

Case Report

Wegener's Granulomatosis : A Case Report

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ABSTRACT

Wegener's Granulomatosis is a rare disorder, presenting with granulomatous vasculitic lesions, mainly involving the respiratory tract (including the lungs) and associated with glomerulonephritis. We present the case of a 33-year old male patient who was admitted with complaints of cough and hemoptysis associated with vasculitic skin lesions. He had high levels of serum cytoplasmic-antineutrophil cytoplasmic antibody (C-ANCA). The chest X-ray revealed extensive infiltrates in both lung

fields. As the patient was too ill on account of severe hypoxia, lung biopsy could not be carried out, but skin biopsy revealed leukocytoclastic vasculitis. Based on these findings, a clinical diagnosis of Wegener's granulomatosis was made and combined therapy of steroids and cyclophosphamide started. The patient showed dramatic improvement and recovered fully from this life threatening condition.

KEY WORDS: vasculitis, Wegener's granulomatosis

INTRODUCTION

Wegener's Granulomatosis was first described by Friedrich Wegener, a German pathologist^[1]. It is a distinct clinico-pathologic entity characterized by granulomatous vasculitis of the upper and lower respiratory tract together with glomerulonephritis. In addition, variable degrees of disseminated vasculitis involving both arteries and veins may occur. Even though the disease was known to have a high mortality in the past, the recent introduction of combined therapy with cyclophosphamide and steroids helped in reducing the morbidity and mortality. We present the case of a patient with Wegener's granulomatosis who showed dramatic response to therapy and recovered fully.

CASE REPORT

A 33-year-old Kuwaiti male was admitted with skin lesions on both legs of two weeks duration. He had a road traffic accident in 1997, resulting in dysarthria and quadriplegia, which had made him wheelchair bound. On examination, there were painless palpable purpuric eruptions on both legs (Fig. 1). There was no history of fever, epistaxis, bleeding gums or hematuria. On the second day after admission, he developed cough with hemoptysis, followed the next day by shortness of breath and mild knee pain. He had no orthopnea, paroxysmal nocturnal dyspnea or any evidence of inflammation in the joints. Examination of his chest revealed only scattered rhonchi which progressed

two days later into generalized diminished air entry with scattered rhonchi and coarse crepitations.

Laboratory and other investigations revealed the following: Hemoglobin 11.9 g%, WBC 9000/cmm, platelets 302,000/cmm, ESR 110/1st hour. FDP was raised, DDimer >1000, Glucose 7.2 mmol/L, urea 3.2 mmol/L, creatinine 83 µmol/L, Sodium 133 mmol/L and potassium 3.9 mmol/L. Urine analysis showed few epithelial cells with no RBC or casts. Blood and sputum culture grew no organism. Chest X-ray revealed bilateral basal haziness (Fig. 2). A biopsy was taken from the skin lesion (Fig. 1).

Course in the hospital:

The biopsy specimen showed thickening and fibrin deposition in the wall of the small vessels. There was perivascular and interstitial inflammatory cell infiltrate that contained neutrophils which showed leukocytoclasia and nuclear dust formation, as well as extravasated red blood cells. The histopathological diagnosis of the skin biopsy was leukocytoclastic vasculitis

Repeat chest X-ray on the third day revealed extensive infiltrates in both lung fields (Fig. 2). A ventilation perfusion scan of lungs was performed to rule out pulmonary embolism, but was reported as a low probability. CT scan of the chest revealed bilateral extensive alveolar infiltrates multiple nodules and some cavitating nodules (Fig. 3 and 4).

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Fig. 1: Vasculitic skin lesion on the forearm



Fig. 2: X-ray chest on the 3rd day of admission



Fig. 3 and 4: show C.T. Scans with bilateral extensive alveolar infiltrates, multiple nodules, some of them with cavitation

C-ANCA was 117.2 u/ml (normal < 20), antinuclear antibody, anti-ds and anti-cl antibodies were all negative. Anti-GBM antibody was 0.6u/ml (normal < 2), Anti-HCV, HbsAg, and HIV were all negative. Bronchoscopy and lung biopsy were planned but could not be carried out due to deterioration in the patient's condition. The diagnosis of Wegener's granulomatosis was based on histological findings of leukocytoclastic vasculitis in the skin biopsy associated with alveolar hemorrhage, cavitating nodules in the CT scan and a high titer of C-ANCA (Fig. 3 and 4).

The patient was started on pulse therapy of methyl prednisolone (1 g iv daily for 3 days), followed by oral prednisolone and cyclophosphamide (1 g iv once/month). His cough subsided, hemoptysis did not recur, E.S.R. came down to 4 mm/hour, C-ANCA decreased to 49.8 u/ml, and repeat chest X-ray showed resolution (Fig. 5).

DISCUSSION

In view of the symptoms of shortness of breath, hemoptysis and increasing radiological evidence of deterioration, the patient was initially suspected of having pulmonary embolism and heart failure. This was however excluded by a pulmonary V/Q scan that showed low probability and an

echocardiogram that showed good systolic function with no regional wall motion abnormalities. Once the skin biopsy was positive for leukocytoclastic vasculitis with high ESR and high levels of serum C-ANCA, the differential diagnosis of C-ANCA positive vasculitis was considered. The typical lung biopsy evidence of vasculitis with granulomatous inflammation establishes a diagnosis of Wegener's granulomatosis. As the patient was too ill, lung biopsy could not be carried out. Skin biopsy occasionally reveals the typical granulomatous vasculitis, but frequently shows only acute vasculitis but not the full spectrum of pathological changes necessary for the pathologist to be certain. In such cases as in ours, clinical judgment by the physician is needed in arriving at a diagnosis.

Other ANCA positive vasculitic conditions have to be excluded. As there was no bronchospasm and eosinophilia Churg-Strauss vasculitis was unlikely. In microscopic polyangitis, granulomas are absent, there is usually renal involvement and P-ANCA is present in 60% of cases^[2].

Wegener's granulomatosis is a rare disease with an estimated incidence of three per 100,000 in USA and occurs equally in both sexes. Mean age of onset is between 40 and 55 years. In the upper airways, it



Fig. 5: X-ray at discharge from hospital shows marked resolution.

can present with epistaxis, ulceration and perforation of nasal septum. In the lower respiratory tract, it can involve the lung parenchyma, bronchi and rarely, the pleura. Here, it can present as alveolar hemorrhage, nodular infiltrates and cavitating lesions. Endobronchial disease can lead to dyspnea, hemoptysis and bronchial stenosis. The associated glomerulonephritis leads to proteinuria, microscopic hematuria and renal failure. Other organs involved include the skin, eyes, and the nervous system^[3]. The clinical subgrouping according to the severity at presentation of ANCA associated vasculitis is as follows:

1) Localized, 2) Early systemic, 3) Generalized, 4) Severe and 5) Refractory (refractory implies progressive disease despite at least six weeks treatment with an appropriate regimen)^[6].

The disease entity in severe form is fatal if untreated. The life expectancy of untreated cases is only about five months^[4]. The life expectancy of cases treated with steroids improved to 12.5 months^[5]. This indicates that this is a disease, which has high mortality and morbidity, if not recognized and treated early. Combination therapy of cyclophosphamide and steroids has improved the life expectancy and remission rate of the disease.

Though the current treatments are toxic and contribute to morbidity and mortality, immunosuppressive therapy now saves lives and salvages organ function.

Our case illustrates the potential for rapid progression of this disease from simple skin vasculitis and arthralgia to a life threatening alveolar hemorrhage. It also illustrates the usefulness of simple diagnostic procedures like skin biopsy and serum C-ANCA in making the diagnosis of Wegener's Granulomatosis.

We chose to treat patient with a combination our of steroid and iv pulse cyclophosphamide, because it has a lower incidence of long term side effects when compared to steroid and oral cyclophosphamide. Our plan was to combine a tapering dose of prednisolone and pulse cyclophosphamide for six months to induce remission and then change cyclophosphamide to a less toxic immunosuppressive drug like immuran^[6,7].

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