Goodpasture's Syndrome

Dr Amit H Panjwani*, Lt Col RB Deoskar†, Lt Col JJJ Falleiro, SM ‡, Col KE Rajan **

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Introduction

Alveolar haemorrhage is a potentially catastrophic complication of myriad immune and non-immune disorders. Among the immune mediated problems, Goodpasture's syndrome is included as one of the less common causes. In 1919, Goodpasture described an association between pulmonary haemorrhage and glomerulonephritis [1]. Since then, many cases have been reported in world literature. This syndrome is composed of recurrent haemoptysis followed by pulmonary infiltration, anaemia, renal failure and a short fatal course. We present a rare case of Goodpasture's syndrome associated with pulmonary tuberculosis.

Case Report

A 20 year old soldier was admitted to a tertiary referral Chest Centre with the history of cough, minimal mucoid expectoration, streaky haemoptysis, low grade fever, anorexia and weight loss, all of 2 months duration.

At admission, his temperature was 38°C, pulse - 100 / minute, respiratory rate - 22/minute, and BP - 118/70 mm of Hg. There was no pallor, icterus, clubbing, edema, lymphadenopathy, or cyanosis. Chest examination revealed features of consolidation in the right upper lobe. Physical examination was otherwise non-contributory.

Investigations : Haemoglobin 11g/dl, WBC - 10,600/m³, DLC - N₆₂, L₃₀, E₈, M₁. Urine showed albuminuria, 1-2 RBC and 3-4 pus cells/high power field. Urine culture did not grow any pathogenic organism. Blood urea was 30 mg/dl, and serum creatinine was 0.8 mg/dl. Liver function tests were normal.

Sputum study for acid-fast bacilli was reported as negative. However, sputum for *Mycobacterium tuberculosis* culture later grew bacilli sensitive to all first line drugs. Tuberculin skin test and serum antibodies for HIV1 and HIV2 were found to be negative. Chest radiograph (Fig 1) revealed nodular opacities in left upper zone and both mid zones. Patient was diagnosed as a case of sputum smear negative, culture sensitive pulmonary tuberculosis and was exhibited antituberculosis chemotherapy (2EHRZ/4HR). After completion of 15 days of treatment for pulmonary tuberculosis, the patient developed one episode of haemoptysis (200ml/24 hours). Clinical examination at that time revealed bilateral coarse crepitations. Blood study showed haemoglobin of 7.7 g/dl, haematocrit - 24%, and

TLC - 8200 cells/mm³. Blood culture did not show growth of any organism. Platelet count, prothrombin time and activated partial thromboplastin time were normal. Blood urea was 129 mg/dl, and serum creatinine was 4.1 mg/dl. USG abdomen showed enlarged kidneys with increased echotexture of renal cortex. There was no pelvicalyceal dilatation. Repeat radiograph (Fig 2) of the chest showed fluffy opacities in all zones of the lung. Arterial blood gas analysis revealed pH-7.396, PaCO₂ - 27.5 mm Hg, PaO₂ - 42.3 mm Hg, bicarbonates - 17 mEq/L, alveolar-arterial oxygen difference - 132 mm Hg, and SaO₂ - 58%. The serum electrolytes were in the normal range. Bronchoscopy was deferred in view of significant hypoxemia and respiratory distress.

The patient was treated with oxygen inhalation, and parenteral antibiotics, in addition to supportive measures. Within a few hours of the initial episode of haemoptysis, patient had worsening of his respiratory distress and he succumbed to his illness.

Autopsy findings were as follows : Both the lungs were heavy and had a solid feel with many pale and congested areas. There was a scar on the outer aspect of left upper lobe, overlying a necrotic area, with bilateral straw coloured pleural effusion (approximately 200 ml on each side). The pre-tracheal, paratracheal, hilar and mesenteric lymph nodes were enlarged. There were caseating epithelioid granulomas with Langerhan's giant cells on histopathology. There were focal areas of mononuclear cell infiltrates and diffuse alveolar haemorrhage in both the lungs (Fig 3). The kidneys were edematous and proteinaceous casts were seen in the minor calyces. Microscopic examination (Fig 4) showed diffuse involvement of the glomerulus by crescents. There was a dissection of the basement membrane of capillaries and Bowman's capsule. The interstitium was edematous with infiltration of mononuclear cells in the periglomerular region. Proteinaceous casts were seen in the renal tubules. There was no evidence of vasculitis in other organs.

Discussion

Goodpasture's syndrome is an auto-immune disease affecting primarily the lung and kidney. It is a prototype of pulmonary - renal syndromes and accounts for 18 - 32% of immune mediated alveolar haemorrhage. The disease is thought to occur in less than 1 per million of the population annually. The peak incidence is seen between 20-30 years of age with a 4:1 male

*Post Graduate Resident, †Classified Specialist, **Senior Advisor (Medicine & Respiratory Medicine), ‡Classified Specialist (Pathology), Military Hospital (CTC), Pune - 411 040.

Fig. 1 : Chest radiograph (PA view) showing nodular opacities in left upper zone and both mid zones

Fig. 2 : Chest radiograph (PA view) showing fluffy opacities in all the zones of the lung

Fig. 3 : Haematoxylin and eosin section of the lung showing caseous granuloma with giant cells, adjacent air spaces filled with blood

Fig. 4 : Haematoxylin and eosin section of kidney showing circumglomerular crescent formation, periglomerular cell infiltrate

predominance [1].

A second peak is seen in the middle age where women are commonly affected. Our patient was in his early twenties and was a male. The finding of strong association between the abnormality and HLA - DR2, presence of the disease in brothers and identical twins suggests a hereditary factor in the pathogenesis [2].

Goodpasture's syndrome is a prototype of type II cytotoxic antibody mediated immune reaction [3]. The syndrome is characterized by the presence of antibodies directed at collagen in alveolar and glomerular basement membranes. The antibodies react with the carboxyl

terminal region of the alpha - 3 chain of type - IV collagen, which is present throughout the body. But the syndrome is characterised by involvement of lung and kidneys possibly due to the greater accessibility of the antigen and greater exposure of alpha-3 chain in the alveoli and glomeruli than in other tissues. Increased capillary permeability may be required for the antibody to gain access to the alveolar basement membrane. This observation is supported by the clinical observation that recurrent pulmonary haemorrhage may develop after infection, fluid overload, cigarette smoking, and exposure to toxins.

Histologic features include intra-alveolar haemorrhage and numerous hemosiderin containing macrophages in the alveoli. Alveolar necrosis may be present in case of secondary pneumonitis. Electron microscopy may show thickening, splitting, discontinuity or smudging of the basement membrane. Immuno-fluorescence study of fresh lung tissue may demonstrate diffuse linear staining along the alveolar walls. In the kidneys there are epithelial crescents and glomerular - capsular adhesions as well as interstitial infiltrates and focal atrophy of the tubules. Immuno-fluorescent staining reveals linear deposition of Ig along the basement membrane. In our case there were features of diffuse intralveolar haemorrhage in both the lungs with bilateral crescentic glomerulonephritis and disruption of capillary basement membrane.

Goodpasture's syndrome is often preceded by a pulmonary infection [4]. Haemoptysis is found in 80-90% presentations, although it may occur late in the course of the disease. Cough, dyspnea, weakness and fatigue are common complaints. Pallor is common and hypertension is seen in a minority of cases. Acute haemorrhage is often accompanied by chills, fever and diaphoresis.

Inspiratory crepitations may be the only physical finding in the chest. Urinalysis is abnormal in over 90% of the cases with microscopic haematuria, proteinuria, granular casts and occasional frank haematuria. Uraemia occurs in 70% cases. The findings of anaemia and uraemia were present in our case. Examination of sputum or broncho-alveolar lavage may reveal blood or hemosiderin-containing alveolar macrophages. Abnormal chest radiograph is a feature in more than 80% cases and most commonly shows diffuse bilateral patchy consolidation in mid and lower zones with relative sparing of apices and costophrenic angles. In the later stages, there may be features of interstitial fibrosis. CT scan may be useful when the chest radiograph is normal. In our case, there was patchy consolidation in both mid and lower zones. Pulmonary function test usually shows a restrictive pattern while DLCO is increased during the episodes of haemorrhage. The diagnosis of Goodpasture's syndrome can be made by detecting anti-glomerular basement membrane (anti-GBM) antibody in the patient's serum [5].

Prognosis appears to be related to degree of crescent formation, intensity of tubulo-interstitial disease, presence of scarring and fibrosis. Greater the histologic

findings, worse is the prognosis. Patients with advanced renal failure, oliguria, and/or serum creatinine more than 5-6 mg/dl, rarely respond to therapy [6]. In case of life threatening alveolar haemorrhage, plasmapheresis may be required for rapid lowering of the circulating level of anti-GBM antibodies. This should be continued for 2 weeks until the antibodies are reduced to the baseline level.

The renal manifestations warrant treatment with high doses of prednisolone (60 mg daily reducing to 20 mg over 4 weeks) and cyclophosphamide (2-3 mg/kg daily). The former may be tapered off over 6 months. The latter can be stopped after 2-3 months as the patient responds. In severe renal failure, there may be a need for dialysis, followed by renal transplantation, if recovery of renal function does not occur. In the era before plasmapheresis and immunosuppressive therapy, the outcome was death in more than 90% cases. With the current therapy, long term survival is more than 50%. We have reported a case of sputum smear negative, (MTB culture sensitive) pulmonary tuberculosis, who had Goodpasture's syndrome. This syndrome per se, is a rare entity and till date there is no association reported between tuberculosis and Goodpasture's syndrome. The prognosis of this condition is not good and some of the patients could have a rapid downhill course as seen in our case.

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