Goodpasture Syndrome with Negative Serum Test for Anti-GBM Antibodies: A Rare Case Report

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Abstract

Goodpasture syndrome is a rapidly progressive and fatal disease. Serum anti-glomerular basement membrane (GBM) antibody is used for diagnosis, but the test is time-consuming and a false-negative is possible. Most hospitals in Taiwan, the test would be performed when the samples collected up to a certain amount. Thus, renal biopsy is the gold standard for a definite diagnosis. The case presented here was negative for serum anti-GBM antibody, but immunofluorescence microscopy of tissue from a renal biopsy indicated linear deposition of IgG on the glomeruli. Patients who present with suspected pulmonary renal syndrome should be considered for renal biopsy, and pulse corticosteroid therapy with plasmapheresis should be promptly initiated. (J Intern Med Taiwan 2017; 28: 108-111)

Key Words: Goodpasture syndrome, Pulmonary renal syndrome, Anti-GBM antibody

Case Report

A 26-year-old man, without known underlying medical diseases, presented to our emergency room with severe dyspnea and hemoptysis for the previous 3 days. He reported being healthy until approximately 2 weeks previously. At that time, he developed an intermittent low grade fever without chills, a dry cough, malaise, and fatigability. His primary care physician prescribed diclofenac, benzonatate, and levocetirizine, but these had little effect. His cough worsened, he developed blood-tinged sputum, and began to have progressive shortness of breath.

On physical examination, the patient’s temperature was 37°C, his pulse was regular at 95 beats per min, his respiratory rate was 22 breaths per minute, and his blood pressure was 167/111 mm Hg. He had hypoxemia, with an oxygen saturation of 88% while breathing ambient air, and his conjunctiva were pale. All other findings of the physical examination were normal.

A complete blood count indicated a white cell count of 16,500/µL, 81.2% neutrophils, hemoglobin of 8.6 g/dL, and a platelet count of 418,000/µL. The prothrombin time/international normalized ratio was 11.8 s/1.08 and the activated partial thromboplastin time was 35.8 s. His blood urea nitrogen was
54 mg/dL, serum creatinine was 10.42 mg/dL, Na was 140 mmol/L, and K was 2.2 mmol/L.

The presence of combined renal and pulmonary dysfunction led us to perform several additional tests. The results of serum tests for anti-glomerular basement membrane (GBM) antibody, anti-neutrophil cytoplasmic antibodies (ANCA), and cryoglobulin were all negative. More specifically, fluorescence enzyme immunoassays indicated the level of Anti-GBM antibody was 6.7 EliA U/mL, and ANCA, including anti-myeloperoxidase antibody and anti-protease 3 antibody, was less than 0.2 IU/mL. A complement test indicated normal levels of C3 and C4. A chest X-ray and chest computed tomography revealed the presence of a bilateral alveolar infiltration with an air bronchogram (Fig. 1).

The patient was intubated with mechanical ventilator support due to a pulmonary hemorrhage complicated by acute hypoxic respiratory failure. Pulse corticosteroid therapy was initiated after the bronchoscopy exam to exclude active pulmonary infection.

An ultrasound-guided renal biopsy was performed on day 4. The result indicated the presence of glomerular crescent formation in hematoxylin and eosin staining (Fig. 2) and a linear deposition of IgG in immunofluorescence staining of glomeruli (Fig. 3). These results are consistent with deposition of glomerular basement membrane antibody and Goodpasture syndrome. Plasmapheresis was initiated after the preliminary pathologic report, and cyclophosphamide (500 mg) was given intravenously after the pulse corticosteroid therapy. The patient’s clinical condition stabilized, and he exhibited great improvement. There were also improvements in the chest X ray. Extubation was performed on day 9 but the renal function was irreversibly impaired and led to end-stage renal disease.
Discussion

Goodpasture syndrome is a rare but life-threatening disease, characterized by rapidly progressive crescentic glomerulonephritis and pulmonary hemorrhage. It was estimated to occur in fewer than one case per million population\textsuperscript{12}. Seronegative anti-GBM disease may occur in 2–3\% of these patients\textsuperscript{8}. The prognosis of patients with untreated disease is extremely poor. More than 90\% of patients die or undergo dialysis\textsuperscript{1}, so rapid diagnosis is needed. Anti-GBM antibody disease is most often idiopathic, although it occasionally follows pulmonary infection or injury. Smoking or inhaled hydrocarbons and the ensuing damage leads to expression of an epitope that incites an immune response.\textsuperscript{2,3,4,5}

A circulating autoantibody is directed against an antigen intrinsic to the GBM. The target of this anti-GBM antibody is the NC1 domain of the alpha-3 chain of type IV collagen, one of 6 genetically distinct gene products present in the GBM collagen.\textsuperscript{5}

Timely initiation of pulse corticosteroid therapy and plasma exchange can be lifesaving.

Serum anti-GBM antibody is indicative of Goodpasture syndrome, but false negatives may occur.\textsuperscript{8} The sensitivity of tests for the autoantibody depends on the specific method used such as indirect immunofluorescent and radioimmunoassay techniques. Some studies reported IgA or IgM deposited on the GBM and in the circulation.\textsuperscript{8,9} A more common method is the detection of anti-GBM antibodies in serum using a direct enzyme-linked immunoassay (ELISA); the specificity of the antibody can be confirmed by western blotting. High antibody titers are usually present in patients with rapidly progressive disease.\textsuperscript{7,10} The sensitivity of the serum tests depends upon the commercial kit used, and ranges from 63\% to nearly 100\%. However, pathological examination of a renal biopsy is the gold standard for diagnosis. Plasmapheresis in combination with immunosuppression therapy is the main treatment\textsuperscript{11,12,13} but the optimal duration of treatment is unknown. Spontaneous cessation of autoantibody formation can take 6 to 9 months or longer.\textsuperscript{14} Relapses are uncommon, but data on the relapse rate are inconclusive.\textsuperscript{9,15,16, 17}

Conclusion

Goodpasture syndrome is a rapidly progressive and fatal disease if untreated. The serum anti-GBM antibody test takes time, and false-negatives are possible. A renal biopsy should not be delayed, and is the gold standard for confirming diagnosis. The present case was serum-negative for the anti-GBM autoantibody, making diagnosis more difficult.

References


一個罕見的病例：
抗基底膜抗體陰性 Goodpasture 症候群

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摘 要

Goodpasture症候群是個進展快速且致命的疾病，血清中的抗基底膜抗體被用來診斷這疾病，但等待這結果相當耗費時間且結果可能呈現陰性。腎臟切片是用來確認診斷這疾病的黃金準則。這個案例正是抗基底膜抗體陰性但腎臟切片以免疫熒光染色下呈現以 IgG 線狀沉積在腎絲球基底膜上的分布。病人以疑似肺腎症候群表現來就醫時，必須要考慮做腎臟切片且儘速開始作脈衝式類固醇給予以及作血漿置換。