Case Reports and Reviews: Open Access

Case Report| Vol 2 Iss 1

Isolated Glomerulonephritis as a Classic Presentation of Goodpasture Disease: A Case Report

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Received: April 11, 2021; **Accepted:** April 26, 2021; **Published:** May 04, 2021

Abstract

Goodpasture disease is very rare, and occurs in about two cases per million population. It is an autoimmune small vessel vasculitis where anti-glomerular basement membrane antibodies are targeted to the glomerular basement membrane and alveolar basement membrane. Our report highlights the importance of early recognition and nephrology referral for prompt initiation of treatment.

Keywords: ***Goodpasture disease; Glomerulonephritis; Autoimmune vasculitis; Glomerular basement membrane; Alveolar hemorrhage; Crescentic proliferation.***

1. Introduction

Goodpasture syndrome, also known as Anti-GBM disease, is an autoimmune small vessel vasculitis where anti-glomerular basement membrane antibodies are targeted to the glomerular basement membraneand alveolar basement membrane. This results in rapid progressive glomerulonephritis and alveolar hemorrhage [1]. This disorder was first described in 1919 by Ernest Goodpasture when he reported a caseof pulmonary hemorrhage and glomerulonephritis. It was confirmed in 1967 by Lerner, Glassock, and Dixon when they found antibodies from a diseased kidney produced nephritis on experimental animals [2]. Anti-GBM antibodies primarily target the alpha-3 chain in the type IV collagen; this type of collagenis predominantly found at the glomerular and alveoli basement membrane [3]. The exact cause of Anti- GBM disease is unknown, and is often idiopathic. It is believed that when a blood vessel becomes compromised, it allows anti-GBM antibodies to come in contact and damage the glomerular and alveoli basement membranes. Examples of this include exposure to organic solvents/hydrocarbons, tobacco smoke, infections/sepsis, cocaine inhalation, metal dust inhalation and high oxygen environments.

Citation: Dubey A, Dhanjal J, and Penaherrera J. Isolated glomerulonephritis as a classic presentation of goodpasture disease: A case report. Case Rep Rev Open Access. 2021;2(1):121.

Familial cases of anti-GBM disease are rare, but patients with HLA-DR15 and DR4 have been found to be at an increased risk [4]. Anti-GBM antibodies either in the serum or kidney are required for diagnosis of this disease. Kidney biopsy should also be performed as it can show the extent of renal involvement and exclude other causes of glomerulonephritis. Although Goodpasture syndrome is very rare, this diagnosis should be suspected in patients presenting with rapidly acute glomerulonephritis, and especiallyin patients with concomitant alveolar hemorrhage. We present a case of a 70-year-old male who presentedwith acute renal failure, and was found to have Goodpasture syndrome confirmed by kidney biopsy and presence of serum anti-GBM antibodies.

2. Case Presentation

A 70-year-old male w/ underlying uncontrolled hypertension presented to the ED with complaints of abdominal discomfort. As per the patient, for the past week, he had been experiencing a dull, non- radiating, pressure like sensation located in his mid-abdomen. During this time, he had accompanying symptoms of nausea and vomiting and claimed that he was unable to tolerate liquids or solids for the past3 days. His emesis was non-bloody and non-bilious. On review of systems, the patient further revealed that he had also not urinated or had a bowel movement for the past two days. He had never had any issues with urination prior to admission. On admission, a CMP was obtained which revealed Na 127, K 6, BUN151, and a Cr of 23.49. A urinalysis was done which revealed 50-75 dysmorphic RBCs and urine protein of 300mg/dL**.** The patient was treated accordingly with IV fluids, Insulin, and calcium gluconate.

Additionally, nephrology was consulted, and a hemodialysis-catheter was placed for dialysis initiation. As per nephrology recommendations, a kidney biopsy was performed and laboratory tests were ordered to further assess for glomerulonephritis. A full workup including Antineutrophil Cytoplasmic Autoantibodies (ANCA), anti-glomerular basement membrane antibodies (Anti-GBM), antinuclear antibodies (ANA), anti-double stranded DNA antibodies (Anti-dsDNA), Myeloperoxidase antibody (MPO), serum complement levels (C3 and C4), and serum free light chains and immunofixation was obtained. The patient had markedly elevated serum Anti-GBM levels at 186. He tested negative for ANCA. His diagnosis was further confirmed with the kidney biopsy which revealed diffuse crescentic glomerulonephritis with extensive destruction of glomerular capillaries [Figure 1]. The patient was started on a 5-day course of IV Solumedrol 500mg and was subsequently discharged on PO Prednisone once he was cleared by nephrology and had been setup for dialysis as outpatient.

3. Discussion

Goodpasture disease is very rare, and occurs in about two cases per million population [1]. Anti-GBM disease predominantly occurs in Caucasian and Asian populations, and occurs less in African populations. It accounts for 15 percent of all crescentic glomerulonephritis, and only 0.8 percent of all end stage renal disease patients [5]. Anti-GBM disease has been shown to have a bimodal age distribution, with peak incidences occurring in patients in their 30s and 70s [6]. The younger age group appears to be predominantly male, and the older age group is largely female. Younger patients with Anti-GBM disease more often present with pulmonary hemorrhage, whereas the elder patients tend to present with glomerulonephritis, as was the case with this patient. Anti-GBM disease should be suspected in any patient presenting with clinical or laboratory signs concerning for acute and/or subacute nephritic syndrome including

hematuria, RBC casts, acute renal failure, proteinuria etc. Additionally, if these signs are accompanied with alveolar hemorrhage, this disease should be given special consideration to as this may be the predominant symptom in rare cases. A diagnosis is usually achieved with demonstration of anti-GBM antibodies either in the serum or in the kidneys. A kidney biopsy should be performed as well, if not contraindicated as this can dictate management by providing information on the activity and chronicity of renal involvement [2], [6]. Classic findings of Anti-GBM disease are crescentic glomerulonephritis seen on light microscopy [Fig. 1a,1b] and linear IgG deposition seen on immunofluorescence [Fig. 2a, 2b].

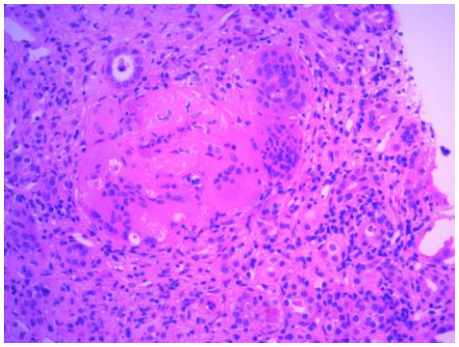

Figure 1a

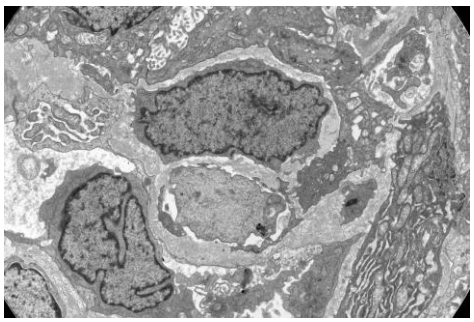

Figure 1b

Fig. 1. (a) H&E section demonstrating crescentic proliferation with disruption of Bowman's capsule and surrounding periglomerular multinucleated giant cell granulomatous reaction. (b) Electron microscopy section demonstrating glomeruli replaced by crescentic proliferation with destruction of capillary loops.

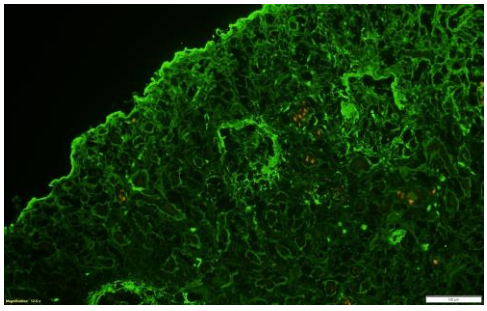

Figure 2a

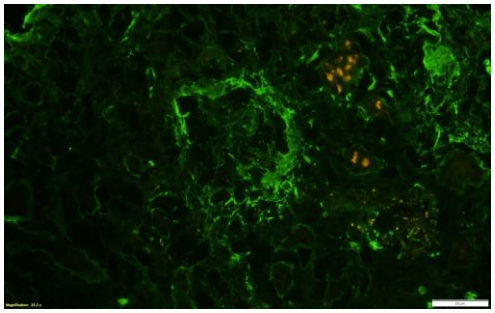

Figure 2b

Fig. 2. (a) Immunofluorescence microscopy showing characteristic linear deposition of fibrin in anti-GBM antibody disease. (b) Immunofluorescence microscopy focusing on single glomerulus demonstrating fibrin deposition within a circumferential crescent surrounding the glomerular tuft.

Anti-GBM can rapidly progress to ESRD if left untreated, and early diagnosis and treatment is key in preserving kidney function. In general, the recommended treatment for Anti-GBM disease consists of plasmapheresis, steroids, and immunosuppressive agents such as cyclophosphamide. This treatment combination is recommended for all patients who have pulmonary hemorrhage (regardless of kidney involvement), and all patients who have kidney involvement but do not require dialysis. For patients who develop Goodpasture syndrome that already are dialysis dependent, there are no clear guidelines for treatment and is usually handled on a case by case basis. There are no large randomized controlled trials that support the use of plasmapheresis, however its benefit of rapid removal of the anti-GBM antibody

can significantly decrease the risk of becoming dialysis dependent [6]. Plasmapheresis is performed by daily 4 L exchanges for 2 to 3 weeks, with albumin given as a replacement fluid [7]. Fresh frozen plasma may also be given instead of albumin if the patient developed pulmonary hemorrhage or had a kidney biopsy. The preferred initial glucocorticoid therapy is intravenous Methylprednisolone. It is administered as a 15 to 30 mg/kg pulse dose, daily for three days, then followed by oral prednisone 1 mg/kg daily, which can be tapered as the patient begins to improve. Oral steroids can be continued for about six months to achieve remission. In addition to plasmapheresis and steroids, the preferred immunosuppressive agent is cyclophosphamide. It is dosed at 2mg/kg daily for at least three months, but a maximum of up to six months. Inpatients who cannot tolerate cyclophosphamide, rituximab or mycophenolate mofetil can be used as alternatives, but are not considered first line therapies due to the insufficient evidence of their efficacy.

Relapses are uncommon, but it is recommended that the anti-GBM antibody levels should be monitoredon a weekly basis for at least six months to ensure the antibody levels remain undetectable.

4. Conclusion

Anti-GBM disease is a rare autoimmune disease where anti-glomerular basement membrane antibodies are targeted to the glomerular basement membrane and alveolar basement membrane. It commonly has abimodal age distribution and can manifest itself as acute crescentic glomerulonephritis or pulmonary hemorrhage. We present the case of a 70-year-old male displaying who had symptoms of nausea and abdominal discomfort and was diagnosed with advanced Anti-GBM disease.

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