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Case Report

Renal transplantation from a donor with a nail–patella syndrome

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Introduction

Nail–patella syndrome or hereditary osteo-onychodysplasia, is an autosomal dominant syndrome with variable expression and penetrance. It is characterized by hypoplasia or complete abscence of the patellae, dysplasia of the nailbeds, presence of iliac horns, elbow abnormalities, and sometimes renal disease. The nail–patella syndrome was described by Little in 1897, who compiled 42 previously reported and personally studied cases of congenital absence of patellae [1].

The disorder has been mapped to the long arm of chromosome 9 (9q34) and the locus for the nail–patella syndrome gene is closely linked to adenylate kinase and ABO group [2]. Hawkins and Smith reported in the English literature the first cases of family members with nail–patella syndrome who also had proteinuria, cylindruria, and haematuria [3]. Renal disease has a variable clinical expression from normality to renal failure. More than 50% of the patients have no apparent clinical renal involvement, and in the remainder the nephropathy is characteristically benign, although about 10% of them develop end-stage renal disease [4]. The characteristic lesion is a change in the glomerular basement membrane (GBM), consisting of presence of mottled and lucent rarefactions of the GBM and less commonly the mesangium, which results in a characteristic 'moth-eaten' appearance [5–8]. Several reports have described these renal changes in patients without skeletal, or other manifestations of classic nail–patella syndrome ('forme fruste' or 'nephropathy only variant') [3,7,9].

The aim of this paper is to present a patient who received a cadaveric renal transplant with morphological features of nail–patella syndrome. To our knowledge, this is the first case reported in the literature.

Case history

A 43 year-old woman suffered a chronic renal failure secondary to chronic primary glomerulopathy that manifested 16 years ago. After 2 years of regular programme of dialysis, she received a cadaveric renal allograft. The donor was a 18-year-old man who died after a craneocephalic trauma in a motorcycle accident. There was no suspicion of nephropathy in the donor prior to transplantation and he maintained a good renal function before donation (creatinine 0.36 mg/dl).

The immunosuppressive therapy was based on steroids and azathioprine. The recipient had an initial non-graft function requiring 16 sessions of haemodialysis because she suffered five episodes of acute interstitial rejection at 8, 19, 40, 83 and 100 days post-transplantation, treated with methylprednisolone in bolus.

The renal biopsy showed 35 glomeruli, 10 of which were completely hyalinized. Many glomeruli showed glomerular enlargement and mesangial increase (Figure 1). The glomerular capillary walls were

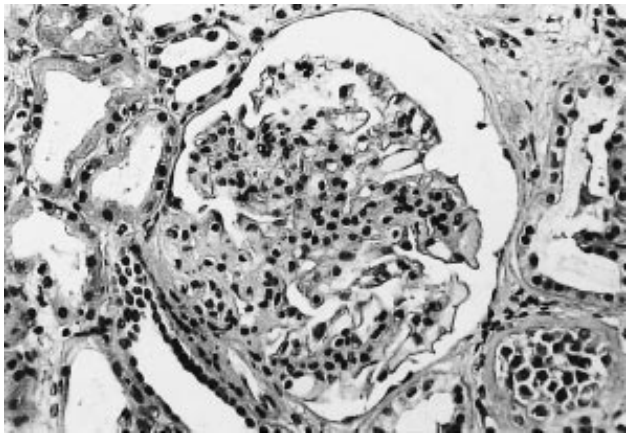

Fig. 1. Glomerulus showing segmental mesangial proliferation and sclerosis. The basement membrane shows normal thickness. The tubules show slight atrophy with interstitial fibrosis. (H&E × 250).

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thickened and the GMB was thickened due to a combination of widening of the subendothelial zone and diffuse mesangial-cell interposition. There was mesangial proliferation, and/or accumulation of homogeneous eosinophilic material that expanded the periphery, collapsing some capillaries. The tubular architecture was preserved, although there was interstitial focal fibrosis. Ultrastructurally, there was a striking widening of the subendothelial zone of the GMB together with normal areas. Interposition of mesangial cells between endothelial and epithelial cells was common. GMB and mesangium had a 'moth-eaten' appearance (Figure 2) with coarse cross-banded collagen fibres arranged in small clusters (Figure 3). There were several areas with effaced epithelial foot processes. Immunofluorescence studies were negative. These pathological findings confirmed the diagnosis of nail–patella syndrome. We did not perform additional biopsies.

In the following years, between 1980 and 1991, the patient suffered arterial hypertension with difficult control, episodes of leukopenia, chronic mild active hepatitis, hypogammaglobulinaemia, arteriosclerotic stenosis of the renal artery, repeated episodes of anxious depression, hypercholesterolaemia, proteinuria, microcrystalline arthritis (uric acid or chondrocalcinosis) treated with colchicine and allopurinol, which produced an allergic rash and lymphocytic vasculitis, cardiac failure, pericarditis, ascites and impairment of hepatic function probably due to cytomegalovirus infection, and carcinoma '*in situ*' of the vulva complicated with sepsis by *E. coli*.

The renal function gradually deteriorated within 9 years. In 1991, due to an infection of surgical wound and sepsis after vulvectomy because of a carcinoma '*in situ*', immunosuppression was decreased. Subsequently a definitive deterioration of renal function occurred, requiring once again periodic haemodialysis. In 1991 the patient was included again on a waiting list for renal transplantation.

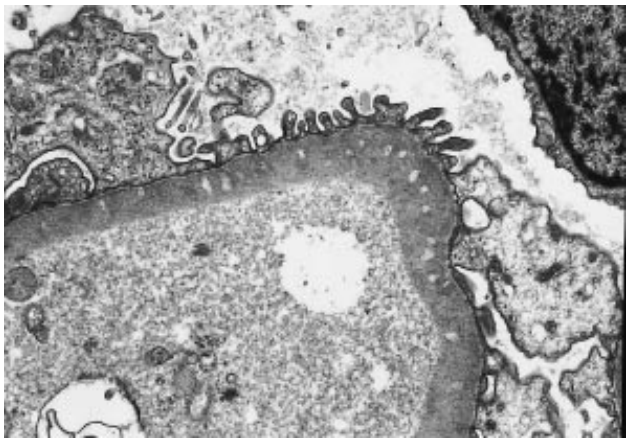

Fig. 2. Nail–patella syndrome. Glomerular basement membrane shows slight thickening of the basement membrane and rounded clear holes (Lead citrate and uranyl acetate, ×6500.).

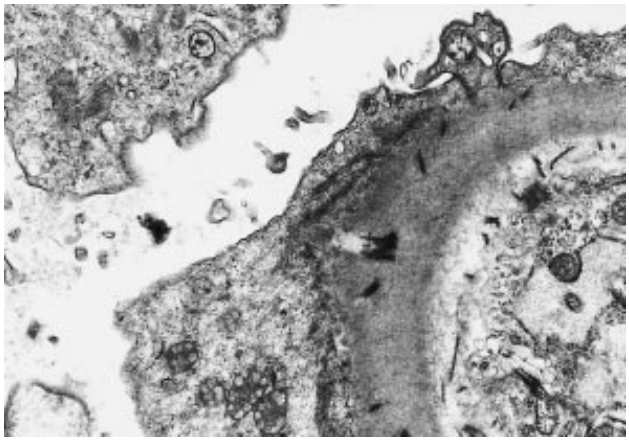

Fig. 3. Dense collagen and holes in the same segment of the glomerular basement membrane. (Lead citrate and uranyl acetate ×10 000.).

Discussion

The diagnosis of nail–patella syndrome was based in an electron-microscopic study and was supported by the appearance of glomerular lesions in a biopsy performed 8 days after transplantation, when the patient had the first acute rejection episode.

When clinical manifestations and renal disease are present, light-microscopy shows increased amounts of mesangial matrix, either diffuse or segmental [8]. Cell proliferation may be absent in the mesangium, although in some cases the mesangium is hypercellular and the glomerular basement membrane is generally thickened [5].

Ultrastructural renal lesions of nail–patella syndrome are characteristic [5,8]. On electron-microscopic examination, the epithelial cells show focal fusion of foot processes [6]. The basement membrane is generally thickened in an irregular fashion with electron-lucent areas, thus giving a moth-eaten appearance [8]. Fibrils characteristic of collagen are seen in the electron-lucent areas in the basement membrane and mesangial matrix [5,8].

It is known that renal transplantation is a viable therapeutic modality in the treatment of end-stage renal disease in patients with nail–patella syndrome, and the disease does not recur in the kidney grafts [10,11].

The most important differential diagnosis of the nail–patella syndrome—at least from a morphological point of view—is collagenofibrotic glomerulopathy (collagen type III glomerulopathy). Renal lesions in nail–patella syndrome are similar to those described in collagen type III glomerulopathy [12]. However, we favour the diagnosis of nail–patella syndrome because the donor had no evidence of early and progressive glomerular symptoms and hypertension, which are characteristic of collagen type III glomerulopathy.

We tried to obtain information concerning the donor and his family, but were unsuccessful. The contralateral donor kidney was transplanted at another Institution

and we were not able to follow its evolution. Unfortunately we do not know whether the donor had other stigmata of nail–patella syndrome. If they were absent, the case should be considered a 'forme fruste' of nail–patella syndrome.

The evolution of the recipient might be considered as normal for a patient with five acute rejection episodes and development of a carcinoma, which required a decrease of immunosuppression. This clinical history suggests that nail–patella syndrome did not have much influence in the development of renal failure. Thus, we should conclude that kidneys from donors suffering from nail–patella syndrome could be useful for transplantation, if no renal impairment is present before donation.

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