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Case Report / Приказ болесника

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En bloc kidney transplantation of an infant to an adolescent girl – one-year follow-up

En bloc трансплантација бубрега одојчета адолесценткињи – једногодишње праћење

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SUMMARY

Introduction *En bloc* kidney transplantation (EBKT) overcomes the problems of insufficient nephron mass of the solitary kidney of the youngest donors and the creation of a vascular anastomosis with small blood vessels. Although there are positive experiences with EBKT in adult patients, there is little data in pediatric recipients.

Case outline The kidney donor was a six-month-old male infant (7 kg), and the recipient was a 16-year-old adolescent girl (58.7 kg). The estimated glomerular filtration rate increased during the one-year follow-up after EBKT and reached 88.8 ml/min/1.73m^2, which was accompanied by an increase in the dimensions of the medial and lateral kidneys. Normalization of proteinuria and tubular functions occurred 6 and 12 months after transplantation, respectively.

Conclusion EBKT in an adolescent girl was performed without vascular complications, with satisfactory kidney function and physiological values of proteinuria after a one-year follow-up. EBKT of infants could increase the number of cadaveric donors but also enable better function and survival of the graft, given that the growth and functional maturation of the infant's kidneys continue postnatally in the body of the graft recipient.

Keywords: *en bloc* kidney transplantation; small infant donor; pediatric recipient; postnatal kidney maturity

САЖЕТАК

Увод Ен блок трансплантацијом бубрега (ЕБТБ) превазилазе се проблеми недовољне нефронске масе солитарног бубрега најмлађих донора и креирања васкуларне анастомозе са малим крвним судовима. Иако постоје позитивна искуства са ЕБТБ код адултних болесника, мало је података код педијатријских реципијената.

Приказ болесника Донор бубрега било је шестомесечно мушко одојче (7 *kg*), а реципијент адолесценткиња узраста 16 година (58,7 *kg*). Процењена јачина гломерулске филтрације током једногодишњег праћења након ЕБТБ је расла и достигла 88,8 *ml*/*min*/1,73 *m*^{2}, што је праћено порастом димензија медијалног и латералног бубрега. До нормализације протеинурије дошло је након 6 месци од трансплантације, а тубулских функција после 12 месеци.

Закључак ЕБТБ код адолесценткиње је протекла без васкуларних компликација, са задовољавајућом функцијом бубрега и физиолошким вредностима протеинурије после једногодишњег праћења. ЕБТБ одојчади могла би да повећа број кадаверичних донора, али и да омогући бољу функцију и преживљавање графта обзиром да се раст и функционално сазревање одојачких бубрега настављају постнатално и у телу примаоца графта.

Кључне речи: Ен блок трансплантација бубрега; одојче донор бубрега; педијатријски реципијент; постнатално сазревање бубрега

INTRODUCTION

Kidney transplantation is the gold standard for renal replacement therapy in children [1]. Although pediatric recipients have priority in the allocation of cadaveric grafts [2], the number of pediatric cadaveric transplants is low primarily due to the small number of quality cadaveric grafts. By changing the demographic characteristics of adult cadaveric donors after brain death (older age, higher body mass index, comorbidities such as hypertension and diabetes), the quality of the cadaveric graft worsened [3]. Having in mind that every pediatric patient with end-stage renal disease (ESRD) needs at least two to three kidney transplants for an average life span, the importance of long-term survival of the transplanted kidney is clear, from which it follows that borderline donors are not the best solution for them. *En bloc* kidney transplantation (EBKT) implies transplanting both kidneys in a pair together with part of the aorta and inferior

vena cava, which overcomes the problems of insufficient nephron mass of the solitary kidney of the youngest donors and the creation of a vascular anastomosis with small blood vessels [4]. Application of this transplantation method is one way to increase the donor pool of quality grafts for pediatric patients [5–8]. There are numerous positive experiences with EBKT in adult patients [3, 9–13]. However, there are few studies related to the outcome of EBKT in pediatric recipients, especially if the graft donor was an infant [5, 7, 8, 14, 15]. The aim of our work is to present the one-year clinical course of EBKT of a six-month-old infant to an adolescent girl.

CASE REPORT

The kidney donor was a six-month-old infant (7 kg), whose cause of death was a ventricular arrhythmia caused by a fetal rhabdomyoma of the heart. The recipient of the kidney was a 16-year-old girl (58.7 kg), with a congenital anomaly of the urinary tract. At the age of 12.5 years the girl was referred to a nephrologist for the first time, due to unrecognized advanced chronic kidney disease. She was on chronic hemodialysis from the age of 13.5 years, until transplantation. EBKT was performed by creating a venous T-L anastomosis between the external iliac vein of the recipient and inferior vena cava of the donor, and the arterial anastomosis was created between the external iliac artery of the recipient and the aorta of the donor (Figure 1). Cold ischemia lasted 6 hours and 35 minutes, and warm ischemia 52 minutes. Immunosuppressive therapy with basiliximab, corticosteroids, tacrolimus and mycophenolatemofetil was administered. Due to delayed graft function, the patient required three hemodialysis sessions. The urinary catheter, clogged by a large coagulum, was removed on the eighth post-transplantation day, after which the patient spontaneously passed out several more coagulums (Figure 2). On the tenth post-transplantation day, a perirenal collection was verified by ultrasound, positioned in front of both transplanted kidneys and ureters, which progressively increased and on the seventeenth post-transplantation day its dimensions were 97x61x25 mm. Due to compression on the venous flow in the lateral kidney, two months after transplantation, drainage of this perirenal collection was performed. Cytological and biochemical findings indicated a lymphocele. Recurrent lymphocele was treated by laparoscopic fenestration at the end of the third post-transplantation month. During the second post-transplantation month, the clinical course was complicated by cytomegalovirus disease, treated with valganciclovir, human cytomegalovirus immunoglobulin and immunosuppressive therapy reduction. In the fourth post-transplantation month, the patient was diagnosed with SARS-CoV2-infection, which was successfully treated

with immunosuppression therapy reduction and supportive therapy. None of the listed complications did affect the functional maturation of the grafts (Table 1). The estimated glomerular filtration rate (eGFR) during the one-year follow-up increased, which was accompanied by an increase in the dimensions of the medial and lateral kidney, measured by ultrasound. Normalization of proteinuria occurred 6 months after transplantation. Tubular functions reached physiological values one year after transplantation.

The authors declare that the article was written according to ethical standards of the Serbian Archives of Medicine as well as ethical standards of medical facilities for each author involved. No personal data of the patient were presented in the manuscript. Written consent was obtained from the patient and her parent.

DISCUSSION

Survival, growth, cognitive development and quality of life of transplanted children are incomparably better and morbidity rate is lower, compared to children on dialysis [1]. Pediatric patients on dialysis have a 78% higher risk of cardiovascular death compared to age-matched transplanted patients [16]. On the other hand, early transplantation in children limits the accumulation of cardiovascular risk such as intima-media thickness, marker of atherosclerosis, which increases in children on dialysis over time, and remains stable for years after kidney transplantation [17]. Worldwide there is a growing discrepancy between the number of available cadaveric grafts and the number of potential recipients, which is the cause of longer waiting time for a cadaveric kidney [7]. Also, with changing the demographic characteristics of adult cadaveric donors, the number of borderline donors increased [3], however they are not a good option for pediatric patents due to the extreme importance of long-term graft survival in this population. Therefore, the importance of increasing the donor pool of organs for child transplantation is clear, and EBKT is one of the possible solutions to this problem [8, 18]. Furthermore, children who receive a kidney from a pediatric donor have a better long-term graft outcome compared to children who receive a kidney from an adult donor [19]. EBKT remains a challenge for surgeons, given that it is accompanied by a higher frequency of vascular and urological complications [18]. A good selection of donors and recipients, improvement of surgical technique, shorter cold ischemia time, better immunosuppressive therapy, as well as postoperative anticoagulation and antiplatelet therapy, contributed to a significant reduction in the rate of these complications [4, 7, 8, 12, 13]. Regarding early post-operative complications, our

patient had large coagulums in the urinary bladder (Figure 2) and perirenal lymphocele which was successfully treated by laparoscopic fenestration.

Utilization of very small pediatric donor kidneys can provoke hyperfiltration injury, but careful recipient selection and EBKT technique (doubling the nephron mass) with adequate follow-up of transplanted patients, successfully overcomes this problem, and provides similar graft survival in comparison with adult deceased donor or even living donor kidneys [4, 7, 11]. One year after transplantation, our patient had eGFR 88.8 ml/min/1.73 m^2 with normal proteinuria values, which points against hyperfiltration damage of EBKT.

The newborn kidney differs from the mature kidney anatomically, histologically and functionally. The GFR of a term newborn is low and after birth it continuously increases. Functional maturation of the nephron is completed by the end of the second year of life [20]. In case the kidney donor is an infant, the functional maturation and growth of the infant kidneys continue in the body of the graft recipient [4, 8, 21]. Table 1 clearly shows the functional maturation of nephrons and the growth of infant kidneys transplanted in a pair to the adolescent girl.

Numerous studies have shown the excellent outcome of EBKT of small pediatric kidneys in adult graft recipients in terms of graft function and survival [4, 11, 12, 22]. Recently published follow-up results (mean follow-up of 65 months, range 7–220) of adult patients after EBKT indicated excellent results: 100% patient survival and creatinine clearance which increased during the first 3 years before reaching stabilization (at 10 years, the mean creatinine clearance was 112 ml/min, 95% confidence interval 107–117) [4]. During the last year, in the literature have been described two EBKT to adults from preterm neonates donors after circulatory death (<30 weeks' gestation and weight <1.2 kg) with acceptable results 5 and 9 months post-surgery [23]. On the other hand, a low percentage of EBKT was performed in pediatric recipients [7]. This is why there is a small number of studies assessing the long-term survival of grafts transplanted with this surgical technique in pediatric graft recipients. However, the experience of individual centers indicates promising results [5, 7, 8, 14, 15]. Yaffe HC et al. and Winnicki et al., compared pediatric recipients with grafts from small pediatric donors and pediatric recipients with grafts from standard donors, and showed that the one-year survival of grafts was slightly worse in the group of recipients of small pediatric grafts, but five years after transplantation the outcome was practically the same [7, 14]. Chesnaye et al. analyzed the 5-year graft survival of small pediatric donors under 5 years of age who were transplanted into pediatric recipients. They divided the recipients according to age into 4 groups (0-3 years, 4-5 years, 6-

11 years and 12-19 years) and showed that the 5-year graft survival was 70%, 75%, 81% and 83%, respectively [15]. This year, Azzam A et al. published the results of a follow-up (mean duration 6.86±1.35 years) of pediatric patients after EBKT from donors <15 kg [8] and showed excellent renal function outcome on the last follow-up (eGFR 79.8±30.8 ml/min/1.73 m^2). The outcome of EBKT of infant kidneys in our adolescent girl one year after the transplant was excellent, despite numerous complications in the first four months after the surgical intervention. EBKT from infants could increase the number of cadaveric donors, as well as the quality grafts for pediatric recipients, and also could enable better function and survival of the graft given that the growth and functional maturation of the infant kidneys continue postnatally. We should not hesitate to use this potential pool of donors because the data in the literature is truly positive and encouraging. Certainly, in the future, multicenter studies are necessary, considering the small number of pediatric patients transplanted with this technique per center, which will show us the long-term outcome (> 10 years) of grafts transplanted with the *en bloc* surgical technique in the youngest patients.

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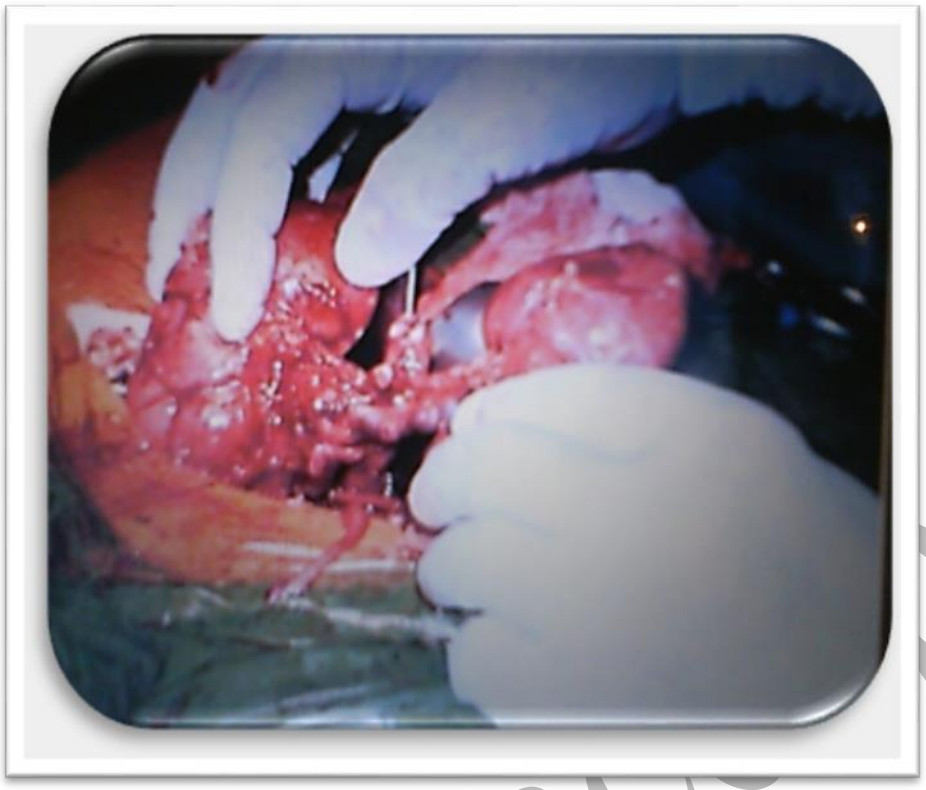

Figure 1. Kidneys transplanted using the *en bloc* surgical technique, after the creation of vascular anastomoses and established reperfusion

Figure 2. Spontaneously voided coagulums from the urinary bladder after removal of the urinary catheter on the eighth post-transplantation day

Table 1. Functional maturation and growth of infant kidneys transplanted in pair

Parameters	Months after EBKT				
	1	**3**	**6**	**9**	**12**
eGFR (ml/min/1.73m^2)	26.1	46.2	68.6	77.2	88.8
Medial kidney size (mm)	68 × 35	86 × 38	95 × 34	95 × 42	102 × 44
Lateral kidney size (mm)	64 × 41	76 × 44	91 × 44	100 × 44	105 × 49
Tubular functions (%)	FeNa 5.5 FeK 46.7 TRP 53		FeNa 2.47 FeK 18.9 TRP 74.2		FeNa 1.96 FeK 12.01 TRP 84.3
Urine protein creatinine ratio (UPCR) (mg/mg)	1.27		0.21		0.14

EBKT – en bloc kidney transplantation; eGFR – estimated glomerular filtration rate; FeNa – fractional excretion of sodium; FeK – fractional excretion of potassium; TRP – tubular reabsorption of phosphate; UPCR – urine protein creatinine ratio

