Narain and Gupta et al. J Nephrol Ther 2015, 6:1
DOI: 10.4172/2161-0959.1000230

Journal of Nephrology & Therapeutics

Case Report Open Access

Pauci Antibody Anti-GBM Nephritis: A Case Report

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Background

Anti-glomerular basement membrane (GBM) disease is characterized by autoantibodies directed against the anti-GBM antigen, which is part of the non-collagenous domain of the alpha 3(IV) collagen chain. These antibodies bind to the GBM and most patients show rapid progressive form of glomerulonephritis. The alveolar basement membrane also contain the anti-GBM antigen, and some patients pulmonary haemorrhage [1].

Case Report

A 41-year-old non diabetic male patient with a 6-weeks history of malaise, loss of appetite, persistent low grade fever and cola colour urine off and on. There was no history of respiratory symptoms and, in particular, no haemoptysis. He had no family history of renal disease.

Laboratory findings detected proteinuria and haematuria, and blood tests showed an elevated serum creatinine. On admission, he was febrile with edema. Pulse was 100 beats/minute and regular, and blood pressure was 120/70 mm Hg. Clinical examination of the heart, lungs, abdomen, and nervous system were normal. Urinalysis showed 2+ RBC, 3+ protein and dysmorphic red cells. Serum creatinine was 6.3 mg/dL and urea 82.0 mg/dL. Electrolytes were in the normal range, but albumin was reduced at 2.3 g/dL. Blood picture showed haemoglobin 8.7 g; white blood cell count 9.6 × 10^9/L; and platelets 654 × 10^9/L. Oxygen saturation with the patient breathing room air was 94%, and chest radiograph was normal. Patient had normal sized and echogenic kidneys. No evidence of haemolytic anaemia and S. electrophoresis was negative for monoclonal proteins.

An enzyme-linked immunosorbent assay for anti-GBM antibodies done by CHORUS was negative at 15 AU/ml (normal range below 18 AU/ml). Kidney biopsy reveals seven glomeruli show presence of cellular crescents. Necrotising lesions seen in underlying glomerular tufts. Tubules show patchy areas of acute tubular necrosis. Tublar atrophy comprises <10% of cortex. Interstitium shows mild edema and lymphomononuclear cell infiltrate. Direct immuno flouresence (DIF) core showed eleven glomeruli with diffuse strong linear IgG in glomerular capillary wall with granular C3 and fibrinogen are positive in necrotic areas of glomerular tufts. IgA, IgM and C1q were negative, as shown in Figure 1. No light chain restriction was noted. DIF findings favour Anti GBM Crescentic glomerulonephritis.

Patient was treated with intravenous methylprednisolone 1gm infusion for five days and oral cyclophosphamide 3mg/kg daily without plasma exchange. Patient did not afford PE as he belongs to low socio economic status. He has given negative written consent for PE. After five days of treatment patient started improving interm of afebrileness, clearance of colour of urine, increase in HB, and fall in renal parameters. He was discharged on 12th day as there were no symptoms with lab parameters of HB 10.2, S. urea of 20 and S. creatinine 3.5.

Discussion

Cases of anti-GBM disease without detectable circulating antibodies were seen in many series. Moulis et al. [2], Dash et al. [3] and Kussman and Gohara [4] all describe classic clinical presentations of RPGN with negative serologic testing for circulating anti-GBM IgG autoantibodies. Interestingly, the case reported by Moulis et al. [2] showed on IF linear staining which was stronger for IgA than for IgG, promoting them to re-test their patients for anti-GBM IgA autoantibodies, which were positive. There are several possible reasons for negative test results. The half-life of kidney bound antibodies is longer than the half-life for those in the circulation, and thus circulating antibodies might have disappeared when the serum sample was drawn [5].

Another possible explanation for false negative results is auto antibodies reacting with a different antigen or epitopes as compared with "regular" anti-GBM antibodies, that all react with two well defined epitope regions of the NC1- domain of Type IV collagen α3-chains [5]. Such findings were recently described in four Chinese patients with biopsy proven anti-GBM disease [6].

In some instances, a false-negative serology in anti-GBM nephritis can be explained by antibodies that bind to the kidney with high affinity but circulate in levels too low for the ELISA [7]. These autoantibodies may be detectable by a more sensitive biosensor analysis [8], available only in research settings and not employed in any of the above mentioned and current case reports. Bazari et al. reported a case of serum antibody-negative anti GBM nephritis, 'even a test that is 98% sensitive will be negative in 2% of patients with anti-GBM disease'

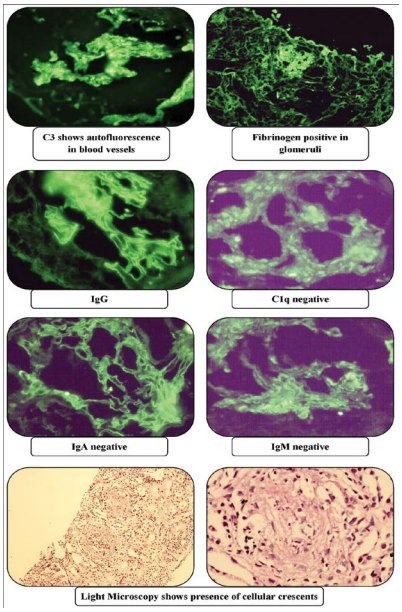

Figure 1: IgA, IgM and C1q were negative

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Received: December 09, 2015; **Accepted:** December 16, 2015; **Published:** December 23, 2015

Citation: Narain U, Gupta A (2015) Pauci Antibody Anti-GBM Nephritis: A Case Report. J Nephrol Ther 6: 230. doi:10.4172/2161-0959.1000230

[9] Bowman et al. reported a patient where no clinical symptoms were seen when IgG4 anti-GBM antibodies reappeared four years after diagnosis [10]. According to Bomback a renal biopsy not always 'makes' a diagnosis. The histopathology, rather, presents a pattern of injury that in turn allows the treating physicians to seek out an etiology behind that pattern. Routine IF staining of kidney biopsies do not stain specifically for anti-GBM autoantibodies, but a linear deposition of IgG along the GBM suggests that the IgG, which was 'lighting up,' is from anti-GBM autoantibodies. Serologic testing for circulating antibodies then confirms the presence of such autoantibodies [7].

As mentioned above in few cases serology was negative, in few cases symptoms were vague and sometimes histopathology was not conclusive. In our case circulating antibodies were not detectable in serum by well-established enzyme-linked immunosorbent assay. The diagnosis of anti-GBM disease was only confirmed by renal biopsy, Hence anti-GBM nephritis thus exemplifies the glomerular disease whose firm diagnosis relies on a combination of clinical, serologic and histopathologic findings.

Declaration

The authors declaring that the results presented in this paper have not been published previously in whole or part, except in abstract format.

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