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BRIEF REPORT

Living-donor transplantation after excision of unrecognized renal cancer diagnosed after transplant

Marta Melgosa Hijosa · Angel Alonso Melgar · Mª José Martínez Urrutia · Carmen García Meseguer · Enrique Jaureguizar Monereo · Mercedes Navarro Torres

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Abstract
Background Published data on kidneys transplanted after resecting small renal cancers during the transplantation surgery are very rare and, to the best of our knowledge, no pediatric cases have been reported in the literature.
Case-Diagnosis/Treatment Our patient was diagnosed with a bilateral Wilms tumor when he was 15 months old. A total bilateral nephrectomy was required to control the disease. Two years later, a human leukocyte antigen (HLA)-identical living-donor transplant from his father was performed. A small mass in the father's left kidney was diagnosed as an angiomyolipoma during the pretransplant donor evaluation. During the surgery, the mass was excised and the kidney implanted. One week later, the pathological study revealed the mass to be a clear cell renal carcinoma. After joint discussion, the urologic and nephrologic teams and the family decided to maintain the transplant, managing the patient with monotherapy based on rapamycin and close ultrasound control. To date, 8 years after transplantation, no signs of malignancy have been detected, and renal function is normal.
Conclusion This is the first reported pediatric case of a living-donor graft with a small renal carcinoma excised in the operating room. No malignancy has been observed in 8 years of follow-up.

Keywords Renal cancer · Kidney transplantation · Pediatric · Living donor · Outcome

M. Melgosa Hijosa (✉) · A. Alonso Melgar · C. García Meseguer · M. Navarro Torres
Pediatric Nephrology Service, Hospital "La Paz", Pº Castellana nº 161, 28045 Madrid, Spain
e-mail: mmelgosa.hulp@salud.madrid.org

M. J. Martínez Urrutia · E. Jaureguizar Monereo
Pediatric Urology Service, Hospital "La Paz", Madrid, Spain

Introduction

Renal transplantation is considered the best therapy for end-stage renal disease (ESRD), particularly for the pediatric population. The shortage of available cadaveric donors with the added evidence of better long-term function by living-donor allografts has led our center to encourage patients to consider living donation as the preferred option.

The every-day use of more powerful immunosuppression has greatly improved graft survival but has provoked an increased incidence of organ transplantation malignancies. According to Coutinho et al. [1], the transplanted pediatric population has an estimated risk of malignancy ten times higher than the nontransplanted population; a higher standardized rate ratio of 15–30 was reported by Webster et al. [2]. To minimize this risk, an individualized immunosuppression approach should be used for every patient. A complete and meticulous evaluation of every potential donor is also performed before acceptance into the program. Occasionally, the routine evaluation will reveal any incidental renal masses in the donor kidney and, historically, these kidneys have been rejected as a transplant source. In recent years, some papers have reported sporadic adult experiences using kidneys with small renal tumors for transplantation after excision of the mass [3]. We present the evolution of a kidney transplanted from a father to his son after excision of a small renal mass that was originally thought to be an angiomyolipoma but was later diagnosed as renal cell carcinoma (RCC) . To the best of our knowledge, this is the first pediatric case to be reported in the literature.

Clinical case

Our patient is a boy who was diagnosed with a bilateral Wilms tumor in March 2002, when he was 15 months old.

Subtotal bilateral nephrectomy and chemotherapy were not able to control the disease, and a total nephrectomy was required in October 2002, when hemodialysis therapy was begun. Two years later, a human leukocyte antigen (HLA)-identical living-donor transplant from his father was performed.

A small 2.5×2 cm mass was discovered in the left kidney and diagnosed as an angiomyolipoma during the pretransplant donor evaluation. During the surgery, the mass was excised and the kidney implanted, with immediate diuresis and rapid decline of creatinine to a normal value of 0.5 mg/dl after 48 h. One week later, the pathological study revealed the mass was a clear cell renal carcinoma with a histological Furhman grade II/IV. After joint discussion, the urologic and nephrologic teams and the family decided to keep the graft, managing the patient with monotherapy based on rapamycin due to its antitumoral properties, and close ultrasound (US) control. To date, 8 years after transplantation, no signs of malignancy have been detected. The boy is clinically excellent, with a normal renal function [glomerular filtration rate (GFR) estimated by Schwartz formula: 130.7 ml/min/1.73 m^2; GFR calculated by Cystatin C-based Filler formula: 112.95 ml/min/1.73 m^2] and has not suffered from any rejection episodes.

Discussion

Renal transplantation is considered to be the best therapy for ESRD, particularly for the pediatric population. The use of ever more powerful immunosuppression has offered considerable improvement in graft survival but has provoked an increased incidence of malignancies. Published data show a malignancy incidence during the pediatric age of 2.2–3.4 % [4, 5]. The risk increases exponentially with survival, and there are various reports of disease in adults who received a graft during childhood. A recent study in Sweden [6] reported the risk after a median of 15.5 years of follow-up to increase to 8.4 %; in the Dutch series published in 2001, with a longer follow-up, the probability of developing a malignancy at 25 years after the first renal replacement was 17 %. Compared with the general population, the overall incidence for cancer was ten times higher in adults who had received a kidney transplantation in childhood [1].

When a tumoral disease is known or suspected in a potential cadaveric kidney donor, the organ is discarded except in cases of brain tumors with complete certainty of no spreading. In the living-donation option, a complete evaluation with exhaustive biochemical and anatomical study, including US and angioresonance, is always done, not only to visualize the anatomy as well as possible to reduce surgical risks, but also to exclude any unknown tumoral disease; the finding during the routine donor evaluation of a solid renal mass suggestive of a tumor has always been considered a cause for donor rejection. In our case, image studies suggested an angiomyolipoma, and surgical excision was planned during the transplantation procedure.

As a consequence of these policies, the reported incidence of unsuspected RCC being found in cadaveric renal transplants after organ harvest but before transplant is very low, <0.5 % [7]. Historically, all these organs have been discarded for transplantation, and very little information is available on the very isolated cases. Thus, the Israel Penn International Transplant Tumour Registry, a voluntary registry collecting data on malignancies in transplant patients since 1968, reports only 14 cases of kidneys (11 from living and three from cadaveric donors) in which small RCCs were unexpectedly discovered at the time of donor kidney harvesting, and after excising the tumor, the kidney was transplanted. After a median follow-up of 69 months, no recurrences had been observed, with excellent patient and graft survival rates [8].

In the last 5 years, some cases have been published reporting isolated experiences using organs transplanted after excising small renal tumors [9]. The first such case was published by Whitson et al. in 2007 [10], and some months later, Nicol et al. [3] published their experience: 43 patients with a suspected diagnosis of small (<3 cm) RCC chose radical nephrectomy as the treatment option. After the decision was made, they were asked to donate the organ for transplantation, and all kidneys were implanted. The final pathological diagnosis reported 25 clear cell carcinomas, five papillary carcinomas, one chromophobe carcinoma, four oncocytomas, thre angiomyolipomas, and three complex cysts. After a mean follow-up of 32 months, with regular 3-monthly US follow-up, only one possible tumor recurrence was detected, and that was 9 years after transplantation; the patient refused nephrectomy or radiofrequency ablation and the lesion was followed by serial US, which revealed very slow growth.

RCC comprise 5 % of malignancies in the renal transplant population, a higher incidence compared with 2–3 % in the general population [10, 11]; in pediatric series, data are scarce, but isolated cases have also been diagnosed [12, 13]. In non-transplanted patients, a small localized renal mass suggestive of renal tumor is treated with surgical removal by radical or partial nephrectomy. Radical nephrectomy has been the standard management for many years, whereas partial nephrectomy was originally reserved for patients with a solitary or functionally compromised contralateral kidney. In recent years, however, partial nephrectomy has become more frequent, and excellent results have been reported [3].

There are no clearly defined treatment and follow-up protocols for managing RCC in the transplant population. Although transplantectomy is the most reported treatment, excision of only the tumor [14] and even percutaneous minimally invasive techniques have been described in some specific cases. Tsaur et al. [15], in 2010, published the largest single-center series with 30 RCC diagnosed in 2,001 transplanted patients after 58.6±62.3 months of follow-up: 25

developed in native kidneys and five in the allograft. Native kidney tumors were treated with radical nephrectomy; in the case of allograft tumors, three cases were treated with transplantectomy and two with tumor enucleation: one patient is alive in complete remission, and the other died from non-tumor-related causes 76 months after surgery.

In conclusion, to the best of our knowledge, this is the first reported pediatric case of a living-donor graft implanted after a mass that was eventually diagnosed as a renal carcinoma that had been excised in the operating room. No malignancy has been observed in 8 years of follow-up, and growth and renal function are both normal. We think that tumoral disease discovered during donor evaluation is an unacceptable risk for the child and, in general, the donation should be discarded; however, our unexpected experience suggests that organs with very localized tumors might be considered in some special cases after a meticulous balance of for-and-against discussion among the medical team and family, followed by close surveillance and the use of minimal immunosuppression based on rapamycin, an immunosuppressor with antitumoral qualities.

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