SANAMED
2020; 15(2): 189–194
ISSN-1452-662X

DOI: 10.24125/sanamed.v15i2.405
UDK: 616-097:616.61-008.65
ID: 18296585
Case report

LOST KIDNEY IN GOODPASTURE SYNDROM - CASE REPORT

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Primljen/Received 02. 04. 2020. god.

Prihvaćen/Accepted 10. 06. 2020. god.

Abstract: **Introduction:** Goodpasture syndrome is a rare autoimmune syndrome with alveolar hemorrhages and glomerulonephritis caused by circulating antibodies against the glomerular-basement-membrane. Anti-glomerular-basement-membrane were administered against a non-collagen *(NC-1)* α*3* chain of collagen type IV, which was found at the highest concentration in the basal membrane of renal and pulmonary capillaries. The aim of case report is a clinical overview of this rare and severe syndrome.

Case report: The patient, 22-years-old was sent to Center of Urgent Medicine of Clinical Center Kragujevac from General Hospital of Paraćin because of blood poisoning, fever, symptoms and signs of renal and respiratory weakness, and suspected of Wegener's disease. Antibodies were taken on the basement membrane of the glomerulus were resulted of enormously high. After due to the clinical and immunology diagnosis of Goodpasture syndrome, plasmapheresis treatment was initiated. The standard hemodialysis was continued. Following the guidelines protocols, patient received pulse dozes of cytostatics, corticosteroids, etc.

Conclusion: The case report of our patient points to the necessity of multidisciplinary approach of the expert team, consisting of a nephrologist, pulmologist, clinical pharmacologist and other specialists. The prognosis is good, if treatment is started before irreversible pulmonary and/or renal changes (respiratory and/or renal insufficiency). Goodpasture syndrome often progresses rapidly, so it can be fatal if it's delayed with the diagnosis and the treatment. Patients with Goodpasture's syndrome require an adequate the socio-medical care as a rare and severe syndrome.

Key words: Goodpasture's syndrome, autoimmune diseases, anti-glomerular basement disease and antibody, pulmonary hemorrhage, glomerulonephritis.

INTRODUCTION

Goodpasture syndrome is a rare autoimmyne syndrome with alveolar hemorrhages and glomerulonephritis caused by circulating antibodies against (anti) glomerular-basement-membrane (GBM) and most commonly affects genetically predisposed in younger men. The estimated incidence of Goodpasture syndrome is one case per million per year (1). Anti-GMB antibodies were administered against a non-collagen *(NC-1)* α*3* chain of collagen type IV, which was found at the highest concentration in the basal membrane of renal and pulmonary capillaries (1). Exposure - the smoking, the viral infection of the upper respiratory tract, the inhalation of carbon dioxide waste, as well as pneumonia induction of the alveolar capillary to circulating antibodies, especially those with *HLA-DRw15 allele*, *-DR4 and -DRB1 allele* (1). GBM circulating antibodies bind to basal membrane, fix complement, and stimulate the cellular inflammatory response, causing glomerulonephritis and/or pulmonary capillaritis. Symptoms and signs of disease include dyspnoea, cough, tiredness, hemoptysis, hematuria, proteinuria, increased body temperature, weight loss, peripheral edema, pale skin and visible mucous due to sideropenic anemia, arthralgia, uremia, hypertension, cotton wool deposits and vasculitis on retina, etc. For diagnosis of Goodpasture's syndrome, it is necessary to demonstrate serum of anti-GBM antibodies with indirect immunofluorescence or ELISA with recombinant or human *NC-1* α*3* directly bound antibodies to the antigen-membrane glomeruli (1). Other serological tests, such as ANA for the detection of System Lupus, Chyrg-Strayss's disease, Bechcet's diseases and the antistreptolysin O-titer for the proving of poststreptococcal glomerulonephritis were used in the differential diagnosis (1). In the case of glomerulonephritis (hematuria, proteinuria, erythrocyte cylinders in urine and/or renal in-

sufficiency), the kidney biopsy is indicated. Progressive focal segmental necrotic zealous glomerulonephritis with sickle (crescentic) creatures was found in the bioptate. The immunofluorescence coloring of lung and kidney samples shows diffusely distributed immunoglobulin deposits of IgG, sometimes IgA and IgM, along the basal membrane of alveoli capsules and glomeruli. In addition to the insufficiency of pulmonary function of the restrictive type with hypoxemia, the diffuse capacity for carbon monoxide has been increased due to the presence of blood in alveoli. It was treated with plasmapheresis, corticosteroids and immunosuppressants. It was treated daily or every other day by plasmapheresis 2 to 3 weeks to eliminate circulating anti-GBM antibodies, in combination with iv pulse dozes of corticosteroids (usually methylprednisolone 1 *g* for 20 *min* every other day in 3 doses, and then 1 *mg/kg* of prednisone 1 ×/day) and cyclophosphamide (in bolus and than 2 *mg/kg* 1 x/day) for 6 to 12 months to prevent the formation of new antibodies (1). After renal transplantation for renal insufficiency, this disease can be recidivated. The prognosis is good if treatment is started before irreversible pulmonary and/or renal changes, i.e. respiratory or renal insufficiency. Goodpasture syndrome often progresses rapidly, so it can be fatal if it's delayed with the diagnosis and the treatment. The aim of this case report is a clinical overview of this rare and severe syndrome.

CASE REPORT

The patient, 22-years-old was sent to the Center of Urgent Medicine of Clinical Center Kragujevac from General Hospital of Paraćin because of blood poisoning, fever, symptoms and signs of renal and respiratory weakness and suspected of Wegener's disease. After the examination in Internist Clinic, patient was immediately admitted to the Stationary Section of Urgent Medicine Center of Clinical Centre of Kragujevac due to the extremely low saturation values measured by the pulse oximeter in the room air. The patient's report had occurred suddenly, by coughing up blood and elevated body temperature. The auscultator findings of the lungs were dominated by inspiratory fractures, both in the middle and lower lungs. The computerized tomography of chest, with the protocol for pulmoangiography excluded the presence of pulmonary thromboembolism. The confluent murmur, alveolar infiltrates with larger consolidations in the lower lobe posterobazal was observed diffusely. Both sides of the lower part of lungs had the pleural effusion. The heart action was tachyarrhythmia and the sounds were good with no noise. The echocardiographic examination was a neat. The radiographic examination of the heart and lungs

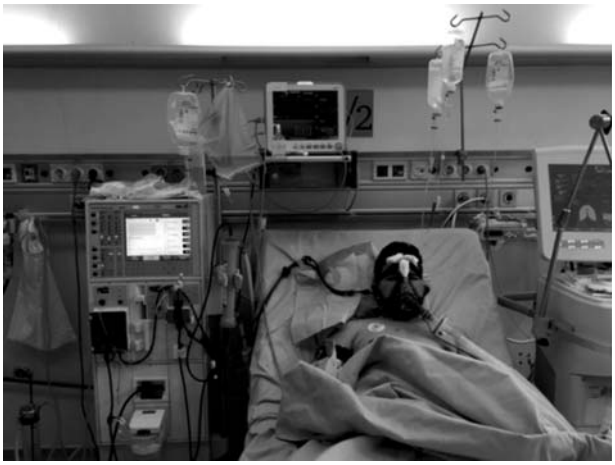

Figure 1. *Patient attached device for noninvasive mechanical ventilation and oxygen catheter*

were record alveolar infiltrations in the middle and lower lung fields on both sides, and more on the left. The upper echo abdominal was tidy. The echo of urinary tract showed an unclear medullocorticular boundary and brighter kidney parenchyma. The pANCA and cANCA antibodies were negative as well as other standard immunological analyzes, that were made due to suspicion of Wegner's disease. Goodpasture's syndrome was suspicion after the consultative review of pulmologist, nephrologist, infectollogist, clinical pharmacologist, ophthalmologist, etc. Antibodies were taken on the basement membrane of glomeruli. The result of the required antibodies was enormously high. Until the arrival of the immunological confirmation, patient with Goodpasture syndrome was treated with antibiotics and symptomatic therapy, as well as standard hemodialysis. After the arrival of high GBM-titer, and due to the clinical diagnosis of Goodpasture's syndrome, the plasma-treatment was initiated. The standard hemodialysis was continued. Following the standard protocols, patient received pulse dozed of cytostatics, corticosteroids, etc. At beginning of the illness, the dieresis was low at level of oliguria, and after two weeks of baking over 2000 ml. Due to respiratory weakness, the patient was attached to the device for non-invasive mechanical ventilation for five days, shortly afterwards on oxygen catheter (Figure 1). In biochemical analyzes, leucocytosis, lower hemoglobin levels, hypoproteinaemia, hypoalbyminemia, hyperasothemia and elevated parameters of inflammation were recorded (Table 1). The control antibody determined by ELISA was significantly reduced with 200 U/mL, 160 U/mL, 110 U/mL, 34 U/mL and10 U/mL compared to the first analysis (Table 2). The computerized tomography of chest reveals the reticulonodular lung infiltrate and extensive bilateral consolidations (Figure 2). Echo of urinary tract showed the unclear medullocorticular boundary and brighter kidney parenchyma in Figure 3.

Table 1. *Biochemical analyzes (erythrocytes, leucocytosis, hemoglobin, hypoproteinaemia, hypoalbuminemia, hyperasothemia, parameters of inflammation, etc)*

Biochemical analyzes	Results	References
Erytrocytes	2.91	4.34 – 5.72 x10^{12}/L
Hemoglobin	84	138 – 175 g/G
MCV	87.6	80 – 97.2 (fL)
Leucocytes	15.54	3.7 – 10.0 x10^{9}/L
Trombocytes	149	135 – 450 x10^{9}/L
Creatinine	261	49 -106 mol/L
Urea	20.1	3.0-8.0 mmol/L
CRP	25.8	0.0 – 5.0 mg/L
Total serum protein	31	64 - 83 g/L
Serum albumin	24	35 – 52 g/L
24-hour-proteinuria	15.4	0.04 - 0.15 g/24h

MCV - Mean Corpuscular Volume
CRP - C-Reactive Protein

Table 2. *ELISA-control antibody reduced with compared to the first analysis*

ELISA - Immunology	Results	Reference	Date
GBM antibody	200 U/mL	‹20.0	5th May 2019 (first analysis)
GBM antibody	163 U/mL	‹20.0	11th May 2019
GBM antibody	110 U/mL	‹20.0	18th May 2019
GBM antibody	34 U/mL	‹20.0	28th May 2019
GBM antibody	10 U/mL	‹20.0	3th June 2019

GBM antibody - antibodies against Glomerular-Basement-Membrane

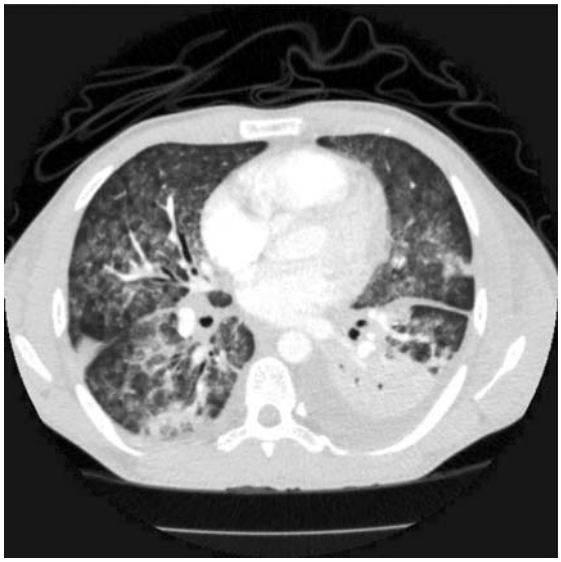

Figure 2. Computerized tomography of chest revealed reticulonodular lung infiltrate and extensive bilateral consolidations

The Social history of our patient wasn't notable. The kidneys of young man were saved.

DISCUSSION

Our case report illustrates the complex nature of Goodpasture's syndrome. Antibodies from our patient were taken on the basal membrane of glomerulus, and

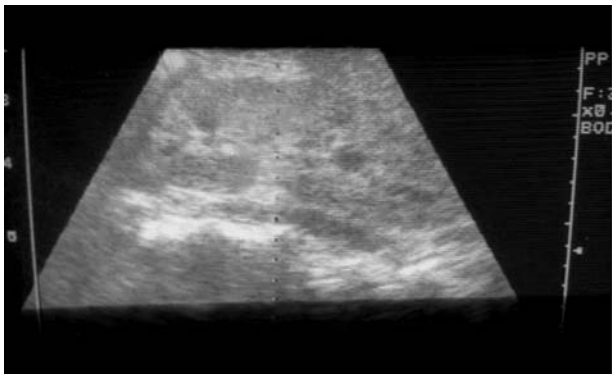

Figure 3. *Echo of urinary tract showed unclear medullocorticular boundary and brighter kidney parenchyma*

desired antibody result was extremely high. Due to clinical and immunological diagnosis of Goodpasture syndrome, plasma treatment has begun and standard hemodialysis has been continued. By using follow-up clinical standard protocols, patient received pulse doses of cytostatics, corticosteroids, and other therapies. Timely diagnosis and adequate therapy saved the "lost kidney" of this young person, which the active life is preserved. The disease of the anti glomeric basal membrane is a rare, and an antibody-mediated disease. Consecutive severe changes are deposited which arise depending on the localization where these antibodies.

The most patients have joint pulmonary, kidney and other lesions. The renal system is the primary localization of damage with catastrophic exacerbation of acute glomerular inflammation of kidneys, from just a few days after diagnosis – Goodpasture's syndrome. Goodpasture syndrome refers to the condition characterized by pulmonary haemorrhagia and glomerulonephritis. Clinicians can use several terms, including the disease against the glomerular basement membrane, as Goodpasture syndrome and as Goodpasture disease. This last term is the most specific term and refers to the presence of kidney and lung infections, together with antibodies to glomerular basement membrane (2). Goodpasture's disease is an autoimmune disease that endangers life and can lead to kidney disease and death in the final phase. The diagnosis of anti-GBM-disease requires high clinical suspicion, necessary for early diagnosis and adequate treatment in order to improve survival rates (3). Antibodies initiate kidney glomeruli destruction, resulting in focal necrotizing glomerulitis, which can rapidly progress to renal failure. Damage to alveolar basal membranes mediated by autoantibodies leads to pulmonary hemorrhage, which causes respiratory failure. The immunofluorescence testing on anti-GBM antibodies on lung and kidney tissues confirms the diagnosis of Goodpasture syndrome. Tests can be falsely negative in 15% of patients with Goodpasture syndrome (4). The pathology is characterized by linear immunofluorescence coloring for immunoglobylin-G on glomerular base membrane, while bronchoscopy doesn't to show the obvious lesion. The kidney biopsy shows the fibrinoid necrosis. The research shows that early and aggressive therapy leads to improved disease forecasts (5). Patients may be twice as positive for anti-GBM and anti-proteinase-3 neotrophili cytoplasmic antibodies (c-ANCA). Other patients may be twice as positive for anti-GBM and anti-myeloperoxidase cytoplasmici antibodies (p-ANCA). The antibodies are associated with serum ANCA in 10-40% of patients and indicate a poor prognosis of this disease. The function of auto reactive T cells is poorly defined, but it may involve a change from T_{H2} to T_{H1} cytokine regulation, thus improving the antigenic specificity of the antibody response. Timely diagnosis and triple therapeutic regimen involving plasmapheresis, corticosteroids and immunosuppressive drugs significantly improve patient outcomes, resulting in a survival rate of 70-90% for one year (6). The common immunodeficiency variable is the primary immunodeficiency that is manifested by hypogammaglobulinemia, the inability to create functional antibodies, and recurrent infections. The clinical course may be complicated by hypertensive encephalopathy, meningoencephalitis, status epilepticus, the change in the retina, the cutaneous-vascylitis, etc (7, 8). Autoantibody stimulates local capillaritis, which is manifested as progressive glomerulonephritis in 80-90% of patients, with concurrent alveolar bleeding in 50%. A small number of cases can be isolated from progressive pulmonary disease. Alveolar bleeding usually responds to treatment, and long-term respiratory complications are rare. Kidney prognosis is variable, although with aggressive treatment, an independent kidney function is maintained for one year in more than 80% of patients who do not require renal replacement therapy. In the case of unusual anti-GBM disease, unless there is the accompanying anti-neytrophili cytoplasmic antibody (30-40%), maintenance of immunosuppression is also recommended (9). Hypertension may be present in 70% of cases, proteinuria (>3.5 g/24 h) in 42% of cases, nephrotic syndrome in 37%, microhematuria in 95%, renal insufficiency in 63%, lung abnormalities and anemia in 16% of patients. The electron microscopy can detect sparse electronic deposits in glomeruli or globally remove the sub-cell (10, 11). A small number of cases have been reported with eye symptoms and visual disturbances in the context of this rare syndrome. Ophthalmoscopic, bilateral cotton wool deposits were detected bilaterally along the blood vessels and bilateral retinal bleeding predominantly on the back half of the eye. By intensifying the existing antihypertensive therapy, vision is significantly improved. Although it is seen more often in Goodpasture syndrome, it is important to be aware of eye pathology because it can refer to diagnosis of this syndrome (12). The pathophysiology of this condition is understood by molecular analysis of the interactions of antibodies and antigens and the use of human leukocyte antigen-transgenic animals, while the association of anti-GBM antibodies with anti-neytrophili antibodies to cytoplasm and their combined effect on the phenotype of the disease is increasingly recognized, providing some insights into the basis of glomerular damage and autoimmunity (13, 14). Tashiro et al points to pathological findings in autopsy with progressive glomerulonephritis, diffuse alveolar bleeding and fibroblast foci in the lungs. The cause of death is diagnosed as respiratory failure and the result of diffuse alveolar damage caused by a combination of diffuse alveolar bleeding and exacerbation of the interstitial pneumonia. Goodpasture syndrome with already existing chronic interstitial pneumonia and anti-neytrophil antibody against neutrophils is associated with poor prognosis (15).

CONCLUSION

The case report of our young patient (Goodpasture's Syndrome) points to the necessity of a multidisciplinary approach in the treatment including medical team consisting of a nephrologist, pulmologist, clinical

pharmacologist, ophthalmologist, and others. The prognosis is good, if treatment is started before irreversible pulmonary and/or renal changes, i.e. respiratory and/or renal insufficiency. Goodpasture syndrome often progresses rapidly, so it can be fatal if it's delayed with the diagnosis and the treatment. Patients with Goodpasture syndrome require adequate the socio-medical care of the society, as a rare and severe syndrome. The kidneys of young man were saved.

Conflict of Interests: The authors declare that there are no conflicts of interest related to this article.

Funding: None

Licensing

Sažetak

IZGUBLJEN BUBREG U GOODPASTURE-OVOM SINDROMU - PRIKAZ SLUČAJA

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Uvod: Goodpasture sindrom je redak autoimuni sindrom s alveolarnim hemoragijama i glomerulonefritisom, uzrokovanim cirkulišućim antitelima na bazalne membrane glomerula. Antitela na bazalnu membranu glomerula usmerena su protiv nekolagenog dela (NC - 1) á3 lanca kolagena tipa IV, koji se nalazi u najvećoj koncentraciji u bazalnoj membrani bubrežnih i plućnih kapilara. Cilj prezentacije pacijenta je klinički osvrt na ovaj redak i težak sindrom.

Prikaz slučaja: 22-godišnji pacijent je zbog iskašljavanja krvi, groznice, simptoma i znakova bubrežne i respiratorne slabosti, a pod sumnjom na Wegener-ovu bolest, upućen je na Urgentnu medicinu Kliničkog centra Kragujevac iz Opšte bolnice Paraćin. Uzeta su antitela na bazalnu membranu glomerula, a rezultat traženih antitela bio je izuzetno visok. Zbog kliničke i imunološke dijagnoze Goodpasturovog sindroma, započeto je lečenje plazmaferezom. Nastavljena je standardna hemodijaliza. Koristeći smernice protokola, pacijent je primio pulsne doze citostatika, kortikosteroida i dr.

Zaključak: Prikaz slučaja našeg pacijenta ukazuje na neophodnost multidisciplinarnog pristupa tima eksperata koji se sastoji od nefrologa, pulmologa, kliničkih farmakologa i drugih specijalista. Prognoza bolesti je dobra, ako se lečenje započne pre pojave ireverzibilnih plućnih i / ili bubrežnih promena, tj. respiratorne i/ili bubrežne insuficijencije. Goodpasture-ov sindrom često brzo napreduje i može biti fatalan ukoliko se sa dijagnozom i lečenjem zakasni. Pacijenti s Goodpastureovim sindromom zahtevaju adekvatnu društveno-medicinsku negu, kao redak i težak sindrom.

Ključne reči: Goodpasture-ov sindrom, autoimune bolesti, bolest glomerularne bazalne membrane i antitela, plućne hemoragije, glomerulonefritis.

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