointerstitial nephritis.

ÖZET
Alışılmamış Böbrek Tutulumu ile Seyreden Wegener Granülomatözü Olgusu

Anahtar Kelimeler: Wegener granülomatözü, tubulointerstisyel nefrit.

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Wegener’s granulomatosis (WG) is a life threatening disease with a mean survival of five months in most untreated patients (1). It is characterized histologically by necrotizing granulomatous vasculitis of both the upper and lower respiratory tracts in association with necrotizing glomerulonephritis and systemic vasculitis (2). The American College of Rheumatology has established the following criteria for the diagnosis of WG:

1. A urinary sediment containing red blood cell casts,
2. Abnormal findings on the chest radiograph,
3. Oral ulcers or nasal discharge,
4. Granulomatous inflammation on biopsy (3).

The most common renal lesion in WG is focal and segmental glomerulitis that may progress to crescentic glomerulonephritis (4-6). We present a case of WG with an unusual renal presentation which is tubulointerstitial nephritis.

CASE REPORT

A 63-year-old housewife was admitted to our clinic with a several week history of migrating arthralgies and for evaluation of solid mass seen in thorax computed tomography (CT). She denied any recent drug usage, a smoking history and occupational exposure to exogeneous toxins. Results of head, eyes, ears, nose and throat examinations were normal. Lung examination showed crackles at right lung bases on auscultation. Cardiac and abdomen examination were normal. We revealed Raynaud’s phenomenon and atrophy of left tenar muscles on the extremity examination.

The results of routine laboratory studies were normal except erythrocyte sedimentation rate (ESR) with 105 mm/hour. Urine analysis disclosed a specific gravity of 1005; protein 25 mg/dL and numerous erythrocyte and leucocyte. The chest roentgenogram is shown in Figure 1. CT scan of thorax showed irregular pleural thickness in the right lower lobe superior and posterior basale segment and a solid mass with a diameter of 27 x 30 cm in the right lower lobe adherent to the dorsal pleura (Figure 2). We performed a CT guided transthoracic fine needle aspiration biopsy twice and no diagnostic findings were determined. Then right thoracotomy, wedge resection and decortication was done. Vasculitis and necrotizing granulomatous inflammation was found in biopsy specimen (Figure 3). Wegener’s granulomatosis was diagnosed, combined with the positive c-ANCA test result. Urine analysis revealing a sterile pyuria and microscopic hematuria and proteinuria led to examination of renal tuberculosis. Tuberculosis culture of urine was performed by using Loewenstein-Jensen media and polimerase chain reaction (PCR) procedure. It was found negative. Renal biopsy was done and eighteen glomeruli was seen in biopsy specimen. No pathologic lesion was revealed except minimal nonspecific proliferation. However; tubuler atrophy, foci of
fibrosis and dense inflammation was seen in interstitium (Figure 4). Amyloid was negative and deposition of IgA, IgG, IgM, C3 and C1q were not found by using immunofluorescence staining. Final diagnosis was tubulointerstitial nephritis. Abdominal ultrasonography and computerised tomogram of paranasal sinuses were found normal. Oral corticosteroids (1 mg/kg), cyclophosphamide (150 mg/day), trimetoprim-sulfa-methoxazole (TMP-SMX) (160/800 mg) twice a day was started. After a two month treatment period; serum c-ANCA value was found negative, ESR began to decrease to 25 mm/hour and one or two erythrocyte were still present in the urine. The patient is well and still under control.

DISCUSSION

WG is characterized by a necrotizing granulomatous vasculitis that most commonly involves the lungs together with the nasal pathways, paranasal sinuses and kidneys, but may affect any organ system. The true incidence of the disease is unknown. The male/female ratio is 1/1 and the mean age of presentation is about 40-55 years (2,5). The typical clinical presentation is characterized by signs and symptoms of upper and lower respiratory tract like sinusitis, cough, hemoptysis, epistaxis, chest discomfort, dyspnea in approximately 90% of patients (5). Abnormal chest radiographic appearance is seen in 75% of patients with infiltrates occurring most frequently (63%), followed by solitary or multiple pulmonary nodules (31%) which have a tendency to cavitate. The nodules usually are well-defined, round and range in size from a few millimeters to 9 cm in diameter. Atelectasis, pleural thickening, pleural effusion, hilar adenopathy and pneumothorax are other less common abnormalities (2,7,8). In our case CT scan of thorax showed pleural based solid mass in the right lower lobe. Thirty-four percent of cases with radiographic abnormalities have been found to be asymptomatic (9). Our patient was also asymptomatic.

Eighteen percent of patients with WG initially exhibit renal involvement. However, 75% of patients eventually develop glomerulonephritis, usually within the first two years of disease initiation (7,8). Urine analysis frequently demonstrates red blood cell casts which are indicator of active glomerulonephritis even though serum creatinine and creatinine clearance is normal as seen in our case (10). Renal biopsy generally shows focal segmental necrotizing glomerulonephritis which may become diffuse in advanced disease. However, the spectrum of renal involvement ranges from diffuse proliferative glomerulonephritis and interstitial nephritis to hyalinization of glomeruli. Glomerular crescent formation may be found (11). Renal disease generally dominates the clinical picture and accounts directly or indirectly for most of the mortality in this disease (1,12).

Bajema and co-workers reported the results of meta-analysis of 349 patients in WG (13). They found the most frequently mentioned lesion to be extracapillary proliferation (70%), followed by fibrinoid necrosis of the glomerular tuft (54%). Vasculitis of interstitial arteries and arte-
rioles was present in almost 20% of all cases. Tubulointerstitial nephritis was identified in renal biopsy samples of our case. The term interstitial nephritis is generally reserved for those cases that are noninfective in origin. These include tubular injury resulting from drugs (antibiotics, analgesics, diuretics), toxin exposure (lead, cadmium, uranium), metabolic disorders such as hyperuricemia, hypokalemia, physical injury such as irradiation and immunologic reactions (14). We ruled out drug usage and toxin exposure by direct questioning. Laboratory findings such as serum electrolytes and abdominal ultrasonographic results helped us to exclude the other etiologies of interstitial nephritis. After excluding potential causes of of tubulointerstitial nephritis, with the presence of positive c-ANCA value, we claim that the renal disease was attributable to WG. Our case is important because tubulointerstitial nephritis is an unusual renal finding in WG.

Characteristic laboratory findings include a markedly elevated ESR. Hoffman and co-workers revealed a correlation between high ESR and disease activity in 80% of patients (7). c-ANCA is present in the majority of patients with active disease with a sensitivity of 88% and a specificity of 98% (8, 12, 15). We also revealed a high ESR and a positive c-ANCA value at presentation.

The standard therapy consists of low dose cyclophosphamide (2 mg/kg/day) and prednisone (1 mg/kg/day). With this regimen, marked improvement or partial remission occurs in 90% of patients; a complete remission occurs in 70% of individuals. Approximately 50% of the patients with complete remissions suffer at least one relapse. Treatment with TMP-SMX (160 mg/800 mg) twice daily appears to reduce the relapses in patients with WG in remission (16). In our case we started combination therapy and the patient is still doing well and under follow up.

We present this case because this is the first reported case of Wegener’s granulomatosis associated with tubulointerstitial nephritis.

REFERENCES