doi: 10.5262/tndt.2018.3073

A Case of Goodpasture's Disease who Relapsed while on Hemodialysis

Hemodiyaliz Tedavisi Altında Nükseden Goodpasture Sendromu

ABSTRACT

Goodpasture's syndrome is a rare autoimmune disease, in which anti-glomerular basement membrane antibodies damage glomerular and alveolar basement membrane. Relapse is very rare when it is compared with other pulmonary-renal syndromes. Herein we presented an unusual recurring case of Goodpasture's syndrome, despite immunosuppressive treatment. After the initial treatment with corticosteroid and cyclophosphamide pulses and plasmapheresis, alveolar hemorrhage ended and anti-glomerular basement membrane antibody became negative but the patient's hemodialysis need continued. After eight months of hemodialysis, anti-glomerular basement membrane antibodies were re-detected and hemoptysis occurred one month later. Then, plasmapheresis, intravenous immunoglobulin, and methylprednisone were given in addition to azathioprine treatment but serum anti-glomerular basement membrane antibody positivity persisted.

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

KEY WORDS: Goodpasture, Hemodialysis, Relapse, Vasculitis

ÖZ

Goodpasture sendromu, anti-glomerüler bazal membran antikorlarının glomerüler ve alveoler bazal membranı hedef aldığı, ender görülen otoimmün bir hastalıktır. Diğer pulmoner renal sendromlarla karşılaştırıldığında nüksü nadirdir. İmmünosüpresif tedaviye rağmen, nüks eden Goodpasture sendromu olgusunu sunduk. Kortikosteroid, siklofosfamid ve plazmaferez tedavileri ile hastamızın alveolar hemorajisi sona erdi, anti-glomerüler bazal membran antikoru negatif hale geldi, ancak hemodiyaliz ihtiyacı devam etti. Sekiz aylık hemodiyaliz tedavisi sonrasında, anti-glomerüler bazal membran antikoru tekrar tespit edildi ve antikor pozitifliğinin görülmesinden bir ay sonra hemoptizi tekrarladı. Nüks eden Goodpasture sendromu tanısı ile takibe alınan hastamıza plazmaferez, intravenöz immünoglobülin ve metilprednizon tedavisine ek olarak, azatiopürin verildi, ancak serum anti-glomerüler bazal membran antikor pozitifliği devam etti.

Goodpasture sendromunda relaps nadir görülmekle birlikte, nüks eden olgular genellikle remisyondan yıllar sonra ortaya çıkmaktadır. Bizim olgumuzda nüks remisyon sonrası erken dönemde görüldü. Ayrıca nüks eden hastalarda immünosupresif tedaviye rağmen antikor pozitifliğinin sebat edebileceği akılda tutulmalıdır.

ANAHTAR SÖZCÜKLER: Goodpasture, Hemodiyaliz, Relaps, Vaskülit

Tuba Elif ŞENEL[1]
Sami UZUN[1]
Egemen CEBECİ[1]
Oktay ÖZKAN[1]
Ahmet BEHLÜL[1]
Ayça EROĞLU[1]
Yasemin ÖZLÜK[2]
Savaş ÖZTÜRK[1]

1 Health Sciences University, Haseki Education and Research Hospital, Department of Nephrology, İstanbul, Turkey
2 İstanbul University, İstanbul Faculty of Medicine, Department of Pathology, İstanbul, Turkey

Received : 18.11.2017
Accepted : 13.01.2018

Correspondence Address:
Tuba Elif ŞENEL
Sağlık Bilimleri Üniversitesi, Haseki Eğitim ve Araştırma Hastanesi, Nefroloji Kliniği, İstanbul, Turkey
Phone : +90 212 529 44 00
E-mail : telifsenel@gmail.com

INTRODUCTION

Goodpasture's syndrome typically presents with acute kidney injury due to rapidly progressive glomerulonephritis, 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 populations. The age distribution is bimodal, respectively 20-30 and 60-70 years old (3). Renal involvement in anti-GBM syndrome is more severe when compared with other types of immune mediated glomerulonephritis. The majority of patients are presented with progressive renal failure, resulting in end stage renal disease (3). Relapse is very rare in Goodpasture's syndrome. It is different from anti-neutrophil cytoplasmic antibodies (ANCAs) associated vasculitis 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 treatment of anti-GBM syndrome which gave clinical and serological response to treatment.

CASE REPORT

A 17-year-old white male was hospitalized with hemoptysis, nausea and vomiting. He and his family had no previous medical problem. Physical examination revealed a pale appearance, bilateral pitting edema, and crackles on lung auscultation. Other system examinations were normal. Laboratory findings were blood urea nitrogen: 251 mg/dL, creatinine: 16.4 mg/dL, hemoglobin 6.2 g/dL, hematocrit: 19%, platelets: 301.000/mm^3, and albumin 2.5 g/dL. Urine analysis showed (+++) proteinuria, erythrocytes and leukocytes. The urine sediment had red blood cell casts. Abdomen ultrasound showed that kidneys' size and shape were normal. Bilateral alveolar infiltrates were detected on chest x-ray.

Hemodialysis was started 1 g pulse methylprednisolone for 3 days was given intravenously to the patient due to suspicion of rapidly progressive glomerulonephritis. Antinuclear antibody, anti-double stranded DNA, ANCA, hepatitis serology were negative and C3 and C4 levels were within the normal range. Anti-GBM titer was 1:100 positive. Light microscopic examination of kidney biopsy showed 28 glomeruli; all of them were crescentic, 14 had fibrocellular and 14 cellular crescents. 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 1A-D). Plasmapheresis was performed for 14 times, every other day. As 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 hemorrhagr. After plasmapheresis and immunosuppressive therapy, lung symptoms were improved but the need for hemodialysis still persisted.

During follow up, steroid doses were gradually decreased. At the end of the third month of the therapy, anti-GBM antibodies were found to be strongly positive and monthly cyclophosphamide pulse and oral corticosteroid therapies were continued. Anti-GBM antibody was found to be negative at the end of the fifth month of the therapy. Renal functional recovery had not been achieved and the patient continued the chronic dialysis program. Oral 4 mg/day methylprednisolone was stopped after the sixth month. Anti-GBM antibody was found positive again at the eighth month. One month later, the patient was admitted to our clinic with fever, dyspnea and hemoptysis. The patient had no history of infection, smoking, cocaine use or hydrocarbon exposure prior to the 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 3 consecutive days. The treatment was continued with steroid and azathioprine 1 mg/kg/day. Anti-GBM antibody positivity persisted under these treatment protocols. At the fourth month of azathioprine, it was stopped due to severe pancytopenia and tunneled hemodialysis catheter infection. In spite of effective immunosuppressive treatment during thirteen month; anti-GBM positivity persisted (Figure 2). Renal transplantation was postponed although there was a donor. Rituximab treatment was planned after resolution of pancytopenia and his infection. The patient was followed with a 3/7 hemodialysis program at another healthcare center afterwards. Since the patient had no alveolar hemorrhage and the anti-GBM titer became negative, he was not given any rituximab treatment.

DISCUSSION

Anti-glomerular 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 years of time 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 paralleled the detection of anti-GBM antibody (8). Detectable amounts of anti-GBM antibody usually do not remain in the circulation for >6-12 months (9). After that time, the recurrence of anti-GBM antibody as well as relapse of glomerulonephritis or/and pulmonary hemorrhage is rare (9). In our case, it is compatible with these information, but negative values of anti-GBM antibody turned into positive after clinical findings of disease appeared and while the patient was already on a chronic dialysis program, relapse was seen as pulmonary involvement. It seems very difficult to explain. Although intense immunosuppression and plasmapheresis are offered to relapsing patients, not enough data is present for treatment of refractory relapses such as in our patient. We preferred administering rituximab based on a recently published case series of eight patients (10).

In the follow-up of anti-GBM syndrome, antibody levels of the patients whose diseases were evaluated as in remission with treatment should be assessed periodically. In our case, alveolar hemorrhage recurrence was seen during standard treatment, and anti-GBM antibody turned to positive again and persisted despite immunosuppressive treatment. On the other hand, this case confirms the suggestion that anti-GBM antibody should be negative for at least 6 months for renal transplantation.

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

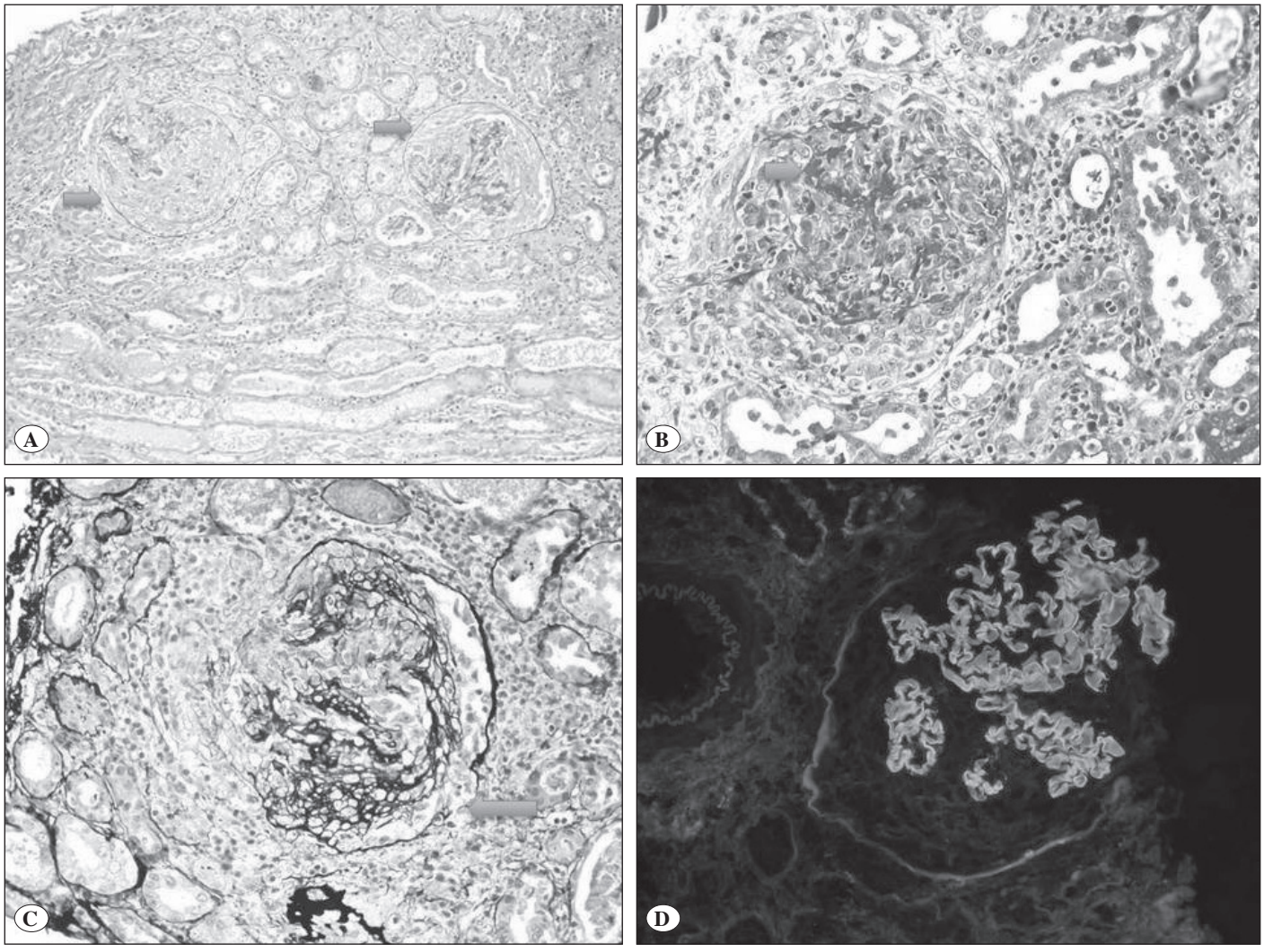

Figure 1: A) *Cellular crescent formation in Bowman cavity in glomeruli (Hematoxylin and eosin)* ***B)*** *Glomerular soft rounded cellular crescent and fibrinoid necrosis in Bowman's cavity (Masson trichrome)* ***C)*** *Cellular crescent formation, rupture in glomerular basement membranes and Bowman's capsule* ***D)*** *Strong linear positivity in basal membranes with anti-IgG antibody (IgG, Fluorescein isothiocyanate)*

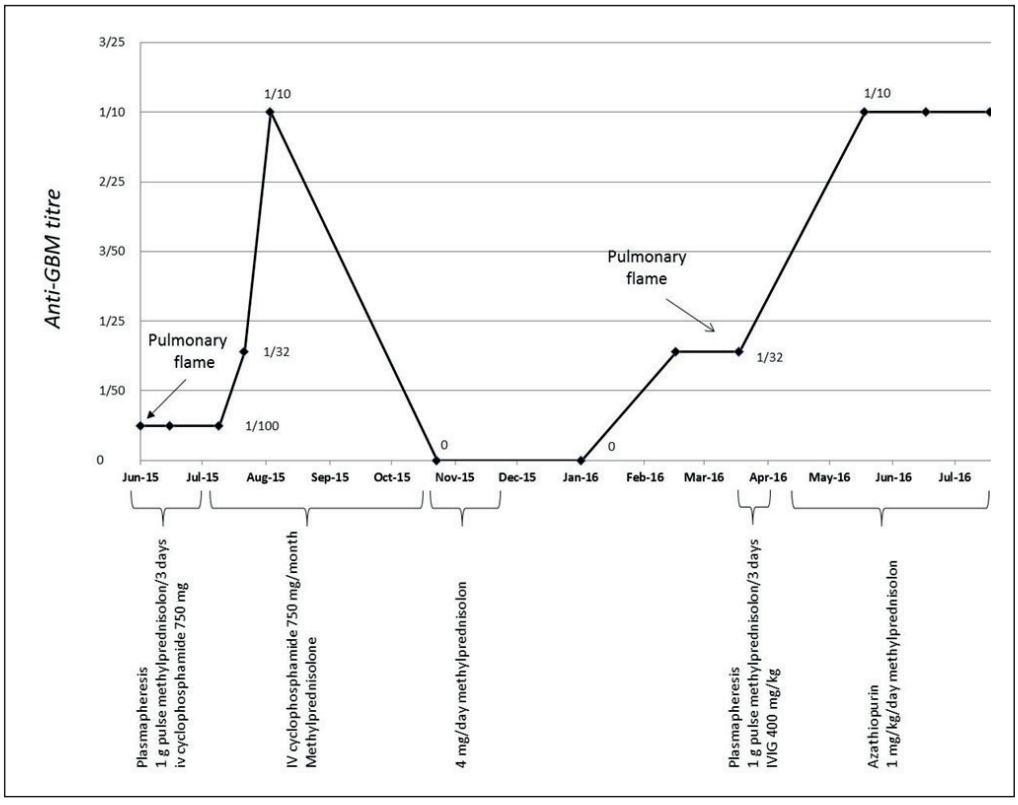

Figure 2: *Anti glomerular basement membrane antibody titers, disease presentations and treatment over time.*

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