Long-term outcome of kidney transplantation in a patient with coexisting lipoprotein glomerulopathy and fibrillary glomerulonephritis

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Abstract
Both lipoprotein glomerulopathy (LPG) and fibrillary glomerulonephritis (FGN) are rare causes of end-stage renal disease (ESRD), and the literature concerning the outcome of kidney transplant in patients with LPG or FGN is scarce. We report a patient who suffered from ESRD with coexisting FGN and LPG and received deceased kidney transplant >10 years ago did not reveal any clinical features of disease recurrence during follow-up. Our case shows that the prognosis of patients with LPG component who received kidney transplant can be good. Kidney transplantation remains a viable therapeutic option for patients with ESRD secondary to FGN with LPG.

Keywords: fibrillary glomerulonephritis; kidney transplant; lipoprotein glomerulopathy

Background
Both lipoprotein glomerulopathy (LPG) and fibrillary glomerulonephritis (FGN) are rare causes of end-stage renal disease (ESRD). LPG is a rare disease of renal lipoidosis, first described by Saito et al. in 1989 [1]. To date, ~150 cases of LPG have been reported in the literature, with most of them in Japan and East Asian countries [2, 3]. It has been shown that half of the patients with LPG eventually develop ESRD at 1–27 years after onset of symptoms [3]. However, the literature concerning the outcome of kidney transplantation in patients with LPG was scarce. Only five kidney transplants have been reported and LPG recurred early in all the transplanted allografts [4–8]. While usually cases without complications are less likely to be reported, it is noteworthy that cases without LPG recurrence have yet been described.

On the other hand, FGN is also a rare deposition disease comprising only ~1% of native kidney biopsies [9, 10]. It is characterized by the deposition of organized microtubules, measuring 16–24 nm in diameter and arranged in a parallel fashion [9]. FGN usually progresses to ESRD within months to a few years but the risk of recurrence in kidney transplant is low according to the limited number of cases [10].

Herein we report a patient with coexisting LPG and FGN, who underwent deceased kidney transplant >10 years ago and did not reveal any clinical features of recurrence of diseases after long-term follow-up.

Case history
A 34-year-old Chinese man first presented to our hospital with 1-year history of ankle swelling. He had no relevant drug history and no family history of renal disease. His blood pressure was 140/90 mmHg. Laboratory investigations revealed a 24-h urinary protein excretion >10 g per day, serum albumin 21 g/L, serum creatinine 123 µmol/L, total cholesterol 10.1 mmol/L and triglyceride 4.7 mmol/L. Ultrasound-guided renal biopsy was performed. Light microscopy revealed 13 out of 36 glomeruli showing advanced sclerosis and another six showing segmental sclerosis. The capillary lumens were markedly dilated and showed occasional fibrin caps. Immunofluorescence studies revealed capillary deposits of IgM and C3 without IgG or IgA. Electron microscopy showed abundant non-branching fibrillary material ranging from 16–19 nm in diameter in the mesangium. Electron-lucent areas were noted in the subendothelial space with fragmented filamentous material ranging from 11–16 nm in diameter (Figure 1A). The diagnosis was FGN. He was put on’accupril and atorvastatin. His renal function gradually deteriorated but he defaulted follow-up thereafter.

Three years later, he presented with uremic symptoms and blood tests showed urea nitrogen 46 mmol/L, creatinine 2011 µmol/L, albumin 28 g/L, hemoglobin 7.5 g/dL with normochromic normocytic indices. Autoimmune markers including antinuclear, antineutrophil cytoplasmic and antiglomerular basement membrane antibodies were all negative. Renal ultrasound showed bilateral small kidneys. He was put on hemodialysis support. Three months later, he received deceased kidney transplant and immunosuppression included prednisolone, tacrolimus and mycophenolate mofetil. The postoperative course was unremarkable. His serum creatinine remained stable (at ~120 µmol/L) without any significant proteinuria. His serum cholesterol was 5 mmol/L and triglyceride was 1.8 mmol/L.
He suffered an episode of acute kidney injury with serum creatinine reaching 201 µmol/L during follow-up at 18-months post-transplant. There was neither fever nor urinary symptoms. Renal graft biopsy was performed and light microscopy revealed marked interstitial inflammation consisting of a large amount of polymorphs which were also noted within the tubular lumens (Figure 1B). All these features were suggestive of infective etiology. A course of ceftriaxone was given and the serum creatinine gradually returned to baseline. He continued to have regular follow-ups in our clinic with unremarkable course.

However, subsequent review of his native kidney biopsy specimen showed that in addition to features of FGN, components of LPG which were characterized by some vacuolated and stringy materials inside the dilated capillary lumens (Figure 1C) were also seen. These materials were weakly eosinophilic, weakly periodic acid–Schiff (PAS) positive and stained pale blue under Chromotrope-Aniline Blue (CAB) stain. On electron microscopy, these intraluminal materials contained fine granular material with small lipid vacuoles, consistent with lipoprotein thrombi (Figure 1D). These features were not present in the graft biopsy specimen obtained 18 months after transplant.

Mutational analysis of the apolipoprotein (APOE) gene by polymerase chain reaction and direct DNA sequencing revealed an E3/E3 genotype and a heterozygous mutation c.480_488del, which is predicted to result in deletion of Leu-Arg-Lys at codons 162–164 (reference sequences NM_000041.2 and NP_000032.1). This is a known mutation called APOE Tokyo causing LPG [11]. A familial genetic study on his son at 18 years of age showed that he also carries the same mutation, though there was no biochemical evidence of proteinuria or renal disease at the time of testing.

His maintenance immunosuppressive regimen remained prednisolone, tacrolimus and mycophenolate mofetil while he was also put on diltiazem and lisinopril for blood pressure control. After >10 years post-transplant, his latest serum biochemistry and other laboratory examination revealed no significant abnormality. These included serum creatinine 125 µmol/L, serum albumin 42 g/L, total cholesterol 4.8 mmol/L, triglyceride 1.2 mmol/L and 24-h urinary protein excretion <0.1 g.

Discussion

FGN and LPG are both uncommon causes of ESRD. The native kidney histology of our patient showed coexisting features of FGN and LPG. Subsequent mutational analysis revealed the presence of APOE Tokyo. LPG is found to be due to mutations of the APOE gene. Up till now, 12 mutations have been reported in the Human Gene Mutation Database (version 27 September 2013) to result in LPG (http://www.hgmd.org/). The more common ones include APOE Sendai (Arg145Pro) [12] and APOE Kyoto (Arg25Cys) [13]. Most patients are asymptomatic. The usual presentation includes proteinuria on routine screening examination and renal impairment. Most patients also have hyperlipidemia with...
In conclusion, our experience shows that kidney transplantation remains a viable therapeutic option for patients with ESRD secondary to FGN with LPG. However, close monitoring of renal function and proteinuria for any recurrence is essential.

Conflict of interest statement. None declared.

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