Case Report

# Pulmonary Renal Syndrome in a Case of Wegener's Granulomatosis

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## ABSTRACT

We report a case of a 42-year-old patient who presented with Wegener's granulomatosis complicated by pulmonary renal syndrome, i.e., diffuse alveolar haemorrhage and rapidly progressive crescentic glomerulonephritis. The patient was treated with plasmapheresis and immunosuppressive drugs — intravenous cyclophosphamide and methyl prednisolone. The clinical, haematological and biochemical parameters improved substantially and remission is achieved. **[Indian J Chest Dis Allied Sci 2013;55:49-52]**

**Key words:** Pulmonary renal syndrome, Wegener's granulomatosis, Plasmapheresis.

## INTRODUCTION

Wegener's granulomatosis is a clinico-pathological entity characterised by disseminated granulomatous vasculitis involving both small arteries and veins as well as of the upper and lower respiratory tracts together with glomeruli. The estimated incidence of Wegener's granulomatosis ranges from 5.2 to 12.9 per million.[1] Pulmonary renal syndrome is characterised by diffuse alveolar haemorrhage and rapidly progressive glomerulonephritis. Wegener's granulomatosis is one of the rare causes of pulmonary renal syndrome.

It is a potentially life threatening disorder and requires prompt diagnosis and treatment with plasmapheresis as well as immunosuppressive drugs that can be life-saving. *To the best of our knowledge, the case presented here is the first reported case of pulmonary renal syndrome in a patient of Wegener's granulomatosis from India* in which effective management was provided with plasmapheresis and immuno-suppressive drugs.

## CASE REPORT

A 42-year-old non-diabetic, non-smoker male presented with progressively increasing shortness of breath for 20 days and haemoptysis for 10 days. Haemoptysis was associated with epistaxis and a reduced urine output for last six days without any hematuria. He had tingling and numbness of fingers and toes. There was no history of chest pain, wheeze, hoarseness of voice, fever, skin rash, any food or drug allergy. He gave a history of multiple joint pains nine months back and serous discharge from the right ear lasting one week about three months back.

General examination of the patient, revealed an alert and conscious patient with moderate pallor, tachycardia (100/min), hypertension (150/104 mmHg), tachypnoea (24/min) and hypoxia (oxygen saturation on room air 85%). Examination of the upper respiratory tract revealed one ulcer in the posterior nares. Chest examination revealed decreased vesicular breath sounds on both the sides in the infrascapular regions, more on the left side, with the presence of coarse crepitations. Examination of the nervous system revealed decreased, supinator, elbow, knee and ankle reflexes bilaterally. Other systems were unremarkable.

Chest radiograph did not reveal any abnormality. High resolution computed tomography (HRCT) of thorax (Figure 1) revealed the presence of a subcentimeter nodule in the right lung field. Initial blood investigations showed anaemia (Hb – 8g%), leukocytosis (TLC-15700/cc), raised blood urea (116mg/dL) and raised serum creatinine (3.87mg/dL). Urine routine examination showed an albumin of 3+ with plenty of red blood cells (RBCs) and RBC casts. The 24 hours urinary protein excretion was 1.52g. The C-reactive protein was raised (60.8u/mL)

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while anti-nuclear antibody, rheumatoid arthritic factor and anti-CCP antibody were negative. The C-ANCA (anti PR3 antibody) was significantly elevated (97.79u/mL; normal value <5u/mL). The P-ANCA was 2.13u/mL (normal value). Ultrasonography of abdomen revealed bilateral renal parenchymal disease.

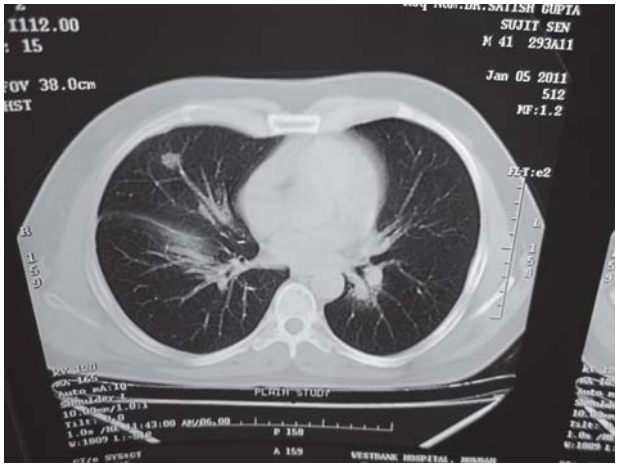


**Figure 1. High resolution computed tomography of thorax showing a subcentimeter nodule in the right lung field.**

On the basis of the upper respiratory tract involvement (nasal ulcer, epistaxis, past history of otitis media), lower respiratory tract involvement (haemoptysis, lung nodule), renal involvement with increased blood urea and creatinine and raised C-ANCA, a diagnosis of Wegener's granulomatosis was made.

After admission, the patient had repeated bouts of severe haemoptysis with significant reduction in the urine output. A repeat chest radiograph (Figure 2) showed bilateral diffuse non-homogeneous opacities. Within a span of three days, the blood urea increased to 256mg/dL and serum creatinine rose to 7.39mg/dL with complete renal shutdown.

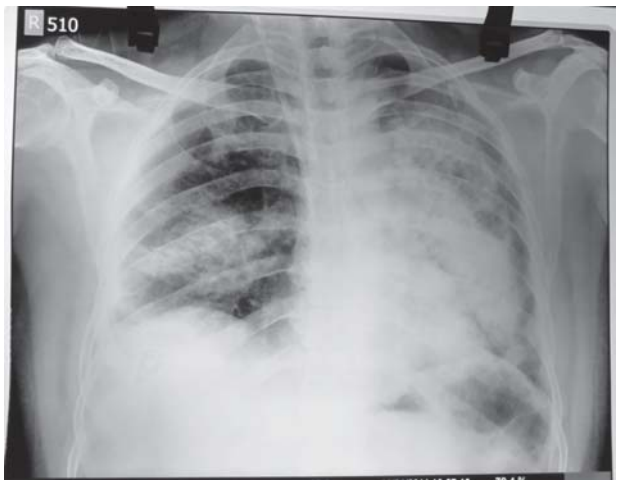


**Figure 2. Chest radiograph (postero-anterior view) showing bilateral diffuse non-homogeneous opacities.**

A pulmonary renal syndrome was diagnosed. The Nephrologist advised plasmapheresis and haemodialysis.

The patient underwent four days of plasmapheresis with fresh frozen plasma and five days of haemodialysis with packed RBCs. He also received intravenous cyclophosphamide 500mg and intravenous methyl prednisolone 1g daily for three days.

Following haemodialysis and plasmapheresis, the patient improved symptomatically. The urine output increased from 1500 to 1600mL per day. Blood urea and serum creatinine decreased to 49mg/dL and 2.6mg/dL, respectively. Urine RBCs decreased in number and urine casts disappeared. At this stage, the patient was subjected to further investigations. Nasal biopsy was normal. Electromyography and nerve conduction velocity study revealed axonal type of symmetric polyneuropathy involving all the four limbs. Subsequently, renal biopsy was done that revealed necrotising and crescentic glomerulonephritis of pauci immune variety (Figure 3). A fibreoptic bronchoscopy (FOB) revealed a normal tracheobronchial tree.

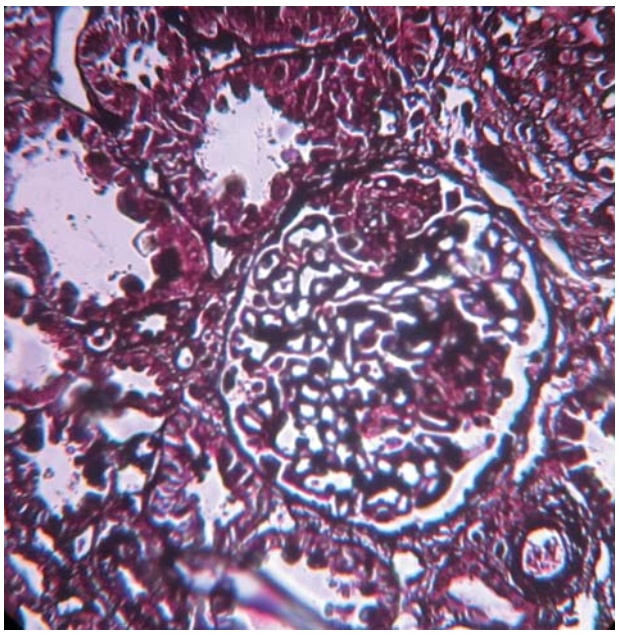

**Figure 3. Renal biopsy showing necrotising and crescentic glomerulonephritis (Periodic Acid Schiff (PAS) stain×400).**

Bronchoalveolar lavage (BAL) fluid stained with pearl stain for iron (Figure 4) revealed a fair number of haemosiderin containing macrophages suggesting diffuse alveolar haemorrahage. Other BAL fluid reports were normal.

The patient received intravenous pulse cyclophosphamide 500mg every three weeks for 11 cycles, with oral prednisolone in a tapering dose and antihypertensive drugs.

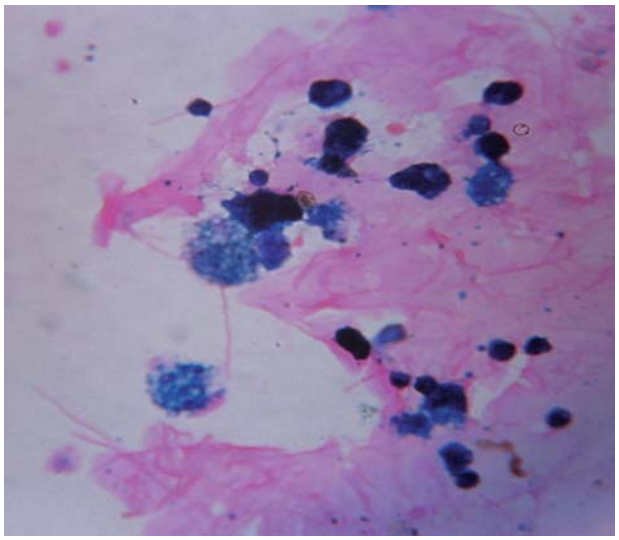

**Figure 4. Bronchoalveolar lavage showing a fluid cytology, large number of haemosiderin containing macrophages are seen (Pearl stain for iron-A×400).**

A follow-up chest radiograph taken after two weeks shows complete resolution of the radiological opacities. Blood investigations showed a progressive increase in Hb% and progressive fall in serum urea and creatinine levels, and in the 24 hours urinary protein excretion. After one month, the urine RBCs and casts had disappeared completely. Currently, the patient is in the remission and receiving maintenance azathioprine and tapering dose of oral steroids.

## DISCUSSION

Pulmonary renal syndrome is a life-threatening condition that complicates a variety of diseases like Goodpasteur's syndrome, primary systemic vasculitis, systemic lupus erythematosus, cryoglobulinemia, systemic sclerosis and intake of certain drugs. According to European Vasculitis Study Group (EUVAS)[2] grading of disease severity, our patient can be classified as severe as he had renal involvement and life-threatening diffuse alveolar haemorrhage.

Diffuse alveolar haemorrhage, characterised by haemoptysis, hypoxia, new radiological infiltrates and bloody BAL fluid, is the most serious complication[3] with a mortality rate of 60 percent. It can rapidly lead to respiratory failure and death unless diagnosed early and treated promptly with plasmapheresis and immunosuppressive therapy.[3] In the present case, treatment was started promptly with plasmapheresis and immunosuppressive drugs. Immunosuppressive therapy alone is unlikely to succeed in such a critical condition.[4]

The pathogenesis of pulmonary renal syndrome is poorly understood. The PR-3 antibody is believed to play a role by directly or indirectly damaging endothelial cells.[5] A necrotising capillaritis involving both renal and pulmonary vascular bed occurs leading to a leakage of RBCs and other plasma products into the extravascular space. Leakage into Bowman's space of the glomerulus leads to the formation of crescents whereas leakage into the alveolar space of lung causes pulmonary haemorrhage. As plasmapheresis rapidly removes PR-3 antibodies and other inflammatory mediators from the circulation, it is thought to be the most effective therapy for pulmonary renal syndrome.

According to one Indian study[6] reporting clinical features, treatment and outcome of 25 patients with Wegener's granulomatosis, the disease can be effectively treated with oral prednisolone and oral cyclophosphamide regimen or with intravenous cyclophosphamide regimen. Median time for achieving remission was six months. Among patients with a relapse, one developed diffuse pulmonary haemorrhage and died.

According to European MEPEX (methyl prednisolone *versus* plasma exchange as additional therapy for severe ANCA associated glomerulonephritis) trial, combination therapy with plasmapheresis and methyl prednisolone has shown a benefit over methyl prednisolone therapy alone.[7]

The diffuse alveolar haemorrhage in our patient resolved completely within two weeks with intensive treatment whereas the renal abnormalities persisted even after six weeks, suggesting that necrotising capillaritis of lung is more responsive to intense treatment compared to necrotising capillaritis of kidney. One study showed that plasmapheresis reduced mortality by 50%[8] in cases of pulmonary renal syndrome. Another study[9] showed diffuse alveolar haemorrhage resolved in all 20 patients receiving plasmapheresis.

To conclude, pulmonary renal syndrome is a rare manifestation of Wegener's granulomatosis. It responds well to prompt and aggressive treatment with plasmapheresis and immunosuppressive drugs.

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