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Case Report

A rare cause of nephrotic syndrome in autosomal-dominant polycystic kidney disease

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Abstract

We report the case of a 49-year-old lady who presented with hypertension, breathlessness and malaise. She was thrombocytopenic, with polycystic kidneys on imaging, and was found to have nephrotic syndrome. Serological results were consistent with systemic lupus erythematosus (SLE) and a renal biopsy confirmed WHO class V lupus nephritis. This is the first reported case of nephrotic syndrome due to lupus nephritis in a patient with autosomal dominant polycystic kidney disease (ADPKD) and underlines the importance of renal biopsy in patients with ADPKD and nephrotic range proteinuria.

Keywords: lupus; nephrotic syndrome; polycystic

Introduction

Autosomal dominant polycystic kidney disease (ADPKD) is an inherited disease with a prevalence of 1:700–1:1000 people, and accounts for 7–10% of patients on haemodialysis in the United States [1]. Although proteinuria has been reported to occur commonly in ADPKD [2], nephrotic syndrome is rare [2,3]. We report the case of a patient who was found to have ADPKD and later nephrotic syndrome, in whom renal biopsy showed WHO class V lupus nephritis.

Case report

A 49-year-old lady presented with a 5-month history of dyspnoea, malaise and weight loss. There was a family history of ADPKD in her father, although he had not progressed to established renal failure. She had been diagnosed with hypertension 6 years previously, at which time her serum creatinine was 1.2 mg/dL (102 μmol/L), urinalysis unremarkable and urinary catecholamines normal, and an ultrasound had shown multiple cysts in her kidneys.

On admission, her pulse was 88 beats/min and blood pressure (BP) 198/113 mmHg; an electrocardiogram showed lateral T-wave flattening and chest radiograph showed interstitial oedema. Serum biochemistry revealed a creatinine of 1.7 mg/dL (151 μmol/L), albumin 2.7 g/dL [27 g/L (36–52 g/L)] and normal liver enzymes. Serum haemoglobin was 1.3 g/dL (13.0 g/L), WCC $7.9 \times 10^3/\mu L$ (7.9×10^9/L), platelet count $45 \times 10^3/\mu L$ (45×10^9/L), ESR 62 mm/1st hour, CRP 0.4 mg/dL (4 mg/L) and troponin I was elevated at 0.3 ng/mL [0.34 μg/L (normal range <0.04 μg/L)]. An autoantibody screen, including antinuclear antibodies, was negative, and a renal tract ultrasound showed multiple cysts throughout both kidneys, in keeping with ADPKD, subsequently confirmed by computed tomography (CT). Echocardiography revealed concentric left ventricular hypertrophy, an immobile posterior mitral valve leaflet resulting in an eccentric jet of moderate-to-severe mitral regurgitation. A bone marrow biopsy was performed, revealing an increase in megakaryocyte activity in keeping with peripheral destruction of platelets. There was normal erythroid and megakaryocyte morphology and normal XX karyotype. On discharge, the patient was referred to the renal service for follow-up.

On review in the renal clinic, she was markedly hypertensive (238/130 mmHg) although clinically and radiographically euvolaemic. Fundoscopy revealed grade III hypertensive retinopathy, urinalysis showed blood (2+) and protein (3+) and blood results revealed serum creatinine 1.5 mg/dL (130 μmol/L), estimated glomerular filtration rate (eGFR) 40 mL/min/1.73 m^2, platelet count $116 \times 10^3/\mu L$ (116×10^9/L), ESR 63 mm/1st hour and serum albumin 3.0 g/dL (30 g/L). She was admitted, and her BP normalized with supervised administration of her usual antihypertensives. Investigations revealed significant proteinuria [6.4 g/L (urinary protein to creatinine ratio of 810.13 mg/mmol)], a moderately positive ANA (titre 1/640, homogeneous pattern), low complement C3 and C4 at 82 mg/mL and 14 mg/mL (0.82 g/L and 0.14 g/L), respectively, elevated double-stranded DNA antibodies at 51 units and detectable lupus anticoagulant. Further investigations revealed elevated anticardiolipin antibodies: cardiolipin antibody (IgG) 22 GPLU/mL (1–13), cardiolipin antibody (IgM) 14 MPLU/mL [1–10].

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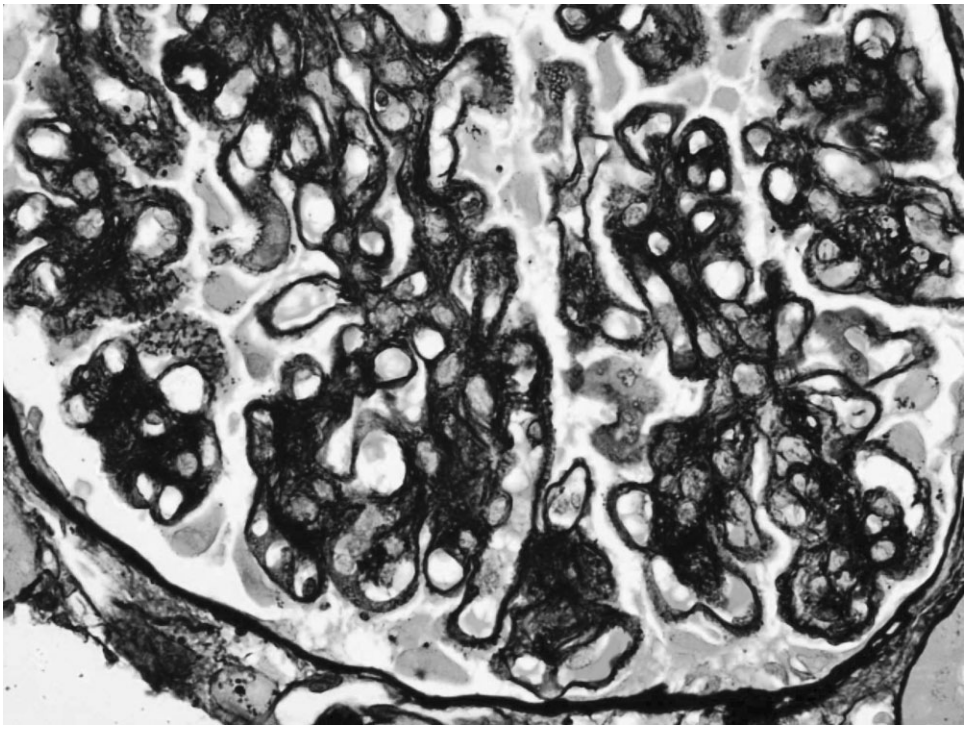

Fig. 1. Global epimembranous spikes and capillary wall vacuolations, and a mild increase in mesangial matrix and cellularity. Silver stain, high power.

A CT-guided renal biopsy was performed. By light microscopy, there were 7 obsolescent and 30 viable glomeruli showing global diffuse capillary wall thickening with widespread epimembranous spikes and focal basement membrane vacuolation on silver stain (Figure 1), a mild increase in mesangial matrix and cellularity, a moderate degree of chronic tubulo-interstitial damage, and severe chronic arteriopathy.

Electron microscopy (Figure 2) showed many subepithelial and intramembranous electron dense deposits surrounded by the basement membrane, many mesangial electron dense deposits, a few subendothelial deposits and a few tubuloreticular inclusions in endothelial cells. Unfortunately, no tissue was obtained for immunofluorescence, but the appearances were consistent with membranous lupus glomerulonephritis (WHO Class V).

She was commenced on prednisolone 20 mg and azathioprine 100 mg, and at 2 months' follow-up her renal function had deteriorated slightly with a serum creatinine of 1.71 mg/dL (152 μmol/L) and eGFR 33.4 mL/min/1.73 m^2, but proteinuria was stable at 1.8 g/L, urinary protein:creatinine ratio was 327.27 mg/mmol and albumin was 3.1 g/dL (31 g/L). The platelet count had increased to 154 × 10^3/μL (154 × 10^9/L), and ESR had decreased to 43 mm/1st hour.

Discussion

Mild proteinuria is common in ADPKD, along with other features of glomerulopathy such as haematuria and hypertension, but nephrotic syndrome is unusual [2,3]. In 1995, Contreras *et al.* reviewed the literature for case reports of ADPKD and nephrotic syndrome [3]. They found 21 patients, of whom 14 had a histopathologic diagnosis. A further review of the literature has revealed only two more recent reports [4,5]. A variety of histological diagnoses have been reported: most commonly focal glomerular sclerosis [3], followed by minimal change disease [6] and membranous nephropathy [7], and there are rare reports of IgA nephropathy [4], membranoproliferative, post-infectious mesangioproliferative glomerulonephritis and diabetic nephropathy. There is only one other report of lupus nephritis in a patient with ADPKD, although this patient did not have nephrotic syndrome [8].

Proteinuria >2 g/24 h is rare, and the presence of nephrotic syndrome should prompt investigations for underlying glomerular disease. Importantly, both proteinuria and microalbuminuria are independent risk factors for the development of kidney failure in ADPKD [2,9], along with hypertension [9]. A co-existent glomerulonephritis may accelerate the progression of renal failure and may require specific treatment. Interestingly, our patient initially had a negative ANA that later became positive as has been previously described in a case series of 17 patients with class V lupus nephritis where the predominant biopsy finding was membranous glomerulonephritis [10]. Although the treatment of class V lupus nephritis is controversial, we elected to give immunosuppression because of the additional extra-renal manifestations (haematological and possible cardiac involvement). This case supports the need to perform renal biopsy in patients with ADPKD and nephrotic range proteinuria.

Conflict of interest statement. None declared.

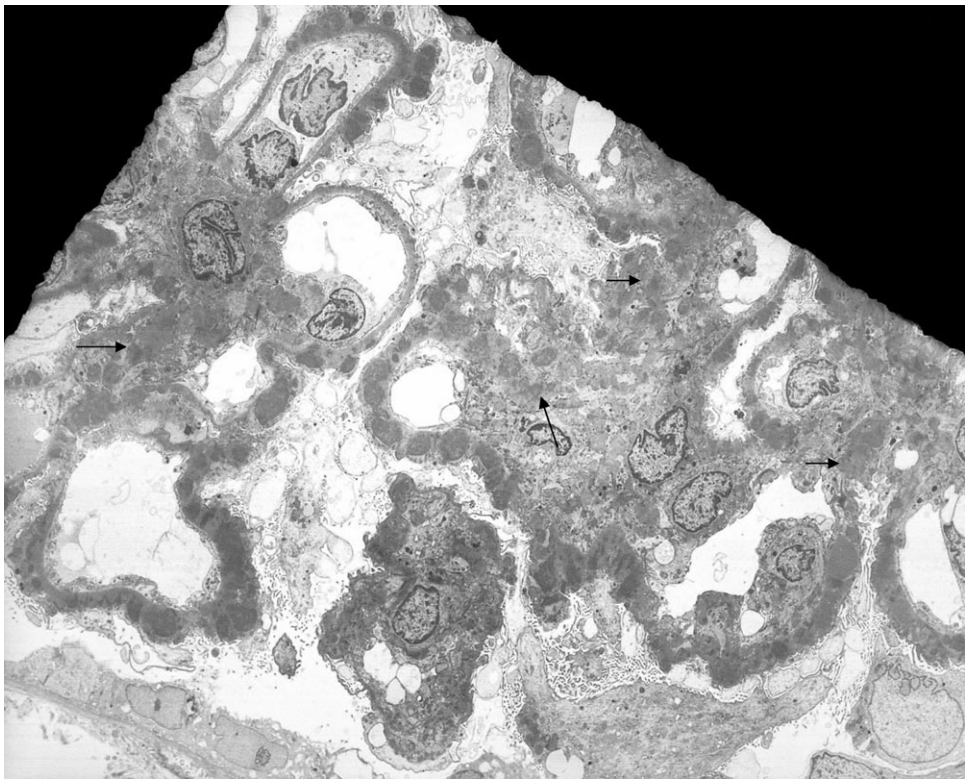

Fig. 2. Electron microscopy showing many subepithelial and some mesangial (arrows) electron dense deposits.

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