GOODPASTURE'S SYNDROME MIMICKING IDIOPATHIC PULMONARY HEMOSIDEROSIS

(Received 7 April, 1993)

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SUMMARY

A 20 year-old man, developed severe anemia due to occult pulmonary hemorrhage and was falsely diagnosed as having hemolytic anemia. Subsequently, lung biopsy and BAL (bronchoalveolar lavage) suggested idiopathic pulmonary hemosiderosis. Immunofluorescence stain of renal biopsy and serum assay for AGBMA (Anti glomeruli basal membrane antibody) was positive, although renal function and urinary sediment were normal. This case report illustrates that renal biopsy is an important diagnostic procedure in the investigation of occult alveolar hemorrhage syndromes even if the renal function is normal.

Key Words: Occult pulmonary hemorrhage, Goodpasture's syndrome.

INTRODUCTION

Diffuse pulmonary hemorrhage, iron deficiency anemia and infiltrates on chest radiography are well-known features of Goodpasture's syndrome and idiopathic pulmonary hemosiderosis (1-3). Kidney lesions with antiglomerular basement membrane antibodies are present in classical Goodpasture's syndrome, but not in idiopathic pulmonary hemosiderosis (4). In most of the reported cases of Goodpasture's syndrome, pulmonary hemorrhage has preceded overt renal disease by some weeks and in a few cases by years. Recently, a subgroup of these patients has been described having immunoglobulin positivity in the glomeruli basement membrane without any evidence of renal dysfunction (5,6).

We present a case with unusual presentation of ABMA (Anti basement membrane antibody) disease with anemia, occult alveolar hemorrhage and normal renal function and no evidence of proteinuria and hematuria.

CASE REPORT

A 20 year-old man was admitted to a local hospital in 1989 with complaints of weakness, shortness of breath and pallor for 1 week. Physical examination revealed rales in bilateral lung fields and icteric sclera. Laboratory investigation revealed a hemoglobin of 5,8 g/dl, reticulocyte count of 11% and a normal white cell differentiation. Bone marrow examination demonstrated increased erythropoiesis. Serum direct and indirect bilirubin was 0,6 and 5.6 mg/dl. Serum BUN, creatinine levels and urinalysis were normal. These findings suggested hemolytic anemia. Bilateral lung infiltration was noted on the P-A chest radiograph. The patient was hospitalized with the diagnosis of congestive heart failure due to severe hemolytic anemia. 1.5 mg/kg day methylprednisolone was began orally and he was transferred to our hospital for further investigation.

At the time of admission to our hospital, hemoglobin was 10 g/dl, reticulocyte count was 1%, hemolysis tests (haptoglobin, sucrose-lysis,acid-ham, direct and indirect Coomb's, sickling tests), ANA and RF were negative. Serum iron level and iron-binding capacity revealed iron deficiency anemia. 20 mg po methylprednisolone per day was insufficient to stabilize his hemoglobin level. On the 10th day of this treatment hemoglobin decreased to 5.8 g/dl, reticulocyte increased to 8 % and a severe abdominal pain developed. Emergency laparotomy was performed considering the possibility of splenic infarct or pancreatitis. No abnormality was found in the abdomen however splenectomy was performed for the treatment of "hemolytic anemia". After surgery supplemental iron therapy was given besides the 16mg/day po methylprednisolone which resulted in stabilization of hemoglobin at 11.9 g/dl.

Three months later, the patient was readmitted with a complaint of fever. He did not give any history of dyspnea, cough, sputum, hemoptysis or chest pain. Diffuse alveolar infiltration of both lung fields was seen on chest radiography (Fig. 1). Patient was not in respiratory distress and auscultation of the lungs were normal. Fever decreased spontaneously within 24 hours. Hemoglobin was 11 g/dl, arterial blood gas analysis on room air revealed PaO_2 of 68.9 mm Hg, $PaCO_2$ of 34.5 mm Hg and pH of 7.43. Spirometry showed mild restrictive pattern. Diffuse interstitial and alveolar infiltration was remarked on the CT of thorax. Bronchoscopy revealed bloody secretions throughout the airways. Bacterial and fungal cultures, cytologic

studies were negative. Transbronchial biopsy revealed hemosiderin-laden macrophages within normal alveoli and no evidence of vasculitis or granulomatosis. The presence of anemia and diffuse alveolar hemorrhage suggested diagnosis of idiopathic pulmonary hemosiderosis. Despite normal serum creatinine level and normal urinary sediment, for the possibility of diagnosis of ABMA disease renal biopsy was performed. The light microscopy of renal biopsy showed minimal mesengial hyperplasia (Fig. 2), but immunofluorescence microscopy revealed dramatic linear for IgG along all glomerular basement membranes (Fig. 3). The serum AGBMA determination with indirect immunofluorescence was positive (1/20 dilution). These results were compatible with ABMA disease. Cyclophosphamide (100 mg/day) po was added to the methylprednisolone 1 mg/kg/day po therapy. One month later the dose of prednisolone was slowly tapered down to 16 mg every other day and cyclophosphamide to 50 mg per day. He was discharged with normal hemoglobin level, normal renal functions and normal urinary sediment and without any chest complaint under this maintenance therapy.

Six months later, he presented again with dyspnea and fever. Chest radiography was similar to the previous ones. Recurrence of Goodpasture's syndrome or pulmonary infection was considered, urinary sediment revealed microscopic hematuria and proteinuria (550 mg/24 h), BUN and creatinine were normal. Dyspnea was resolved with pulse steroid therapy (1 g/day, three consecutive days). Since then, he is receiving 20 mg methylprednisolone every other day and 100 mg/day cyclophosphamide without any discomfort or detoriation of renal function for 36 months.

DISCUSSION

Since Goodpasture's syndrome was first reported in 1919, pulmonary hemorrhage and crescentic glomerulonephritis with detectable antiglomerular basement membrane antibodies classically characterize this disease (1,2). But the clinical symptoms always did not correlate with the pathologic changes. Matthew et al first described a case of Goodpasture's syndrome in which there was characteristic immunofluorescence findings of Goodpasture's syndrome without any clinical renal abnormality (5). Some authors have speculated that these patients with ABMA are now recognized more often because of improved immunodiagnostic techniques (6,7). Linear immunoglobulin deposition along alveolar and renal glomerular basement membranes are diagnostic features of ABMA disease (1-3). Antiglomerular basement membrane antibody level in the serum can be detected in the acute phase of the illness but a negative result does not exclude ABMA disease (8).

Our case illustrates several interesting features. Initial presentation mimicked hemolytic anemia and congestive heart failure, therefore patient was treated with the diagnosis of hemolytic anemia for 6 months. The diagnosis was wrong, but therapy was effective, corticosteroids resolved anemia by decreasing the intrapulmonary hemorrhage. At the second episode, abnormal lung infiltration was remarked and invasive diagnostic methods were used to define occult lung hemorrhage. Patient had no hemoptysis, anemia was the only objective data to measure the degree of lung hemorrhage. Despite normal renal function, renal biopsy was performed. ABMA in renal tissue and serum was positive. The immunofluorescence staining of lung biopsy was not performed. These

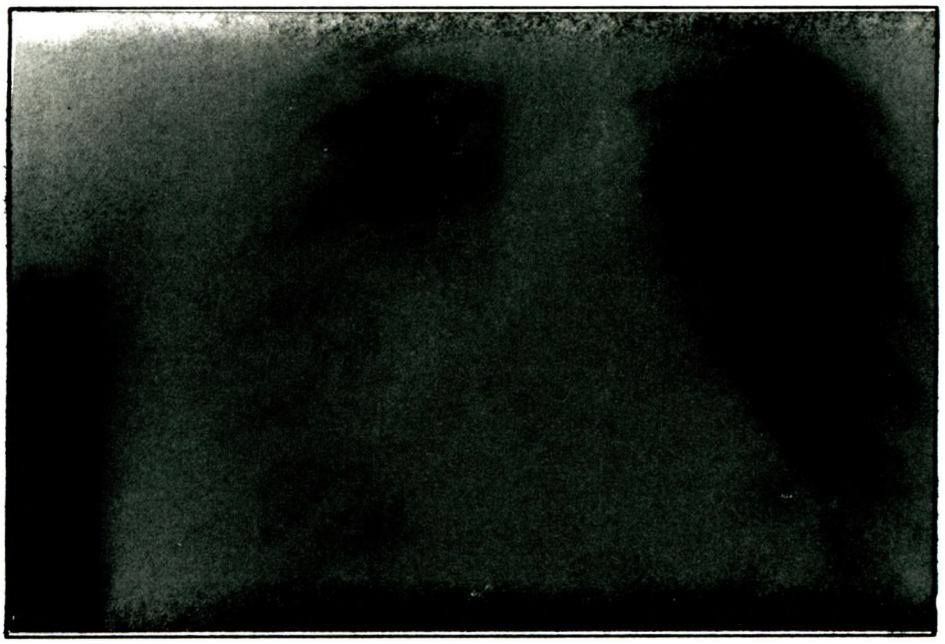

Fig 1. P-A chest x-ray showing diffuse infiltration.

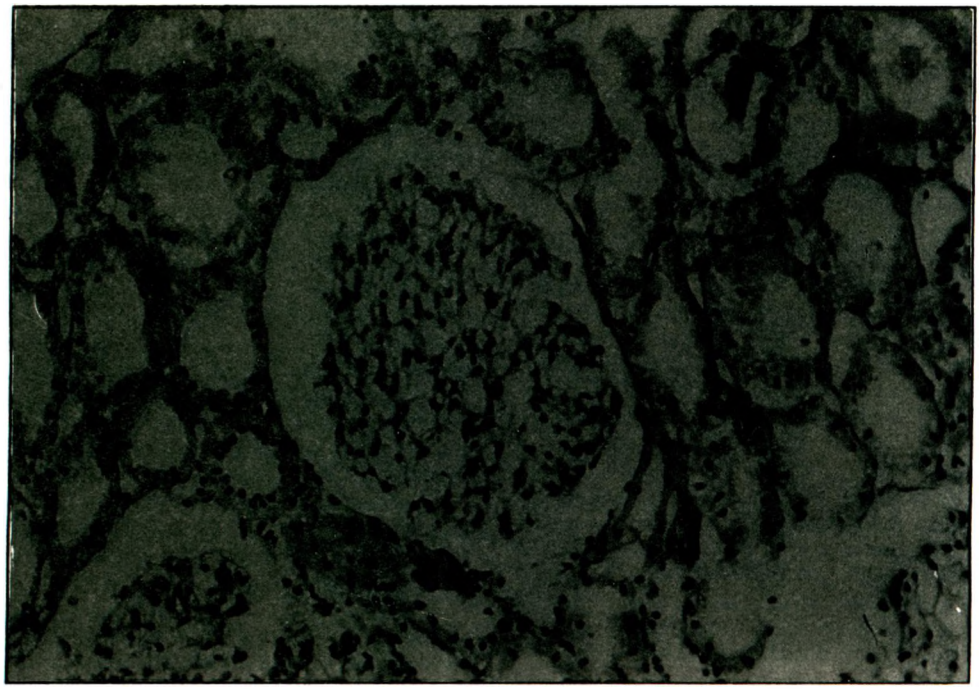

Fig 2. Renal biopsy showing minimal mesengial hyperplasia.

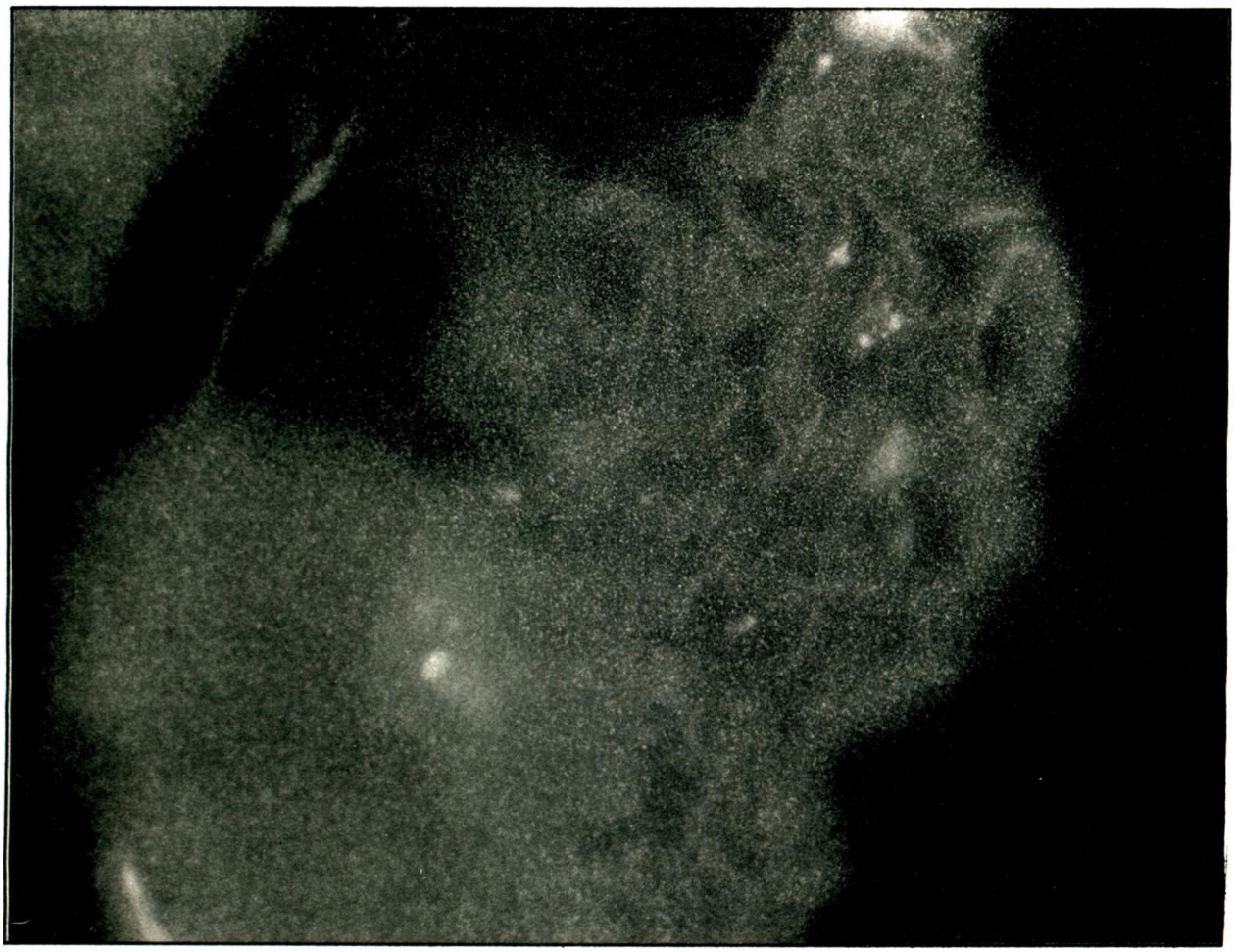

Fig 3. Immunofluorescence microscopy of renal biopsy showing linear staining for IgG.

positive tests were enough to diagnose the Goodpasture's sydrome. At this time, patient had no clinical symptoms of renal involvement, overt microscopic hematuria and proteinuria occurred 6 months after the diagnosis.

A literature review revealed 27 cases of ABMA disease with normal renal function (5-7,9-12). The present case without any renal symptoms at the initial presentation was atypical of Goodpasture's syndrome. It seems reasonable to suggest that pulmonary hemorrhage of uncertain etiology even with normal renal function and urinary sediment should be investigated to rule out Goodpasture's syndrome.

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