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LETTER TO THE EDITORS

Allotransplantation of kidney from unrelated living donor with loin pain haematuria syndrome

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Dear Sirs,

The unavailability of kidney for transplantation to meet the ever-increasing demand has resulted in organ shortage crisis [1]. Among the main actions proposed to overcome, this major health challenge is the extension of criteria defining acceptable deceased donors and the promotion of living donation. Because the last option offers shorter waiting times, lower costs and better results, the use of organs from living donors has regularly augmented over the last decades [2]. Following this trend, bioethical legislations, which once restricted donation to genetically related donors, have evolved to extend this possibility to emotionally related (but genetically unrelated) donors. The transplantation of kidneys from living unrelated patients requiring a nephrectomy has remained unexplored so far.

Loin pain haematuria syndrome (LPHS), which affects predominantly young white females, corresponds to recurrent episodes of loin pain associated with gross or microscopic haematuria without underlying cause [3]. First-line therapy usually consists in pain management with nonsteroidal anti-inflammatory drugs and opiates. Thirty to fifty per cent of patients experience spontaneous resolution of their symptoms after a few years on conservative treatment [4]. For the others, the clinical picture persists or progresses despite escalating doses of opiates requiring the surgical denervation of the kidney. While neurectomy is associated with a high incidence of recurrent renal pain, autotransplantation achieves pain relief in 75% of the cases [5]. Nephrectomy is ultimately considered for patients with intractable pain [4].

Given the excellent long-term nephrological prognosis of LPHS in the medical literature [4], we have considered the possibility of transplanting nephrectomized LPHS kidneys to patients on the waiting list for renal transplantation.

Procedures

Ten patients were diagnosed with LPHS in our centre over the last 10 years. Five required autotransplantation, two of which finally underwent a nephrectomy.

These two patients with LPHS were informed and gave consent for the transplantation of their nephrectomized kidney. The Agence de la Biomédecine, the French institution in charge of organ allocation, was informed of the availability of the kidney graft at the time of donor renal hilum clamping. A compatible recipient, registered on the waiting list, was selected following the usual procedure as for a local deceased donor.

Case #1

The donor was a 42-year-old man without significant past medical history except for a LPHS diagnosed 9 years before. Nephrectomy was proposed because of the failure of autotransplantation to control the pain. At this time, estimated glomerular filtration rate (MDRD formula) was 84 mL/min/1.73 m^2 without proteinuria. Renal biopsy (Fig. 1a) showed normal vessels and glomeruli with discrete tubulointerstitial lesions. The recipient was a 64-year-old woman on haemodialysis for 4 years due to glomerulonephritis. Thymoglobulin was used for induction and a combination of cyclosporine A, mycophenolate mofetil and low-dose steroids for maintenance immunosuppression. During the 7 years of follow-up, the patient did not report any episode of graft pain. On this period, graft function has remained stable with eGFR comparable to that observed after conventional living donation (Fig. 1b). Urine analyses found no haematuria and negligible proteinuria (Fig. 1b).

Case #2

The donor was a 31-year-old woman diagnosed with LPHS 2 years before. She had no proteinuria but reported several episodes of intolerable pain with gross haematuria. Autotransplantation was unsuccessful to relieve the patient. At the time of the nephrectomy, eGFR was 90 ml/min/1.73 m^2 and histological analysis of the kidney was normal (Fig. 1c). The recipient was a 41 years old man diagnosed with chronic interstitial nephropathy due to Crohn's

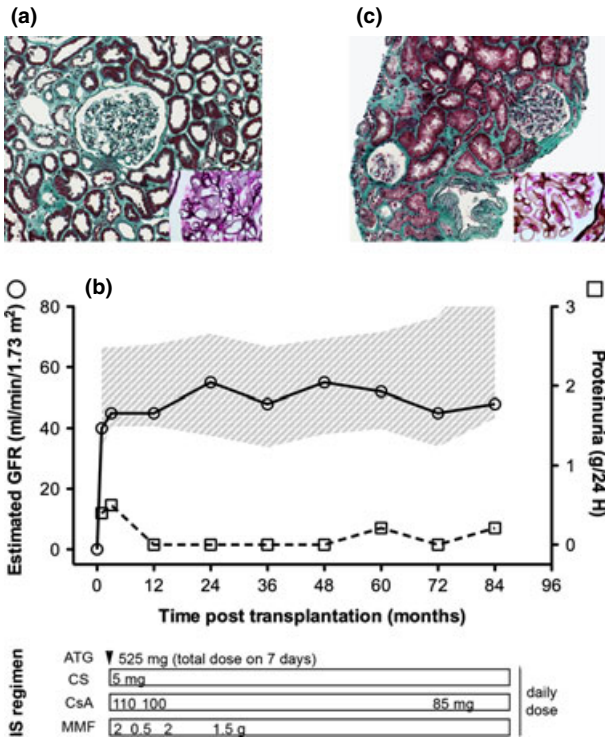

Figure 1 Representative findings of the histological analysis of LPHS kidneys at the time of the nephrectomy. Masson's trichrome (original magnification ×20) and reticulin staining showing normal glomerular basal membrane (thumbnail bottom right; original magnification ×600) for donor #1: (a) (please note the discrete tubulointerstitial lesions: Banff classification: ct1, ci1), and donor 2: (c). (b) Summary of recipient #1 transplantation history. Graft glomerular filtration rate was estimated with the MDRD formula (eGFR). Grey area indicates the mean±standard deviation of eGFR for the conventional living donations performed in our centre in the last 10 years (n = 102). Changes in immunosuppressive regimen are indicated at the bottom of the graph. CS, corticosteroid; Csa, cyclosporine A; MMF, mycophenolate mofetil.

disease, who received the graft before the beginning of haemodialysis. Thymoglobulin was used for induction and a combination of tacrolimus, mycophenolate mofetil and steroids for maintenance immunosuppression. The systematic screening biopsy at 3 months post-transplantation was normal. Eight months after the transplantation, the graft is indolent. Estimated GFR is 63 mL/min/1.73 m^2 without proteinuria or haematuria.

Discussion

We report herein the first two transplantations of kidney from unrelated living donor with LPHS. These transplantations were performed with the consent of the patients with LPHS, who required a nephrectomy to control the renal pain that recurred after autotransplantation procedure. For both transplantations, the outcome, after, respectively, 7 years and 8 months of follow-up, was excellent without pain or haematuria in the recipients and an eGFR within the range of what observed for living donations in our centre (Fig. 1b).

The decision to transplant these kidneys was based on the excellent quality of the grafts, and the available evidence that the long-term nephrological prognosis of LPHS is excellent. As its initial description in the 60s', the pathophysiology of LHPS has remained enigmatic. It has been proposed that ultrastructural abnormalities of glomerular basement membrane could be responsible for episodes of glomerular capillary haemorrhage, leading to intratubular obstruction by red blood cells, and in turn painful stretching of the renal capsule [6]. Many LPHS kidney biopsies (including the ones of our two donors) are however devoid of such intrinsic ultrastructural abnormality [4]. Furthermore, the absence of recurrence of the symptoms in our two recipients argues against a systematic renal intrinsic cause. Instead, it brings indirect evidence for the other proposed hypotheses: the possibility that LPHS represents a type of somatoform pain disorder [7] and/or that it might be caused by transient vasospasm of renal cortical vessels [8].

With the exception of paired donation, where living kidney donors incompatible with their recipients, exchanges kidneys with another donor/recipient pair, donation of an organ to an unknown recipient, the so-called Good Samaritan or altruistic donation is not authorized in France. The two transplantations described herein differ however from altruistic donation inasmuch as the nephrectomy was here required for medical reasons instead of the consequence of a personal choice.

We conclude that transplantation of kidneys from unrelated living donor with LPHS is a viable option to increase the organ pool. This procedure offers excellent outcome. Given the rarity of LPHS, it is unlikely that this procedure will by itself significantly improve organ shortage. It may however be useful to initiate a chain of paired donations; in the same way, altruistic donation has been shown to be valuable in the USA [9].

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Conflicts of interest

No conflict of interest.

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