

Case Report of a Patient with Goodpasture's Syndrome Who Relapsed While on Hemodialysis

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88

Abstract

Goodpasture's syndrome is a rare autoimmune disease in which anti-glomerular basement membrane antibodies damage the glomerular and alveolar basement membrane. Its relapse is very rare, compared to other pulmonary-renal syndromes. Herein, we present an unusual case of Goodpasture's syndrome, which recurred despite immunosuppressive treatment. After the initial treatment with corticosteroid and cyclophosphamide pulses, plasmapheresis, alveolar hemorrhage ended, and the anti-glomerular basement membrane antibody finding became negative, but hemodialysis had to be continued. After 8 months of hemodialysis, anti-glomerular basement membrane antibodies were re-detected, and hemoptysis occurred a month later. Then, plasmapheresis, intravenous immunoglobulin, and methylprednisone were given in addition to azathioprine treatment; however, the serum anti-glomerular basement membrane antibody positivity persisted.

Relapse of this syndrome is rare, and if observed, it generally strikes years following disappearance of anti-glomerular basement membrane antibodies; however, in our case, relapse was observed within a few months. It should be kept in mind that, in patients who achieve remission following immunosuppressive therapy, clinical and serological relapses are rare, and the anti-glomerular basement membrane antibody positivity may persist despite the application of immunosuppressive agents in subjects who relapsed.

Keywords: Goodpasture, hemodialysis, relapse, vasculitis

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INTRODUCTION

Goodpasture's syndrome typically presents with acute kidney injury due to glomerulonephritis that progresses rapidly, as well as pulmonary hemorrhage, which may be life threatening (1, 2). Acute glomerulonephritis due to anti-glomerular basement membrane (anti-GBM) disease is rare and estimated to occur in less than one case per million. The age distribution is bimodal: between 20 and 30 and 60 and 70 years old, respectively (3). Renal involvement in anti-GBM syndrome is more severe when compared with other types of immune mediated glo-

merulonephritis. The majority of patients are presented with progressive renal failure, resulting in the end-stage renal disease (3). Relapse is very rare in Goodpasture's syndrome. It is different from vasculitis associated with anti-neutrophil cytoplasmic antibodies (ANCA), as well as other pulmonary-renal syndromes.

This is a case report of persistent antibody positivity and alveolar hemorrhage with anti-GBM antibody reappearance after the treatment of Goodpasture's syndrome, who showed clinical and serological responses to treatment.



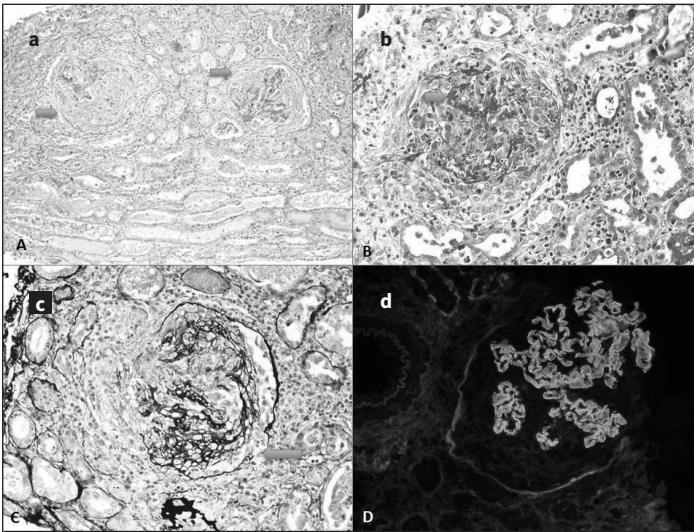


Figure 1. a-d: a) Cellular crescent formation in Bowman's cavity in glomeruli (hematoxylin and eosin) b) Glomerular soft rounded cellular crescent and fibrinoid necrosis in Bowman's cavity (Masson trichrome) c) Cellular crescent formation, rupture in glomerular basement membranes, and Bowman's capsule d) Strong linear positivity in basal membranes with anti-IgG antibody (IgG, fluorescein isothiocyanate)

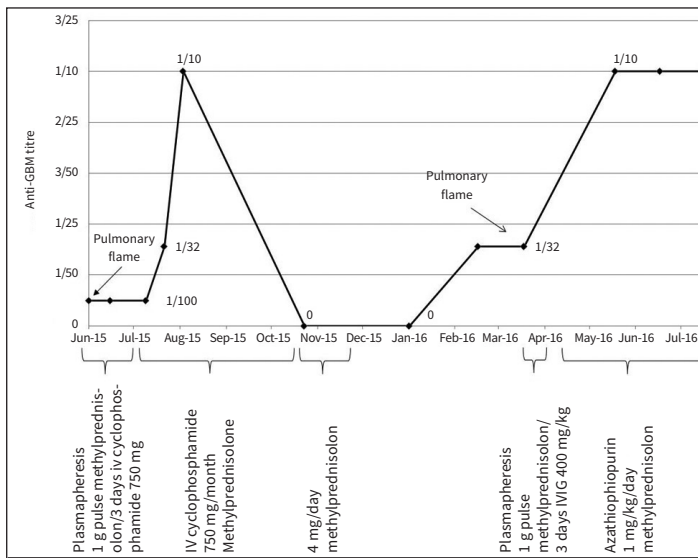


Figure 2: Anti-glomerular basement membrane antibody titers, disease presentations and treatment over time

CASE PRESENTATION

A 17-year-old white male was hospitalized with hemoptysis, nausea, and vomiting. He and his family had no medical problems before. Physical examination revealed pale appearance, bilateral pitting edema, and crackles on lung auscultation. Other systemic examinations were normal. Laboratory findings were the following: blood urea nitrogen, 251 mg/dL; creatinine, 16.4 mg/dL; hemoglobin, 6.2 g/dL; hematocrit, 19%; platelets, 301.000/mm³; and albumin 2.5 g/dL. The urine analysis showed (+++) proteinuria, and erythrocytes and leukocytes were present. The urine sediment had red blood cell

casts. An abdominal ultrasound showed that kidneys' size and shape were normal. Bilateral alveolar infiltrates were detected in the chest x-ray.

Hemodialysis was started. The patient was applied 1 g pulse methylprednisolone for 3 days intravenously due to suspected rapidly progressive glomerulonephritis. Antinuclear antibody, anti-double stranded DNA, ANCA, and hepatitis serology were negative, and the C3 and C4 levels were within normal ranges. The anti-GBM titer was 1:100 positive. Light microscopic examination of kidney biopsy showed 28 glomeruli, and all of them were crescentic: 14 with fibrocellular and 14 with cellular crescents. An immunofluorescence examination of the biopsy revealed linear immunoglobulin G deposition along the glomerular basement membrane, which was compatible with the diagnosis of anti-GBM disease (Figure 1). Plasmapheresis was performed 14 times every other day. As the immunosuppressive therapy, intravenous cyclophosphamide 750 mg/month and methylprednisolone 0.8 mg/kg/day were added. Plain radiographs and thorax computed tomography scan were compatible with alveolar hemorrhage. After plasmapheresis and immunosuppressive therapy, lung symptoms improved, but the need for hemodialysis still persisted.

In the follow-up, steroid doses were gradually decreased. At the end of the 3rd month of the therapy, anti-GBM antibodies were found to be strongly positive, so monthly cyclophosphamide pulse and oral corticosteroid therapies continued. Anti-GBM antibodies were found to be negative at the end of the 5th month of therapy. Renal functional recovery has not been achieved, and the patient continued chronic dialysis program. Oral methylprednisolone dose of 4 mg/day was discontinued after 6 months. Anti-GBM antibodies were found positive again at the 8th month. Then one month later, the patient admitted to our clinic with fever, dyspnea, and hemoptysis. The patient had no history of infection, smoking, cocaine use, and hydrocarbon exposure prior to pulmonary hemorrhage. Plasmapheresis was started again and performed 10 times every other day. Intravenous immunoglobulin 400 mg/kg and pulse steroid 1000 mg were given intravenously to the patient for consecutive 3 days. The treatment continued with the steroid and azathioprine at 1 mg/kg/day. The anti-GBM antibody positivity persisted under these treatment protocols. At the 4th month of azathioprine, it was stopped due to severe pancytopenia and tunneled hemodialysis catheter infection. In spite of effective immunosuppressive treatment during 13 months, the anti-GBM positivity persisted (Figure 2). Renal transplantation was postponed although there was a donor. Rituximab treatment was planned after pancytopenia and the infection resolved. But after that, the patient was followed with a 3/7 hemodialysis program in another health care center. Since the patient had no alveolar hemorrhage, and the anti-GBM titer became negative, he was not given any rituximab treatment. Written informed consent was obtained from the patient.

DISCUSSION

Anti-GBM basement membrane syndrome is an autoimmune disorder in which circulating antibodies are directed mainly against the alpha-3 chain of type IV collagen, which is highly expressed in the glomerular, pulmonary, and other basement membranes (4). There are substantial variations in the clinical manifestations, with 60% to 80% of the patients having manifestations of pulmonary and renal disease, 20% to 40% having renal manifestations alone, and less than 10% having only pulmonary manifestations (5). In our case, the disease presentation was associated with lung and kidney involvement.

Recurrence rates are known to be lower and very rare when compared to ANCA-positive vasculitis and other pulmonary-renal syndromes. Because the recurrence probability is low, we do not give maintenance treatment to patients who are in remission. Relapses are generally seen after many years, but in our case, relapse was seen only after a few months (6). Conventional therapy is based on a combination of plasma exchange with aggressive nonspecific immunosuppression, and relapses are uncommon (6, 7).

Disease severity was parallel with the detection of the anti-GBM antibody (8). Detectable amounts of anti-GBM antibody usually do not remain in the circulation for more than 6-12 months (9). After that time, the recurrence of anti-GBM antibody, as well as the relapse of glomerulonephritis or/and pulmonary hemorrhage is rare (9). In our case, it is compatible with this information, but negative values of the anti-GBM antibody became positive after the clinical findings of disease appeared. The patient was already on a chronic dialysis program, and relapse was seen as pulmonary involvement. This seems to be very difficult to explain. Although intense immunosuppression and plasmapheresis are offered to relapsing patients, there are not enough data present about the treatment of refractory relapses such as the one in our patient. We preferred administering rituximab based on a recently published case series involving 8 patients (10).

In the follow-up of anti-GBM syndrome, antibody levels of the patients whose disease was evaluated as in remission with treatment should be assessed periodically. In our case during the standard treatment, alveolar hemorrhage recurrence was seen, and anti-GBM antibody became positive again and persisted despite immunosuppressive treatment. On the other hand, this case confirms the suggestion that the anti-GBM antibody should be negative for at least six months before renal transplantation.

CONCLUSION

It should be noted that despite the remission of Goodpasture's syndrome with an effective treatment, clinical and serological relapses can be observed rarely, and anti-GBM antibody can persist in relapsing cases despite a long-term immunosuppressive therapy, even if the patient is on a chronic dialysis program. Although intense immunosuppression and plasmapheresis are offered to patients who relapse, these relapses may be more refractory to immunosuppressive treatments.

Informed Consent: Written informed consent was obtained from the patient.

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