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Goodpasture Syndrome; A Look Into A Rare Syndrome

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Abstract

Goodpasture syndrome is a rare autoimmune disorder with manifestations varying from relatively mild renal insufficiency to rapidly progressive glomerulonephritis that leads to life-threatening end-stage renal disease associated with pulmonary hemorrhage. We report our experience with a case of anti - GBM disease in a 45-year-old lady who was admitted in a tertiary care hospital in India with rapidly progressive renal failure and hemoptysis. The renal biopsy showed crescentic glomerulonephritis with linear IgG deposits in immunofluorescence and the anti-GBM antibody titers were elevated. The patient received hemodialysis, immunosuppressants and plasmapheresis to address her pulmonary renal syndrome. The patient succumbed to death due to severe pulmonary hemorrhage.

Keywords

Anti-glomerular basement membrane disease, crescentic glomerulonephritis, pulmonary hemorrhage, Goodpasture syndrome, anti-glomerular basement membrane IgG antibodies, plasmapheresis.

Introduction

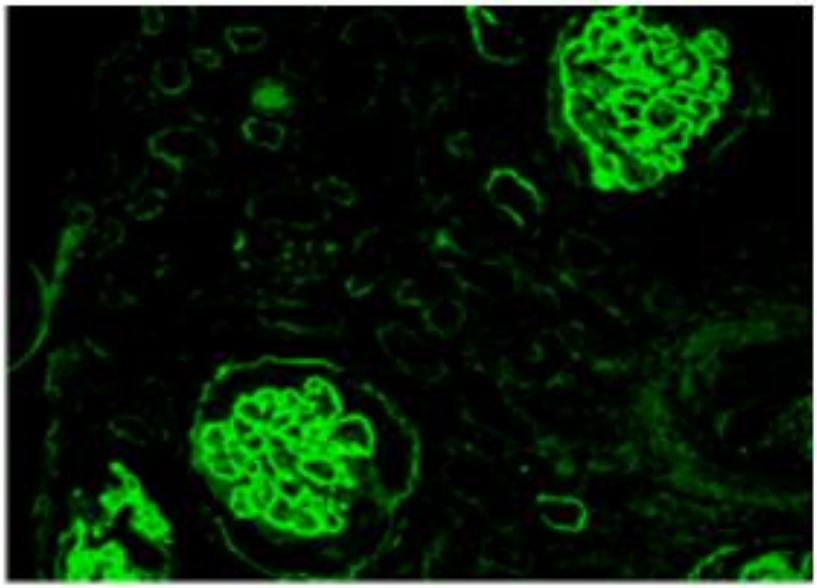
Anti-glomerular basement membrane (anti-GBM) autoimmune disease is a rare small vessel vasculitis that affects glomerular capillaries, pulmonary capillaries, or both. Most patients present with rapidly progressive (crescentic) glomerulonephritis, although some patients may present with relatively mild kidney impairment with or without pulmonary hemorrhage, and typically does not relapse.[1] In general, this disorder is typically associated with severe kidney injury that, if untreated, progresses quickly to end-stage kidney disease (ESKD).[2] Anti-GBM disease is also called Goodpasture syndrome.[3] Some predisposing factors like hydrocarbons, smoking, and the use of hair dye can also increase the risk of Anti GBM disease.

These antibodies will bind to their specific reactive epitopes on the basement membranes and result in the

activation of the complement cascade, leading to the death of the tagged cells, resulting in tissue necrosis. The GBM consists of a network of type IV collagen molecules, each composed of triple-helical protomers of a3, a4, and a5 chains. The principal target of the autoimmune response in anti-GBM disease has been identified as the non-collagenous (NC1) domain of the a3 chain of type IV collagen [4]. Antibody binding occurs in the alveolar basement membrane. Thus, additional nonspecific lung destruction that increases the alveolar-capillary permeability is required for the deposition of antibodies. T cells are also involved. They enhance B cells function and antibody production that can play a direct pathogenic role in the glomeruli of kidneys and tiny alveolar sacs in the lungs.

Symptoms may occur gradually over months or even years, but they often develop very quickly over days to weeks. The majority of patients, especially 80%–90% will present with features of rapidly progressive GN and 40% to 60% will have concurrent lung hemorrhage, and a small minority of patients may present with isolated pulmonary disease [5]. Lungs symptoms may include hemoptysis, dry cough, chest pain, and shortness of breath.

Different tests are used for the diagnosis of Good pasture syndrome. Kidney biopsy is the mainstay of diagnosis. The crescentic glomerulonephritis is the histopathologic hallmark of the anti-GBM disease. Large biopsy series indicates that 95% of patients will have evidence of crescent formation on kidney biopsy, and that in 80% of patients >50% of glomeruli will be involved. Bright linear ribbon-like deposition of immunoglobulin G and complement (C3) along GBM is seen in direct immunofluorescence.[6] The chest x-ray shows the presence of patchy parenchymal consolidations in the lung fields which almost invariably means the patient has pulmonary haemorrhage. Urinalysis is also characteristic and usually demonstrates low-grade proteinuria, gross or microscopic hematuria, and RBC casts.[7]



Kidney biopsy sample immunofluorescence for IgG revealing linear deposits along the glomerular basement membrane [5].

Standard treatment includes immunosuppressive medications, corticosteroids and plasmapheresis. Immunosuppressive therapy consists of cyclophosphamide, rituximab. Plasmapheresis is generally instituted after the diagnosis is established either by renal biopsy or by detection of anti-GBM antibodies which help in rapidly removing the circulating antibodies.When a patient presents with severe pulmonary hemorrhage, plasmapheresis may be initiated if the diagnosis appears very likely, even though confirmation is not available immediately. The plasmapheresis is continued until the patient's clinical course has improved and serum anti-GBM antibodies are not detected.The lifespan has decreased dramatically for people with Anti-GBM which is around 5 years, depending on the severity of comorbidity.

Case Report

45-year-old female patient with history of hypothyroidism, hypertension, and dyslipidemia presented with complaints of

A. Nausea/vomiting and abdominal pain for 2 weeks
B. Dysuria for 4 days
C. Hematuria for 2 days
D. Oliguria for 1 day

The patient was getting treatment for hypothyroidism with Thyronorm 112.5mcg, Losartan 25mg, and Atorvastatin 10mg. She had taken Non-Steroidal Anti-Inflammatory Drug 2 weeks prior to admission. She was being treated for Urinary tract infection

On physical examination, she was conscious and oriented. Her vital signs were stable. Hemogram revealed the following values: hemoglobin 6 g/dL, creatinine 13.10 mg/dL, urea 142.7 mg/dL, albumin 3.1 g/dL, and proteinuria 4.5 g/h. Serum protein electrophoresis showed a decrease in Albumin, Alpha 1 Globulins are slightly elevated. Serum electrolytes were found to be sodium 116 mmol/L, potassium 3.8mmol/L. Prothrombin time 16.4 sec, partial thromboplastin time 40.4 sec, and international normalized ratio 1.27 sec. Her liver function test and serum lipid profile were normal.

Serological tests for viral hepatitis B and C, HIV type 1 and 2, antinuclear antibody (ANA), and cytoplasmic and perinuclear antineutrophil cytoplasmic antibodies (c-ANCA and p-ANCA) were all negative. CT KUB done showed mild bilateral perinephric fat stranding with fascial thickening. Her urine culture did not show significant growth and blood culture showed Micrococcus luteus. USG guided renal biopsy was done after 5 days of admission under aseptic condition. Renal biopsy reports showed 100 % crescentic glomerulonephritis with linear capillary wall IgG (Multiple sections from 3 cortical core stained with H&E, PAS, MT and silver show 21 glomeruli, 2 obsolescent (9.5%). Obsolescent glomeruli show small and globally sclerotic. Viable glomeruli show compression of tufts by 19 crescents (17 cellular,2 fibrocellular (90.4%).Glomeruli reveal fibrinoid necrosis, break in capillary loop,break in bowman capsule). Anti-glomerular basement membrane IgG antibody level was high with a titer of 452 U/ml.

Based on the aforementioned findings, the diagnosis of anti-GBM disease was found. She was treated with Intravenous Methylprednisolone pulse therapy and intravenous Cyclophosphamide.

Discussion

Anti GBM disease is rare in the Asian continent, especially in India. Studies have shown that the peak incidence of anti-GBM antibody disease seems

to be in the third decade mostly in males, and a second peak in the sixth- and seventh-decades affecting men and women equally. [86] Anti-GBM antibodies are strongly associated with rapidly progressive glomerulonephritis. Studies have reported 40-80% incidence of renal insufficiency in anti-GBM disease. Jennette *et al.* found elevated serum creatinine at ~~a~~ presentation in patients of anti-GBM disease with rapidly progressive glomerulonephritis. The pulmonary-renal syndrome is reported in 40-60% of patients with the anti-GBM disease.[97] In our patient Chest X-ray did not show evidence of alveolar involvement but later the patient developed hemoptysis. She was started on intravenous Methylprednisolone 500 mg IV for 3 days after the urine and blood cultures showed no growth. On the next day of renal biopsy after confirming the presence of crescentic glomerulonephritis she was given an Intravenous Cyclophosphamide 500mg pulse. She required five sessions of hemodialysis and 2 units of PRBC transfusion during the hospital stay.

She was advised to undergo plasmapheresis for clearance of antiGBM antibodies, but was not willing for the same. She developed hemoptysis later and was transferred to a government facility for plasmapheresis, due to financial concerns. She received 2 sessions of plasmapheresis, but developed severe pulmonary hemorrhage and succumbed to death.

Conclusion

Goodpasture's disease is a rare autoimmune disease in which antibodies attack the basement membrane in the lungs and kidneys. It may rapidly result in permanent lung and kidney damage, often leading to death.

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