J Korean Med Sci 2000; 15: 99-102
ISSN 1011-8934

A Case of Goodpasture's Syndrome with Massive Pulmonary Hemorrhage

We present a typical case of Goodpasture's syndrome with massive pulmonary hemorrhage and acute deterioration of renal function. A 20-year-old male was admitted due to severe azotemia (blood urea nitrogen 214.7 mg/dL, serum creatinine 30.2 mg/dL) and was treated with emergency hemodialysis. On the 4th hospital day, a sudden onset of pulmonary hemorrhage developed. The circulating level of anti-glomerular basement membrane antibody was then elevated highly, and the kidney biopsy showed crescentic glomerulonephritis and linear deposition of IgG along the glomerular capillary. The patient was treated with intravenous high dose-steroid, oral cyclophosphamide and plasma exchanges. The pulmonary hemorrhage improved with the therapy, however, his renal function did not improve. He is currently on a regular schedule of hemodialysis.

Key Words: *Goodpasture's Syndrome; Hemoptysis; Glomerulonephritis, Anti-Glomerular Basement Membrane Disease*

Young Ok Kim, Jee Yeun Choi, Joon Il Park, Sun Ae Yoon, Chul Woo Yang, Kwan Hyoung Kim, Byung Kee Bang

Department of Internal Medicine, College of Medicine, The Catholic University of Korea, Seoul, Korea

Received: 22 June 1999
Accepted: 17 July 1999

Address for correspondence
Byung Kee Bang, M.D.
Department of Internal Medicine, Kangnam St. Mary's Hospital, College of Medicine, The Catholic University of Korea, 505 Banpo-dong, Seocho-gu, Seoul 137-701, Korea
Tel: +82.2-590-1413, Fax: +82.2-599-3589

INTRODUCTION

Goodpasture's syndrome is a disorder consisting of a triad of glomerulonephritis, commonly of the rapidly progressive type, pulmonary hemorrhage and circulating anti-glomerular basement membrane antibody (anti-GBM Ab) (1-3). Pulmonary hemorrhage precedes or is discovered coincidentally with the renal lesion in most patients (4, 5). Because of rapid progression of the disease and its high mortality, prompt and accurate diagnosis is very important. Initial therapy with plasma exchange combined with oral cyclophosphamide and high-dose steroid has been recommended (1). The incidence is common in the western world. However, it is extremely rare in Korea, and only one case has been reported (6). We report here a case of a 20-year-old Korean with Goodpasture's syndrome in which massive pulmonary hemorrhage and acute deterioration of renal function developed.

CASE REPORT

A 20-year-old male patient was admitted with chest discomfort and general weakness for two weeks. There had been no history of renal or pulmonary disease. On admission, his blood pressure was 120/90 mmHg, pulse rate 75/min, respiration rate 24/min, and body temperature 36.3℃. Heart sounds were normal, but slight inspiratory crackles were audible on both lower lung fields.

The initial laboratory findings were as follows: white blood cell count was 14,500/μL, hemoglobin 10.4 g/dL, hematocrit 30.7%, and platelet count 345,000/μL on complete blood counts. The fasting blood sugar level was 97 mg/dL, blood urea nitrogen 214.7 mg/dL, creatinine 30.2 mg/dL, sodium 141 mEq/L, potassium 5.5 mEq/L, chloride 98 mEq/L, calcium 7.6 mg/dL, phosphorus 7.3 mg/dL, magnesium 3.0 mg/dL, total protein 5.1 g/dL, albumin 2.1 g/dL, aspartate aminotransferase 18 IU/L and alanine aminotransferase 14 IU/L on blood chemistry. Protein was (3+), RBC 30-49/HPF and WBC 5-9/HPF on urinalysis. On admission, 24-hr urine volume was 500 mL, and the amount of protein was 0.9 g/day. Serum complement levels were normal. HBsAg, anti-HCV, ANA, anti-ds DNA, and ANCA were all negative. The initial chest X-ray showed mildly increased interstitial markings without cardiomegaly. The kidneys were normal in size on abdominal sonography.

Since the uremia was very severe on admission, emer-

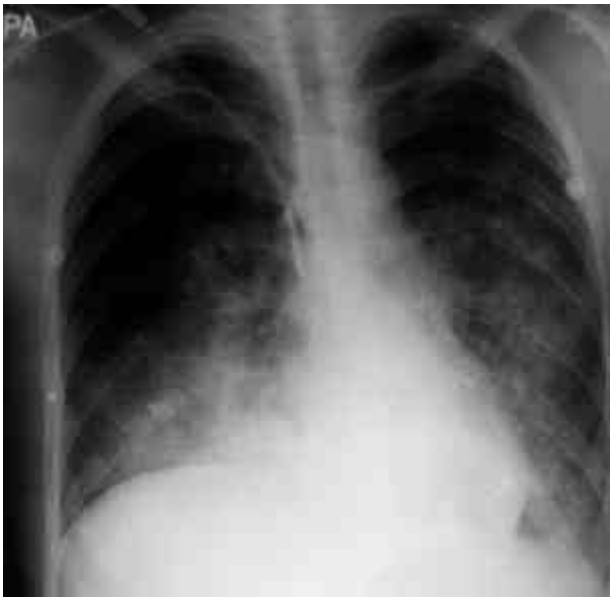

Fig. 1. Chest radiograph shows bilateral alveolar infiltrates predominantly in the mid- and lower lung zones.

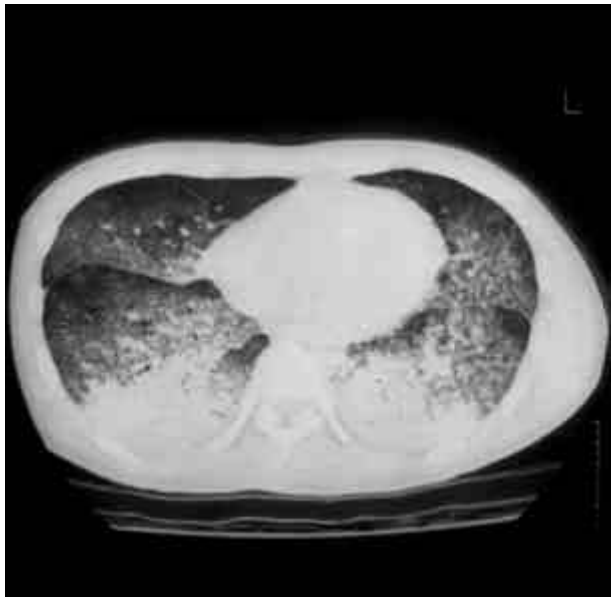

Fig. 2. High-resolution computed tomography of the chest shows bilateral airspace consolidation with ground-glass opacification.

gent hemodialysis was performed. On the fourth hospital day, there was a sudden onset of massive hemoptysis and respiratory distress. Massive pulmonary hemorrhage was then seen on chest X-ray (Fig. 1) and computed tomography (Fig. 2). The level of anti-GBM Ab was 256.7 EU/mL (normal range <5.1 EU/mL). Intravenous methylprednisolone (1,000 mg/day), oral cyclophosphamide (100 mg/day), and plasma exchange of 2.2 L/day were performed. Despite intensive immunosuppressive therapy, pulmonary hemorrhage persisted, and therefore tracheostomy was done on the seventh hospital day. Acute renal failure did not improve as well, and hemodialysis had to be continued. On the 14th hospital day, the pulmonary hemorrhage gradually began to decrease and the steroid was tapered to 125 mg while continuing plasma exchange. Soon after tapering the steroid, however, massive pulmonary hemorrhage developed with increased level of circulating anti-GBM Ab to 400 EU/mL, thus the steroid dosage was increased to 500 mg. Afterwards, there was no more pulmonary hemorrhage. On the 20th hospital day, nausea and seizure developed, but serum ionized calcium level and brain computed tomography were normal. Thereafter, cyclophosphamide and plasma exchange were discontinued, and only steroid was administered. There was neither more nausea nor seizure attack. While tapering the steroid, severe pulmonary hemorrhage recurred on the 24th hospital day, and the steroid dosage had to be increased to 1,000 mg. Pulmonary hemorrhage then began to decrease, and it completely disappeared on the 30th hospital day. Percutaneous renal biopsy was done on the 45th hospital day. Under light microscopy, 19 (86.4%) of total 22 glomeruli demonstrated global sclerosis, and also in the rest of the 3 (13.6%) glomeruli, there were crescentic glomerulonephritis (Fig. 3). Demonstrating an irreversible change, linear deposition of IgG along the glomerular capillary walls was observed under the immunofluorescent study (Fig. 4). To maintain hemodialysis, arteriovenous fistula was made on the 50th day. Anti-GBM Ab level also began to decrease from 178 EU/mL to 93.2 EU/mL, and then to 54.7 EU/mL, on the 28th, 40th, and 66th hospital day, respectively. On the 70th hospital day, the

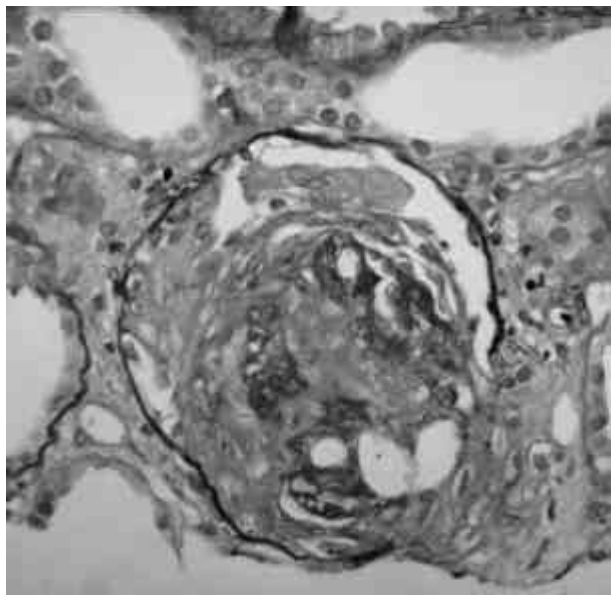

Fig. 3. Light microscopic finding of biopsy specimen from kidney shows circumferential fibro-cellular crescent in a glomerulus (H&E, ×400).

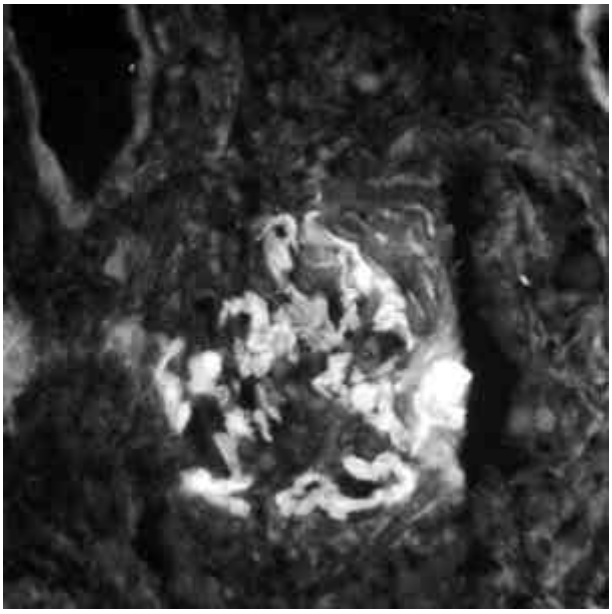

Fig. 4. Immunofluorescent microscopic finding of biopsy specimen from kidney shows linear deposition of IgG along the glomerular basement membrane (×400).

patient was discharged with steroid (oral prednisolone) treatment tapered to 40 mg.

DISCUSSION

Goodpasture's syndrome is defined as a disorder in which circulating anti-GBM Ab reacts with the basement membrane of pulmonary alveoli, leading to pulmonary hemorrhage and acute deterioration of the renal function (1). Linear deposition of IgG along the glomerular capillary walls on immunofluorescent stain of the kidney biopsy material is characteristic of the disease (2). This disease occurs twice more in men than women, and patients from 20 to 30 years of age are usually affected (1, 3). Once the disease sets in, the renal function declines rapidly within several days to several months (3, 4). Episodes of pulmonary hemorrhage precede or coincide with the glomerulonephritis in most patients (4, 5). When rapidly progressive glomerulonephritis develops due to anti-GBM antibodies without the pulmonary hemorrhage, it is not named as Goodpasture's syndrome but designated as anti-GBM Ab-mediated glomerulonephritis (2, 4, 7). The patient in our case was a 20-year-old male, who was admitted for acute renal failure. Acute massive pulmonary hemorrhage occurred on the fourth hospital day. Despite aggressive therapy of high-dose steroid and plasma exchange, there were two more episodes of severe, recurrent pulmonary hemorrhage.

The etiology of anti-GBM Ab production, which is necessary to diagnose Goodpasture's syndrome, is not well known. But, environmental factors, such as inhaled hydrocarbon (8, 9), cigarette smoking (10), cocaine (11) and virus (12, 13) have been considered as causative agents. The anti-GBM antibody titer reaches its peak level when clinical symptoms are manifest and then begins to decrease, hastened by steroid therapy and plasma exchange (14, 15). Although the antibody production usually subsides with time, the elevation of the antibody have been reported in association with symptomatic recurrences (16, 17).

This patient was in a severe uremic state on admission with serum creatinine of 30.2 mg/dL and anti-GBM Ab titer was also markedly elevated to 256.7 EU/mL. Disregarding the aggressive therapy, pulmonary hemorrhage recurred twice and the anti-GBM Ab level reached 400 EU/mL and 178 EU/mL on each episode of hemorrhage, respectively. As the anti-GBM Ab titer gradually dropped to 54.3 EU/mL, recurrent pulmonary hemorrhage was no longer observed. Therefore, we suggest that anti-GBM Ab titer may be directly related to the development of pulmonary hemorrhage in this case.

The pathologic findings of Goodpasture's syndrome under light microscopy shows fibro-cellular crescentic glomerulonephritis, and the immunofluorescent study reveals the characteristic linear deposition of IgG along the glomerular basement membrane (1). Since pulmonary hemorrhage has persisted for quite a long time in our patient, the renal biopsy was delayed and was not performed until the 45th hospital day. Global sclerosis was found in more than 80% of the glomeruli on light microscopy, and fibro-cellular crescents were also observed in the rest of the glomeruli, demonstrating an irreversible change.

For the initial management of Goodpasture's syndrome, a combination therapy of plasma exchange, intravenous high-dose steroid, and oral cyclophosphamide has been recommended (1). The proper time for discontinuing plasma exchange and tapering the dosage of immunosuppressive agents should be decided, depending on the presence of clinical symptoms such as pulmonary hemorrhage and the titer of anti-GBM Ab. Although plasma exchange is believed to be the most effective therapy, there are some controversial reports about its effectiveness (18, 19). Response to therapy chiefly relies on the degree of initial renal function. When the serum creatinine level is above 8 mg/dL, the reversal of renal function is thought to be difficult (1). In our case, a combination of plasma exchange, intravenous high-dose steroid, and oral cyclophosphamide was used as the initial therapy. While tapering the steroid dose, massive pulmonary hemorrhage developed, and the anti-GBM Ab titer was high (400 EU/mL). Oral cyclophosphamide and plasma exchange were discontinued on the 20th hospital day

when nausea and seizure occurred. Afterwards, only the steroid was administered. While tapering the steroid, pulmonary hemorrhage recurred, which was then controlled with increased dosages of steroid. Therefore, we suggest that high-dose steroid therapy is more effective than plasma exchange in our patient.

REFERENCES

1. Glassock RJ, Cohen AH, Adler SG, Ward HJ. *Secondary glomerular diseases. In: Brenner BM, Rector FC, eds. The kidney. Philadelphia: Saunders, 1991; 1280-368.*
2. Lerner RA, Glassock RJ, Dixon FJ. *The role of anti-glomerular basement membrane antibody in the pathogenesis of human glomerulonephritis. J Exp Med 1967; 126: 989-1004.*
3. Kalluri R. *Goodpasture syndrome. Kidney Int 1999; 55: 1120-2.*
4. Wilson CB, Dixon FJ. *Anti-glomerular basement membrane antibody-induced glomerulonephritis. Kidney Int 1973; 3: 74-89.*
5. Ewan PW, Rees AJ. *Pulmonary hemorrhage in Goodpasture's syndrome. N Engl J Med 1977; 296: 574-5.*
6. Chung SH, Kim KH, Kim YS, Hong CS, Lee HY. *A case of Goodpasture's syndrome. J Korean Soc Nephrol 1982; 1: 51-8.*
7. Lee SW, Jung YS, Kim PW, Choi JH, Kim TS, Cha MK, Lee JH, Ha SY. *A case of anti-glomerular basement membrane antibody mediated rapidly progressive glomerulonephritis. J Korean Soc Nephrol 1998; 17: 151-6.*
8. Bombassei GJ, Kaplan AA. *The association between hydrocarbon exposure and anti-glomerular basement membrane antibody-mediated disease (Goodpasture's syndrome). Am J Ind Med 1992; 21: 141-53.*
9. Stevenson A, Yaqoob M, Mason H, Pai P, Bell GM. *Biochemical markers of basement membrane disturbances and occupational exposure to hydrocarbons and mixed solvents. QJM 1995; 88: 23-8.*
10. Escolar Castellon JD, Roche Roche PA, Escolar Castellon A, Minana Amada C. *The modifications produced in allergic alveolitis and in Goodpasture's syndrome due to exposure to cigarette smoke. Histol Histopathol 1991; 6: 535-47.*
11. Garcia-Rostan y Perez GM, Garcia Bragado F, Puras Gil AM. *Pulmonary hemorrhage and antiglomerular basement membrane antibody-mediated glomerulonephritis after exposure to smoked cocaine (crack): a case report and review of the literature. Pathol Int 1997; 47: 692-7.*
12. Wilson CB, Smith RC. *Goodpasture's syndrome associated with influenza A2 virus infection. Ann Intern Med 1972; 76: 91-4.*
13. Tsai CC, Kissane JM, Germuth FG. *Paramyxovirus-like structures in Goodpasture's syndrome. Lancet 1974; 7880: 601-2.*
14. Madore F, Lazarus JM, Brady HR. *Therapeutic plasma exchange in renal diseases. J Am Soc Nephrol 1996; 7: 367-86.*
15. Johnson JP, Moore J Jr, Austin HA 3d, Balow JE, Antonovych TT, Wilson CB. *Therapy of anti-glomerular basement membrane antibody disease: analysis of prognostic significance of clinical, pathologic and treatment factors. Medicine 1985; 64: 219-27.*
16. Mehler PS, Brunvand MW, Hutt MP, Anderson RJ. *Chronic recurrent Goodpasture's syndrome. Am J Med 1987; 82: 833-5.*
17. Hind CR, Bowman C, Winearls CG, Lockwood CM. *Recurrence of circulating anti-glomerular basement membrane antibody three years after immunosuppressive treatment and plasma exchange. Clin Nephrol 1984; 21: 244-6.*
18. Levy JB, Pusey CD. *Still a role for plasma exchange in rapidly progressive glomerulonephritis? J Nephrol 1997; 10: 7-13.*
19. McLeish KR, Maxwell DR, Luft FC. *Failure of plasma exchange and immunosuppression to improve renal function in Goodpasture's syndrome. Clin Nephrol 1978; 10: 71-3.*