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Case Report

Fibrillary glomerulonephritis: presenting as crescentic glomerulonephritis causing rapidly progressive renal failure

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Abstract
We report an unusual case of fibrillary glomerulonephritis (FGN) presenting as rapidly progressive renal failure and extensive crescent formation along with linear staining of capillary walls of the glomeruli on immunofluorescence, mimicking anti-glomerular basement membrane (anti-GBM) antibody-mediated disease. Laboratory results for circulating anti-GBM antibodies were negative. The subsequent electron microscopic findings were that of presence of electron-dense deposits in the glomerular mesangium and capillary walls, comprising of non-branching fibrils with an average diameter of 16 nm consistent with a diagnosis of FGN. This case illustrates the crucial role of electron microscopy in differential diagnosis of crescentic glomerulonephritis.

Keywords: anti-GBM disease; crescentic glomerulonephritis; fibrillay glomerulonephritis; rapidly progressive renal failure

Introduction

Fibrillary glomerulonephritis (FGN) is an uncommon glomerular disease seen in ~1% of native kidney biopsies resulting from glomerular accumulation of non-amyloid fibrillary deposits. The most common mode of presentation is nephrotic range proteinuria, microscopic haematuria and renal insufficiency. Morphologically, FGN exhibits a spectrum of glomerular involvement, the most common pattern being membranoproliferative glomerulonephritis (MPGN). The presentation with rapidly progressive renal failure (RPRF) and associated crescentic glomerulonephritis is uncommon [1–3]. When faced with such a clinical situation in conjunction with immunofluorescence finding on renal biopsy of linear or pseudolinear immunoglobulin staining (IgG staining) of glomerular capillary wall, the possibility of anti-glomerular basement membrane (anti-GBM) glomerulonephritis is often considered. We report a case wherein above clinical scenario was eventually determined to be related to FGN based on electron microscopic findings.

Case report

A 59-year-old man was referred with 6 days history of nausea, headache, severe hypertension (BP 200/100 mmHg) and biochemical evidence of advanced renal failure (serum creatinine concentration of 1150 μmol/L, serum urea concentration of 26.2 mmol/L). A 24-h urinary protein excretion was 5.4 g and midstream urine contained numerous red cells (500×10^6/L), white cells (150×10^6/L) but no casts. There was no evidence of pre-existing renal dysfunction, a serum creatinine concentration done a year ago was normal. He was known to have diet controlled Type 2 diabetes mellitus with no documented clinical or laboratory evidence of micro or macro vascular complications. Laboratory test results for antinuclear antibodies, anti-DNA antibody and antineutrophillic cytoplasmic antibodies were negative. A serum complement profile was normal. Serologic tests results for human immunodeficiency virus, hepatitis B and C infection were negative. The test for circulating anti-GBM antibodies that was available after a week since the commencement of treatment was also negative. There was no evidence of paraproteinaemia on serum and urine electrophoresis. Renal ultrasonography showed normal-sized echogenic kidneys and no hydronephrosis. A computed tomographic-guided renal biopsy was performed.

On light microscopy, 19 glomeruli were seen in one section. Twelve were globally sclerosed and seven contained segmental and global crescents with collapsed glomeruli. Segments away from crescents showed endocapillary proliferation with necrosis in the form of nuclear pyknosis, karyorrhexix and focal deposition of fibrinoid material. Frequent breaks in Bowman's capsule were seen (Figure 1a). There was moderate interstitial infiltrates comprising of lymphocytes, plasma cells, neutrophils along with tubular injury with epithelial sloughing. The blood vessels showed moderate hyaline arteriosclerosis and arteriosclerosis. There was no evidence of vasculitis.

Immunofluorescence microscopy showed intense 4+ linear deposits of IgG with moderate 2+ confluent deposits of C3 along segmental mesangial and capillary loops (Figure 1b). In view of a diffuse proliferative and crescentic

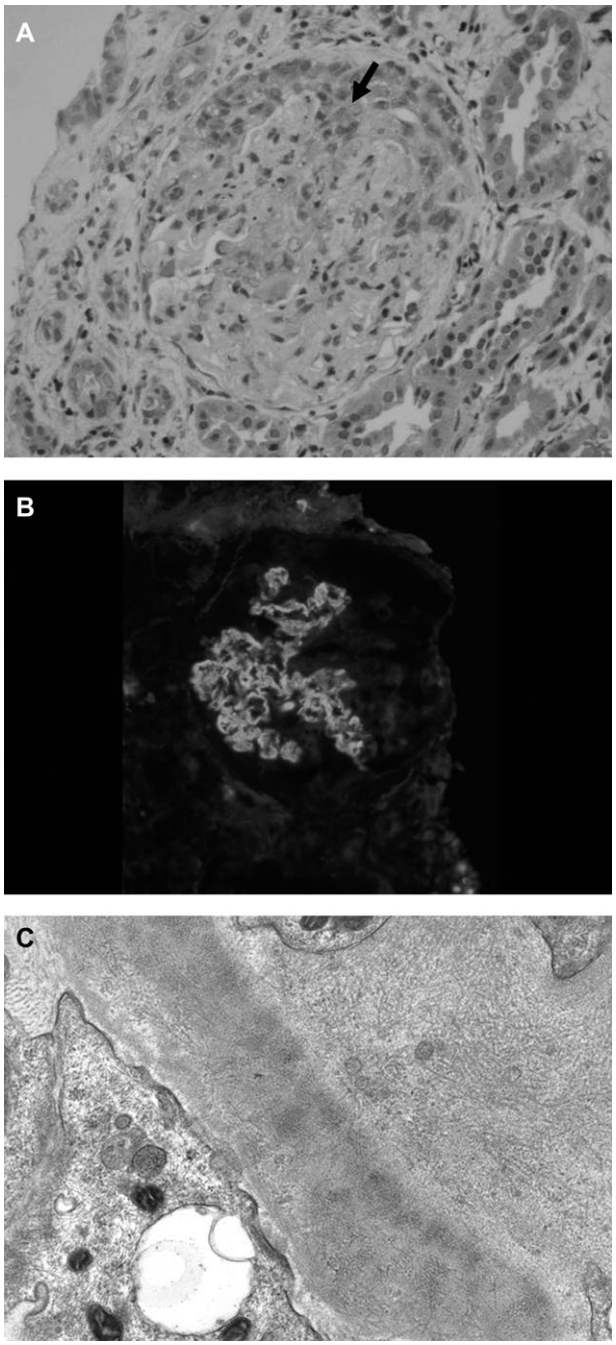

Fig. 1. (**a**) LM: cellular crescents (arrow) and fibrinoid necrosis of glomerular tuft (original magnification ×200). (**b**) IF: linear IgG staining along capillary walls (original magnification ×200). (**c**) EM: non-branching fibrils mesangium and capillary wall (original magnification ×36 000). LM, light microscopy; IF, immunofluorescence.

glomerulonephritis with linear IgG, a diagnosis of anti-GBM glomerulonephritis was made and was treated with combination of methylprednisolone, plasmaphaeresis and cyclophosphamide and haemodialysis. The result of electron microscopy (EM) was available 4 weeks later. This showed electron-dense deposits in the glomerular mesangium and capillary walls. These were composed of non-branching fibrils measuring 16 nm in diameter on average (Figure 1c). Based on these findings, a diagnosis of FGN was confirmed. Computed tomographic examination of chest, abdomen and pelvis done to screen for lymphoproliferative disorders was normal. A full blood count and lymphocyte flow cytometric analysis on peripheral blood was normal. A test for serum cryoglobulins was negative. Immunosuppressive therapy was stopped and patient was consigned to long-term haemodialysis. He continues to remain on dialysis over the past 5 years.

Discussion

In the above vignette, the patient had rapidly progressive glomerulonephritis (RPGN) clinically and crescentic glomerulonephritis pathologically. RPGN is a disease of the kidney characterized clinically by a rapid decrease in the glomerular filtration rate of at least 50% over a short period, from a few days to 3 months. The main pathological finding is extensive glomerular crescent formation. RPGN comprises three major categories: (i) anti-GBM antibody disease (~3% of cases), (ii) immune complex disease (45% of cases) and (iii) pauci-immune disease form of glomerulonephritis, with the highest frequency (50% of cases) [4].

FGN is a non-amyloid glomerulopathy characterized by extracellular deposition of randomly arranged, elongated non-branching fibrils within the mesangium and capillary walls of renal glomeruli [4]. The diameters of the fibrils are approximately twice those of the amyloid fibrils with an average of 20 nm (range 12–30 nm) [4, 5]. Largest single centre series of FGN reported occurrence of diverse morphological patterns on light microscopy, including diffuse proliferative glomerulonephritis (DPGN), MPGN, mesangial proliferative/sclerosing (MES), membranous glomerulonephritis (MGN) and diffuse sclerosing (DS) [4]. However, crescentic variety of glomerular injury is relatively uncommon and occurs in ~20–25% of cases [4, 5]. Immunofluorescence shows polyclonal IgG and C3 staining predominantly in mesangium and granular or pseudo linear pattern along the glomerular basement membrane [3].

The renal disease is commonly manifested clinically as nephrotic syndrome or combinations of proteinuria, haematuria, hypertension and renal insufficiency [1]. Most patients present with significant renal insufficiency and have a poor outcome despite immunosuppressive therapy, and outcome correlates with histologic subtype—mean time to end-stage renal disease being: DS 7 months, DPGN 20 months, MPGN 44 months compared to MES 80 months and MGN 87 months [4]. The presentation with RPRF and dialysis dependency is rather unusual with two such anecdotes of idiopathic FGN being reported in the literature so far [6, 7]. These two cases along with our patient share all the histological features that would allow one to make a reasonable assumption of anti-GBM-mediated glomerulonephritis [6], with potential to expose patients to yet unproven and often unsatisfactory immunosuppressive treatment [7].

The majority of cases of FGN are idiopathic, although association with systemic diseases such as cryoglobulinaemia, lupus, hepatitis C virus infection and rarely dysproteinaemia have been reported [3]. Our patient never demonstrated any clinical or serological evidence of systemic disease and

his continued survival >5 years following diagnosis makes underlying lymphoproliferative disorders unlikely.

This case therefore highlights the crucial role of EM in the differential diagnosis of the anti-GBM antibody negative, crescentic and necrotizing glomerulonephritis with linear immunoglobulin G staining of glomerular capillary wall. Since its first description in 1977 by Rosenmann and Eliakim [8], FGN has been anecdotally reported as an unusual cause of RPGN, the definitive diagnosis of which requires EM.

Conflict of interest statement. None declared.

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