Successful treatment of recurrence of immunotactoid glomerulopathy in a kidney allograft recipient

Xavier Carles¹, Lionel Rostaing¹, Anne Modesto², Claudine Orfila³, Jean-Marc Cisterne¹, Marie-Bernadette Delisle³ and Dominique Durand¹

¹Department of Nephrology/Hypertension/Haemodialysis/Transplantation, ²Department of Immunology and ³Department of Pathology, CHU Rangueil, Toulouse, France

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Introduction

Glomerulopathy characterized by deposits of fibrillary material was first reported in 1977 [1]. Fibrillary immunotactoid glomerulopathy is a clinicopathological entity characterized by extracellular deposition of non-branching microfibrils or microtubules (Congo red and thioflavin T negative) within the mesangium and capillary walls of renal glomeruli. It is clinically characterized by the presence of glomerular proteinuria (often in the nephrotic range), microscopic haematuria, and often hypertension. It can lead to chronic renal failure. Based on the size and the arrangement of the microfibrils or microtubules in intraglomerular deposit, fibrillary immunotactoid glomerulopathies have been divided into two distinct entities: fibrillary glomerulopathy (FG) is characterized by small, randomly organized fibrils (< 30 nm in diameter), whereas immunotactoid glomerulopathy (ITG) is typified by larger fibrils and often organized in parallel arrays (> 30 nm in diameter) [2,3]. Patients with FG are less likely than those with ITG to have associated haematopoietic disease, i.e. monoclonal gammopathies; they also have poorer renal survival [2]. The two above-mentioned entities are primarily renal in most cases. Despite the fact that there is limited information about kidney transplantation in the context of end-stage renal failure related to fibrillar immunotactoid glomerulopathies, the few reports available indicated that fibril deposition occurred in more than 50% of patients, although the allograft functioned satisfactorily for a few years [4–6]. We report the case of a patient with ITG who had an early recurrence of this disease after renal transplantation but who responded favourably to an increase in immunosuppressive therapy.

Case

A 30-year-old woman was first seen in our department in August 1988 for nephrotic syndrome, hypertension, microscopic haematuria, cutaneous vasculitis, and IgA glomerulopathy characterized by deposits of fibrillary lambda microfibrils or microtubules (Congo red and thioflavin T negative) within the mesangium and capillary walls of renal glomeruli. It is clinically characterized by the presence of glomerular proteinuria (often in the nephrotic range), microscopic haematuria, and often hypertension. It can lead to chronic renal failure. Based on the size and the arrangement of the microfibrils or microtubules in intraglomerular deposit, fibrillary immunotactoid glomerulopathies have been divided into two distinct entities: fibrillary glomerulopathy (FG) is characterized by small, randomly organized fibrils (< 30 nm in diameter), whereas immunotactoid glomerulopathy (ITG) is typified by larger fibrils and often organized in parallel arrays (> 30 nm in diameter) [2,3]. Patients with FG are less likely than those with ITG to have associated haematopoietic disease, i.e. monoclonal gammopathies; they also have poorer renal survival [2]. The two above-mentioned entities are primarily renal in most cases. Despite the fact that there is limited information about kidney transplantation in the context of end-stage renal failure related to fibrillar immunotactoid glomerulopathies, the few reports available indicated that fibril deposition occurred in more than 50% of patients, although the allograft functioned satisfactorily for a few years [4–6]. We report the case of a patient with ITG who had an early recurrence of this disease after renal transplantation.

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serological tests as well as ANA and ANCA were negative. There was a mild anaemia (Hb at 8.9 g/dl), schistocytes were negative, platelets were at 291 000/mm³, and liver enzymes as well as LDH were within the normal ranges. The CsA whole-blood trough level was at 105 ng/ml.

Four weeks later since renal failure persisted (serum creatinine at 3.2 mg/dl), a transplant biopsy was performed (see Figure 1): the specimen disclosed 17 glomeruli. There was diffuse mesangial hypertrophy, associated with hypercellularity and thickening of the glomerular basement membranes. In five (30%) of the glomeruli there was segmental or extensive extracapillary proliferation. Most of the glomeruli showed large intracapillary hyaline deposits, which stained positive for periodic acid–Schiff staining. In the interstitium, a mild fibrosis was present without evidence of acute rejection. Congo-red staining was negative and there was no abnormal birefringence. Using immunofluorescence, endomembranous deposits stained with anti-IgG and anti-C3 sera were observed. Using electron microscopy, we found the same findings as in native kidneys, i.e. organized deposits of fibrillar structures (see Figure 2).

Because of the severity of the recurrence of the initial disease, the patient was treated with six plasma exchanges, three methylprednisolone pulses of 10 mg/kg each followed by prednisolone at 1 mg/kg/day; azathioprine was withdrawn and replaced by monthly cyclophosphamide pulses (1 g each). CsA was continued although at a lower dosage (2 mg/kg/day). One month after the beginning of this therapeutic scheme, the serum creatinine was 0.9 mg/dl but nephrotic-range proteinuria persisted. In February 1998, after 6 months of intensive therapy, the serum creatinine was 1.3 mg/dl, proteinuria was mild (2 g/day), and the blood pressure was normal with isradipine. A new transplant biopsy disclosed 14 glomeruli, of which two were obsolescent. There were neither intraglomerular deposits nor crescents. All glomeruli showed an increase in mesangial matrix. Interstitial fibrosis was mild, as on the previous biopsy. Immunofluorescence results of the biopsy were unchanged from the previous one. Cyclophosphamide was stopped and replaced by mycophenolate mofetil 2 g/day, and prednisolone (0.5 mg/kg/day at that time) was progressively decreased. By November 1999 the serum creatinine was normal (1.1 mg/dl) and proteinuria was very mild (0.2 g/day).

**Discussion**

The morphological features of immunotactoid glomerulopathies were initially reported in 1980 by Schwartz and Lewis [8], for Congo-red negative extracellular organized microtubular deposits with an average diameter of 32–50 nm. Although this disease is rare, to date some cases have been reported in the literature [2]. Little is know about the response to therapy in

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**Fig. 1.** First post-transplant renal biopsy. Magnification of one glomerulus showing mesangial proliferation and huge thickening of capillary walls by interposition of hyaline material. Masson’s trichrome (×300).
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Fig. 2. Electron micrograph of the first post-transplant renal biopsy showing foot process fusion and narrowing of the glomerular capillary lumen due to subendothelial and mesangial deposits of numerous fibrils ($\times 21,600$).
patients with immunotactoid glomerulopathies. It appears that steroids alone, steroids with plasma exchanges, and steroids with cyclophosphamide do not generally alter the clinical course of the disease [9]. However, at least two reports described partial remission with long-term alternate-day prednisone [10] or low-dose prednisolone [11].

In contrast to ESRD patients with amyloidosis (primary or AL amyloid), where patient survival is notoriously poor, ESRD patients with FG/mycophenolate mofetil, a new immunosuppressive treatment of glomerular disease.

kidneys, our patient responded very well to plasma exchanges, methylprednisolone pulses, as she had IgA monoclonal gammopathy, after the end of cyclophosphamide pulses we added mycophenolate mofetil, a new immunosuppressive drug known to decrease the synthesis of antibodies by B lymphocytes [13] and also to be efficient in some primary glomerular diseases [14]. However, the follow-up of this patient is too short to draw firm conclusions from our observations, although they show that the recurrence of immunotactoid glomerulopathy on kidney allografts can be successfully managed by increasing and adapting immunosuppression. Finally, the results of a long-term follow-up are obviously needed to draw more definitive conclusions.

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