
*Case report***Different Outcome of Goodpasture Syndrome**Vesna Ristovska¹, Borislav Kondov² and Ladislava Grcevska¹¹Department of Nephrology, ²Department of vascular surgery, Medical Faculty, University "Ss Cyril and Methodius" Skopje, Republic of Macedonia

Abstract

Goodpasture syndrome is a rare autoimmune disease, with significant morbidity and mortality in young people and otherwise healthy population. Complete disease remission is possible with prompt diagnosis and treatment. We report 3 cases with Goodpasture syndrome treated at the Department of Nephrology, University Clinic of Nephrology, with different outcome. All of the patients were with similar clinical feature, with renal failure that needed treatment with hemodialysis. But results of the treatment with plasmapheresis indicate that this procedure reduces morbidity in patients with Goodpasture syndrome. The clinical course and the outcome of the disease were different. The disease is unpredictable, and the early diagnosis and start with the treatment is important for the remission.

Keywords: goodpasture syndrome, kidney function, plasmapheresis, treatment

Introduction

Goodpasture syndrome is a rare, but serious autoimmune disease, that attacks the lungs and kidneys. The disease occurs when the body's immune system, mistakenly produces antibodies against collagen in the lungs and kidneys. It is almost always fatal; if it is not quickly diagnosed and treated [1-3].

Researchers do not fully understand why immune system attacks collagen in the lungs and kidneys. Goodpasture syndrome usually affects young people, between 20-30 years old and sometimes older than 60 years. The first signs of the disease may include fatigue, nausea and vomiting, difficult breathing and pale skin. Because the disease may rapidly involve the lungs, initial symptoms like shortness of breath and cough may occur sometimes with blood. When the kidneys are affected, symptoms include high blood pressure, hematuria, dysuria, swelling and back pain [4,5]. Although Goodpasture syndrome may cause life-threatening bleeding in the lungs, it usually does not cause long-term lung damage,

but the most serious consequence is kidney failure, which may require either dialysis or kidney transplantation [6,7]. We report 3 cases with Goodpasture syndrome, treated at the Department of Nephrology, University Clinic of Nephrology in Skopje. The different outcome of the 3 cases shows that the disease is unpredictable.

Case 1

A 61-year-old woman was admitted to our Department with a history of coughing and mild hemoptysis, associated with fatigue, febrility and inappetence. She was treated as virosis several months ago, with temporary stabilizing, but after that, the malaise and coughing were repeated again, and she was hospitalized at our Department, with similar clinical symptoms. Before admission a computerized tomography of the lungs was done and after that a transthoracic biopsy of a nodular formation in the lungs was performed. The result of the lung biopsy showed granulomatous inflammation. The control chest-x rays disclosed a few scattered pulmonary infiltrates and a small exudative pleuritis. Laboratory findings were as follows: hemoglobin 85 g/l, erythrocytes $3,5 \times 10^9/l$, leukocytes $24,6 \times 10^3/l$, CRP 329. Serum protein was 75 g/l, albumin 29, globulin 46, and proteinuria 1.7 g/24h. Renal function was diminished with urea 21.2 mmol/l and creatinine levels 670 micromol/l, and creatinine clearance 12.5 ml/min. Serum immunoglobulins were within the normal range, and c-ANCA was negative. There was an evidence of circulating anti-GBM antibodies in patient's serum, 6-times higher than reference values. The antibodies were against the glomerular basal membrane, affecting the alfa-3 chains of type IV collagen.

As the renal function was impaired, anuria appeared, and treatment with hemodialysis was started. Renal biopsy was performed, with immunofluorescence estimation that showed massive infiltration of the interstitium with crescent formations, over 90%, anti IGA negative, anti IgG diffuse deposition along the GBM +3. Histopathological analysis showed extracapillary glomerulonephritis, which was in conjunction with Goodpasture syndrome.

The treatment included corticosteroids as pulse therapy, and plasmapheresis was done every day for a period of

one week. This treatment was combined with hemodialysis, because of the renal failure and the high levels of urea and serum creatinine. After 3 weeks the clinical signs were stabilized with the restitution of the pulmonary damage, but the necessity of dialysis treatment was evident. The patient continues with chronic hemodialysis program for the next period.

Case 2

A 28-year-old male, with intensive coughing with hemoptysis and fatigue was hospitalized at the Department of Pulmonology, University Clinic of Pulmonology in Skopje, as pneumonia. The 24-hour proteinuria was 5 g/l, with oliguria. The values of urea were 15.5 mmol/l and creatinine 318 micromol/l; chest radiography detected alveolar infiltrates. Renal biopsy was performed with immunofluorescence estimation for focal necrotizing glomerulonephritis with linear IgG deposits along the GBM and histopathological diagnosis for glomerulonephritis extracapillary proliferative, rapidly progressive-Goodpasture syndrome. Because of the renal failure the patient was admitted to the Department of Nephrology for further treatment. Plasmapheresis, 15 sessions against 2000-2400 ml fresh frozen plasma within 20 days, was done. Because of the renal function deterioration, treatment with hemodialysis was started every second day. Treatment with corticosteroids was also performed 2 times/3 day course of methylprednisolone (500 mg/day) with tapering the dose of orally steroids in the following days. Three courses i.v. cyclophosphamide 500 mg were given for 8 days, followed by oral cyclophosphamide 100 mg/day/7days, proceeding with 50 mg/day afterwards. At first, antibodies against GBM were positive with high positive titer 1:320, but after the treatment the titer was 1:20. Laboratory findings were as follows: Hb 80, Er 3.1, Htc 0.30, Le 22.2...6.2, Tr 397...176, urea 42.8 mmol/l, creatinine 912 micromol/l, proteinuria up to 12.6 g/l. Immunoglobulins: IgA 1.78, IgG 7.13, IgM 0.64, C3=0.50, C4=0.11, circulating immunocomplexes 0.20.

The patient's condition improved, the last h-ray control was completely normal. However, the patient became dependent on hemodialysis. Re-biopsy revealed still active extracapillary glomerulonephritis in 10/14 glomeruli with extensive tubule-interstitial changes that can explain anuria.

After several months of chronic hemodialysis treatment, kidney transplantation was performed, with good effect and further improved condition.

Case 3

An 18-year-old female had breathing problems, coughing with hemoptysis and fatigue for 3 months. The lung biopsy revealed Goodpasture syndrome. After the biopsy and worsening of the condition, with hypoxia, the pa-

tient was treated at the Department of Pulmonology, and the respiratory symptoms were improved. Because renal function impairment with urea 22.8 mmol/l, creatinine 400 micromol/l, oligoanuria, hospitalization at the Department of Nephrology was indicated. The other laboratory findings were as follows: Hb 98, Er 3.2, Htc 0.29, Le 12.4, Tr 124, creatinine clearance 17.8 ml/min, total protein 46, albumin 27, globulin 19, proteinuria /24h: 1.57 g. Anti-GBM antibodies were 5 times higher than normal reference values.

Renal biopsy was performed with immunofluorescence estimation without signs for definitive sclerosis, but the presence of crescent formations is 100% with different expansion. Anti IgG intensive linear deposit along GBM +3. Histopathological analysis showed extracapillary glomerulonephritis-Goodpasture syndrome.

Treatment with plasmapheresis was started and 6 plasmapheresis were performed in the following period of 10 days. A therapy with corticosteroid was also performed, with pulse methylprednisolone therapy 500mg/3 days, followed by steroids per os. Amp. cyclophosphamide was given once, and after that improvement of the symptoms was registered. There was no need of hemodialysis. The renal function slowly improved. During the period of several months after hospitalization the therapy with corticosteroids continued. Proteinuria/24; 0.78-1.6 g/l, persisted, the values for urea and creatinine were normalized (urea 3.6, creatinine 73). One year later complete improvement was noticed and the patient had no need of therapy. At the last control all the results were normal and the patient was clinically stable.

Discussion

Substantial variation exists in the clinical manifestations of patients with anti-glomerular basement membrane (anti-GBM) disease [1,3,8]. From 60-80% of patients have clinically apparent manifestations of pulmonary and renal disease, 20-40% have renal disease alone, and less than 10% have disease that is limited to the lungs. Environmental factors are thought to play a role in triggering the disease. All age groups are affected, but the peak incidence is in the third decade in young men. The second peak may occur in the sixth and seventh decade, affecting men and women equally. Lung hemorrhage is more common in younger men, while isolated renal disease is more frequent in the elderly, with near equal gender distribution [4,5].

In the past, Goodpasture syndrome was usually fatal. Aggressive therapy with plasmapheresis, corticosteroids, and immunosuppressive agents has dramatically improved prognosis [9,10]. With this approach, the 5-year survival rate exceeds 80% and fewer than 30% of patients require long-term dialysis.

We presented 3 cases of Goodpasture syndrome, with similar presentation at onset: severe pulmonary involvement, more than 90% crescents at renal biopsy, with

linear IgG diffuse deposition along the GBM+3 and high titer of antibodies against GBM.

All of the patients were with similar clinical features, with renal failure that needed treatment with hemodialysis. But results of the treatment with plasmapheresis have indicated that this procedure reduces morbidity in patients with Goodpasture syndrome. Although all patients were treated with cytotoxic therapy, it can be used only as an adjunct to plasmapheresis. In one of the cases we used this therapy only once, and the clinical feature was improved after several sessions.

Conclusions

We can conclude that Goodpasture syndrome has different outcome and the course of the disease is unpredictable. The early diagnosis and initiation of plasmapheresis treatment may be important for remission of the disease.

Early diagnosis and treatment lead to improved prognosis. The combination of cytotoxic agents and steroids with plasmapheresis is effective if instituted early in the course of the disease.

Conflict of interest statement. None declared.

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