Grafted kidney, native kidney and proteinuria after pre-emptive pancreas–kidney transplantation: questions and answers

Sir,

Pancreas–kidney transplantation is presently considered as the best therapy for irreversible diabetic nephropathy [1]. Pre-emptive transplant approaches, before the start of dialysis, are increasingly considered as optimal choices; in the setting of an early pre-emptive transplant approach, the behaviour of the native kidneys may be clinically relevant, both for their contribution to the overall glomerular filtration rate (GFR) and because of proteinuria [2,3]. Little is currently known on this issue and the natural history of residual renal function in the case of pre-emptive pancreas–kidney transplantation has not yet been extensively studied [4–6]. The present case may exemplify some of the clinical questions arising from this issue.

A 40-year-old woman, with type 1 diabetes since age of 9 had, at age 25, undergone right nephrectomy for acute papillary necrosis complicated by a large renal abscess (the histology of the kidney showed diffuse and nodular diabetic glomerulosclerosis). Since mononefrectomy, she was macro-proteinuric (proteinuria 1–4 g/24 h) and her kidney function slowly decreased. Ten years later, at the time of the first renal scintiscan (Figure 1, February 2000) her creatinine clearance was 41 ml/min, serum creatinine 1.8 mg/dl and proteinuria 2.2 g/24 h (glomerular and tubular incomplete pattern). At that time, she was on a low protein diet (0.6 g/kg/day), on ACE inhibitors and angiotensin-II antireceptor therapy. On July 27, 2003, she underwent a simultaneous pancreas–kidney graft (at graft, creatinine clearance 35 ml/min, proteinuria 1.3 g/24 h). The post transplant follow-up was uneventful: at hospital discharge, serum creatinine was 1.07 mg/dl and there was no proteinuria on the urinary stick. Therapy consisted of cyclosporine A 175 mg/day (C2 target levels: 700–900 ng/ml), prednisone 10 mg/day, mycophenolate mofetil 2 g/day, omeprazole 40 mg/day, oral anticoagulation with warfarin, anti-infectious prophylaxis with fluconazole, ganciclovir and sulfamethoxazoletrimethoprim.

The second renal scintiscan (Figure 2) was taken in August 2003. The native kidney contributed about 10% to total function, and displayed remarkably contracted functional phases. Proteinuria ranged from 100 to 300 g/24 h, with ‘physiological’ pattern; GFR was 73 ml/min.

In the following months, she progressively developed low grade proteinuria (0.5–0.8 g/24 h), with glomerular and a tubular pattern superimposable on the pattern recorded in the pre-transplant period. The third renal scintiscan showed increased function of the native kidney, which now accounted for 30% of the whole GFR (Figure 3).

This case raises several questions and deserves a few comments. The first point is that after pre-emptive pancreas–kidney transplantation the native kidneys are rapidly ‘turned off’, remaining vital, but contributing little to the overall function [6]. This observation may explain why the nephrotic syndrome of diabetic nephropathy is rapidly reversed after transplantation [6]. The second point is that, at least in selected cases such as the one reported here, kidney function may recover slowly; in keeping with our observations, a small but substantial contribution of the native kidneys to the overall GFR was reported in a large cross-sectional analysis, at distance from transplantation [5].

In our patient, native kidney function increased over time from <10% to ~50% (Figure 1); this behaviour may be of

Fig. 1. The parenchymal curve of the solitary native kidney shows regular morphology, with normal peak time and excretion.

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some clinical relevance, since it could mask moderate functional reductions and hinder the diagnosis of subacute allograft diseases. In such a setting, native kidneys may also be a relevant source of proteinuria. While only kidney biopsy or invasive catheterisation may eventually demonstrate the source of proteinuria, the hypothesis of a pathogenetic role of the native kidney may be suggested by the temporal relationship between the recovery of kidney function and the appearance of proteinuria, whose pattern, indicative of chronic damage, is superimposable on the pre-transplant pattern. The reasons for these functional behaviours, in ‘early’ pre-emptive pancreas kidney transplantation, are not known. The description of a new functional pattern (slowly recovering native renal function) may stress the need for further studies on this issue; from the practical-clinical point of view, it may also suggest consideration of the native kidney contribution in the evaluation of functional alterations after pre-emptive kidney–pancreas transplantation.

Conflict of interest statement. None declared.

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