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Autotransplantation of the kidney in surgery of retroperitoneal sarcomas

R.I. Rasulov[1,2], A.A. Muratov[1,2], V.V. Dvornichenko[1,2,3], D.D. Morikov[1,2], Y.K. Batoroev[1], G.I. Songolov[3]

[1] Irkutsk State Medical Academy of Postgraduate Education – Branch Campus of the Russian Medical Academy of Continuous Professional Education, Irkutsk, Russia;

[2] Irkutsk Regional Oncological Hospital, Irkutsk, Russia;

[3] Irkutsk State Medical University, Irkutsk, Russia

Correspondence to: Rodion I. Rasulov, Dr. Med. Sci., Head of Surgical Department of Irkutsk Regional Oncological Hospital, Irkutsk, Russia, e-mail: gava2010@yandex.ru

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The paper presents the analysis of 5 clinical cases that demonstrate the potential of using organ-saving technologies in surgery of locally advanced retroperitoneal sarcomas. The clinical example shows step by step the technique of organ-preserving surgical intervention: an extended tumour nephrectomy followed by the extracorporeal precise dissection of the kidney from the tumor bulk with inducing a reversible pharmaco-cold ischemia and the isolated kidney autotransplantation into a heterotopic position with regard to intraoperative rapid cytology monitoring results. The article describes the characteristics of anesthesia, the early postoperative period, subsequent rehabilitation, and prophylactic medical screening of this group of patients.

Keywords: kidney autotransplantation, extracorporeal surgery, liposarcoma, non-organ retroperitoneal tumor, nephrectomy

In the recent decade, the proportion of combined and extended surgical interventions in the treatment of locally advanced retroperitoneal sarcomas has been rapidly increasing. More than half of the cases require multivisceral resections being rather traumatic, and nephrectomy is made in 35-39% of them [1, 2]. However, large studies have demonstrated that the histology examination of an obtained gross specimen containing the "tumor-kidney" complex, find a true infiltrative growth of retroperitoneal sarcoma into the kidney only in 21.5-27% [3, 4]. For many decades, a tumor nephrectomy has been the surgery of choice in the cases of kidney involvement in the tumor process. At present, organ-preserving techniques has become possible for use [5]. There are sporadic reports in the world literature describing a successful kidney autotransplantation procedure as an option of completing the surgical operation for retroperitoneal sarcoma removal [6, 7]. The first kidney autotransplantation was performed for the ureter injury by J.D. Hardy in 1963 [8]. A new technology for extracorporeal surgical treatment of kidney pathology started actively developing in the 60-70s of the XX century. That was facilitated by the development of cooling and perfusion techniques allowing the reversible ischemia of the renal tissue to be prolonged; and currently the organ can be preserved for up to 24 hours. The main technical aspects of extracorporeal removal of a kidney tumor were described by A.C.Novick et al. in 1980. And in 1990, he and co-authors reported the data on the treatment of 108 patients for various urological diseases and injuries using the "bench work surgery" technique [9, 10]. In the 80-90s of the last century, there was a certain decline in the number of ex vivo operations, which was associated with a simultaneous increase in hemodialysis opportunities and with an imprudent refusal from

organ-preserving surgery. Significant interest in "bench work surgery" reappeared at the beginning of the 21st century; most authors attributed that to both the improvement of transplantation technologies and the advances in the anesthesia-resuscitation service, which made such sophisticated surgical interventions technically feasible, and safely performed in that patient population with a subsequent successful nursing care and rehabilitation [11].

Forty one patients diagnosed with retroperitoneal sarcoma were treated in the Irkutsk Regional Oncology Dispensary in the period of 2012-2016. Among 7 cases of the extended-combined retroperitoneal sarcoma removal and nephrectomy, there were 5 in whom the kidney autotransplantation to a heterotopic position was performed. No reimplantations were performed in 2 cases where the tumor cells were found in the impression smears from the kidney.

The treatment of patient T., 51 years old, was taken as an example to describe the stages of the surgery under discussion. The patients had the diagnosis of "retroperitoneal sarcoma" on her admission to the Surgical Oncology (Reconstructive Surgery) Department No. 7 in the Irkutsk Regional Oncology Dispensary. The patient complained of a discomfort in the right abdominal area, occasional pulling pain in the mesogastrium region, the flank abdominal pain, an asymmetrical abdomen distension on the right. The patient's history revealed the disease manifested itself in January 2016, when the above symptoms became disturbing. The physical examination, the abdominal utrasonography and multislice spiral computed tomography (MSCT) performed in the local out-patient clinic identified a retroperitoneal tumor. A fiberoptic colonoscopy demonstrated the external compression to the right colon; no atypia was found at morphological study. The patient was referred to the Irkutsk Regional Oncology Center.

Anamnesis vitae: a builder by profession, currently unemployed, married since 20 years old, having one child; no cancer diagnosis in the family history; no history of allergy; denied having bad habits. The patient had the previous history of cardiomyopathy of a mixed origin; sinus tachycardia; lower limb varicose veins; the 2nd degree chronic vein insufficiency (CVI); mild anemia; the deafness on the left; urolithiasis; chronic pyelonephritis in a remission stage; a chronic kidney disease 0; the previous history of left mastectomy for the left mammary gland phlegmon in infancy. The data of the objective physical examination in the Irkutsk Regional Oncology Dispensary included: height 162 cm, body weight 56 kg, body mass index 18.5 kg/m ^{2}. The general condition of the patient was close to satisfactory. The condition with regard to the underlying disease was moderately severe due to the presence of a giant tumor in the right abdomen; the ECOG performance status, Grade 0; no findings in somatic status. The abdomen was considerably enlarged and deformed in the right part due to the tumor. There was a tumor-like protrusion up to 35 x 25 cm palpated on the right flank of the anterior abdominal wall, further extending to the epi-/mesogastrium, being dense, elastic by structure, non-displaceable at palpation, painless. The abdomen was actively involved in the act of breathing, soft to palpation in all regions, slightly painful in the mesogastrium, more to the right. No peritoneal symptoms, "splash noise" were noted, physiological functions being normal. Laboratory investigations demonstrated mild anemia. The MSCT-guided biopsy of the retroperitoneal tumor was performed along a safe trajectory. A fast-track biopsy technique was used for histological study that demonstrated a moderately differentiated liposarcoma of G2 by the FNCLCC System. The MSCT angiography of the abdominal organs and urinary tract detected a multinodal giant lesion of 31 x

25 x 19 cm, being of a soft-tissue (fatty) density, heterogeneous by structure due to multiple septa in the tumor bulk visualized in the retroperitoneal space. The lesion involved the right kidney in a cuff-like fashion, the border was not clearly traceable, i.e. considering the MSCT results, it was difficult to reliably exclude the true invasion of the tumor into the right kidney. The visceral surface of the liver, the abdominal aorta and its branches, iliac vessels, the right renal vascular pedicle, and the right ureter were intact. There was a cyst of 21 x 16 mm identified in segment III of the liver. There were concrements in the left kidney.

With regard to the preoperative examination findings, the surgery was planned in the following extent: a combined removal of retroperitoneal sarcoma with right nephradrenalectomy and extended retroperitoneal lymphadenectomy; heterotopic kidney autotransplantation.

The patient underwent a total midline laparotomy through extraperitoneal access up to Pirogov-Gibson technique on the left under the general combined anesthesia (endotracheal anesthesia + total intravenous anesthesia + epidural anesthesia).

At the first stage, the access to the retroperitoneal space was obtained extraperitoneally (by making the incision from the symphysis laterally and upward parallel to the inguinal ligament on the left). The external iliac artery and the external iliac vein were isolated and marked, the bed was prepared for the kidney to be reimplanted. The second stage included opening the abdominal cavity through the total midline laparotomy. There were no ascites, carcinomatosis, or metastases to the liver in the abdominal cavity. At revision, a retroperitoneal tumor was found on the right, extending to the 1st, 2nd, 3rd, and 4th zones by V.V.Tsvirkun categorization (2001), and being represented as multiple confluent nodes with a single capsule; the tumor size

was 50.0 x 38.0 cm. The tumor involved the right kidney in a cuff-like fashion. The Cattel maneuver of a right-sided medial visceral rotation was used: the hepatic flexure of the colon was brought lower, the ascending colon was medially mobilized, the duodenum was mobilized by the Kocher maneuver, the aortocaval space was exposed. An elective dissection of para-aortic lymph nodes was performed (16a1-16b2). Renal vessels on the right were isolated and marked. The extraorgan tumor with retroperitoneal tissue, the right kidney, and adrenal gland were mobilized; the right ureter was ligated and transected in the lower third. After the systemic heparinization with 5000 IU had been made, the renal vessels were consecutively ligated and transected; the en-bloc resection of the organ complex together with the visceral fatty tissue was performed (Fig.1, 2). The right adrenal gland was resected. The weight of the specimen was 8.5 kg.

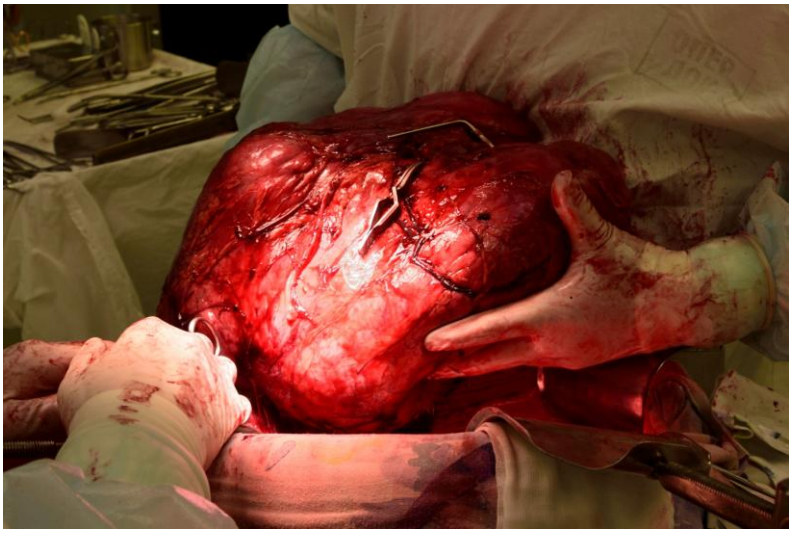

Fig. 1. The general view of retroperitoneal sarcoma and the right kidney after the specimen was obtained

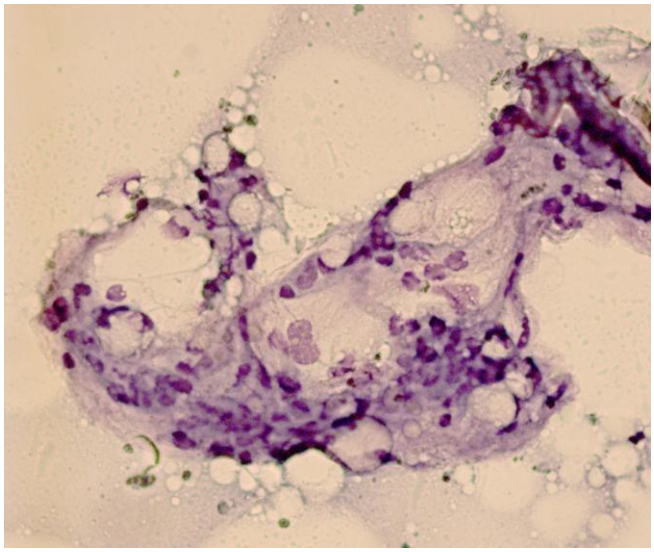

Fig. 2. The specimen for microscopy. A tumor tissue specimen for cytology. Liposarcoma. Magnification 40x, azure-eosin stained.

The third stage included a pharmacological cold preservation of the excised kidney followed by its extracorporeal microsurgical dissection from the adipose tissue and the tumor under temporary hypothermia (Fig. 3).

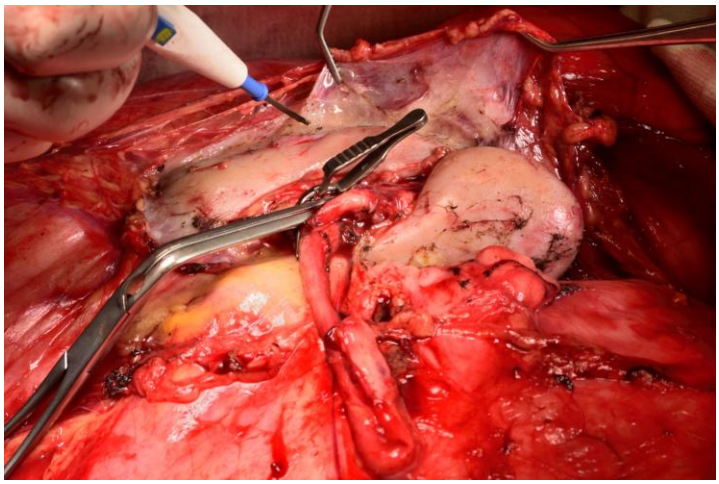

Fig. 3. A microsurgical dissection of the kidney from the tumor bulk ("back-table")

The renal artery was cannulated; the kidney perfusion was performed for 10 minutes with a cardioplegic solution cooled to 4-8° C.

On completing the third stage of the procedure, the impression smears were obtained from the tumor node and 4 glass slides were prepared. The impression smears from the multiple sites of the mobilized kidney capsule (upper, lower poles, anterior, posterior surfaces, the renal hilum) were prepared on 8 glass slides, the kidney was placed on a tray with iced crumbles of isotonic saline (an aqueous solution of sodium chloride) (Fig. 4, 5). The glass slides with impression smears were sent to a fast track cytology study that verified the tumor node as being a liposarcoma; no tumor cells were found at the kidney dissection edges. The indications for heterotopic kidney autotransplantation were displayed.

Fig. 4. Pharmacologically induced reversibe cold ischemia of the mobilized kidney

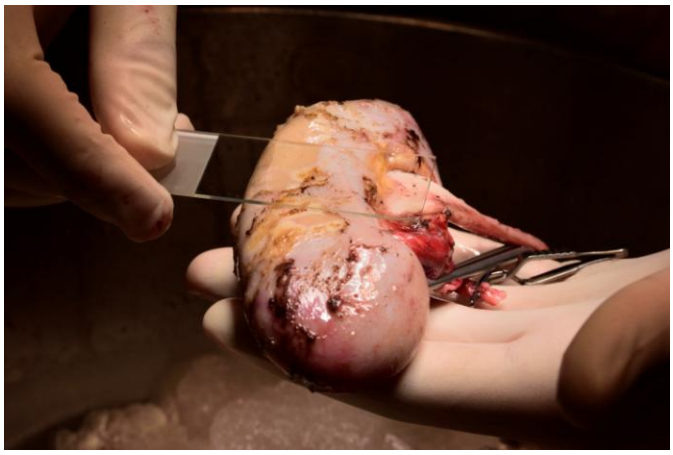

Fig. 5. Impression smears sampled from the surface of the mobilized kidney

During the fourth stage of surgery, the earlier removed kidney was placed retroperitoneally into the left iliac fossa. Consequently, an "end-to-side" anastomosis between the renal vein and the external iliac vein (Fig. 6) and a "side-to-end" anastomosis between the external iliac artery and the renal artery were safely performed (using Prolene 7/0).

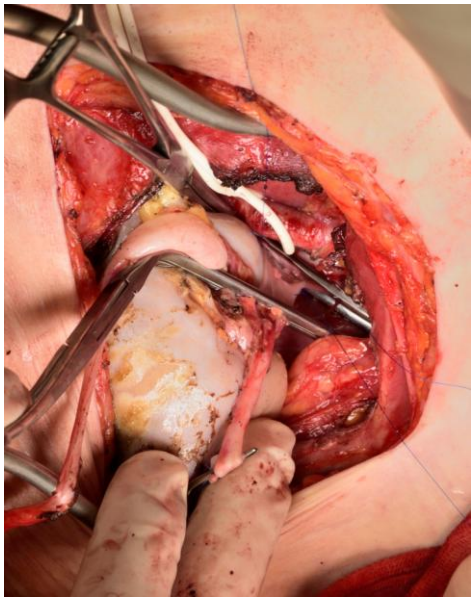

Fig. 6. The stage of the mobilized kidney autotransplantation into a heterotopic position. The venous anastomosis construction

The main blood flow in the kidney was restored. The kidney was viable, the first urine amount was obtained. The kidney ischemia time was 2 hours 10 minutes, the left lower limb ischemia time was 30 minutes. The ureter was anastomosed to the bladder using the Witzel-Sampson-Lich extravesical implantation technique. The anastomosis was performed over the ureteral stent (with PDS 6/0).

The surgery duration was 7 hours 20 minutes, the blood loss amounted to 400.0 mL. The anesthesia duration was 8 hours 00 minutes, including the time of the central venous catheter and epidural catheter placement. The anesthesia was provided in conformity with current concepts of multimode anesthesia based on a low-flow anesthesia with sevoflurane, a thoracic epidural analgesia with narupin, and an intravenous administration of fentanyl. A specific feature of the course was the hemodynamic instability that occurred due to a perfusion syndrome at the time of blood flow resumption in the reimplanted kidney. The decreased hemodynamic parameters required a norepinephrine administration in a dose of 0.5 μg/kg/h. Postoperatively, the patient's condition was consistent with the duration and scope of surgery. No indications to renal replacement therapy arose. The patient was extubated at 7 hours after surgery. No complications occurred in the early postoperative period. The patient was activated on the 1st postoperative day. Tube enteral feeding was started at 16 hours after the surgery. Draining tubes from the small pelvis and the tumor bed were removed on the 2nd-3rd day. The screening ultrasound examination of the kidney on the 1st, 2nd, 3rd, 5th, and 7th postoperative days showed the following: the renal thickness was 42-46 mm, the parenchymal thickness was 12-14 mm, the parenchyma was of normal echogenicity, the pyelocaliceal system was without abnormalities. The blood flow was

preserved; the resistive indices were 0.66 in the renal artery, and 0.75 in the parenchima arteries; no impairments of the venous blood flow were seen. On the 7th day post-surgery, a check MSCT scanning of the abdominal and pelvic organs was performed: the right kidney was displaced to the left iliac region, the contrast agent accumulation in the parenchyma was consistent with the phases of contrast enhancement pattern typical for a normal variant, the kidney function was preserved. The subsequent postoperative period was uneventful; the patient was discharged home in a satisfactory condition on the 16th day after the surgery. The planned histological examination demonstrated the neoplasm being a well differentiated liposarcoma 8851/3.

A month later, the patient underwent cystoscopy, the stent was removed from the neo-ostium of the reimplanted ureter. The follow-up monitoring examination confirmed the adequate function of the reimplanted kidney.

The follow-up period was 10 months, the patient's general condition was satisfactory, without complaints. The instrumental examination demonstrated no signs of tumor recurrence or progression; both kidneys preserved their normal functions.

Seven more patients were operated on using the above described technique. In 2 cases, the kidney was not reimplanted because the tumor cells were found in the impression smears sampled from the isolated kidney. The preliminary results obtained in treatment of 5 patients who underwent the kidney implantation into the heterotopic position are presented below. The mean surgery duration was 388 ± 17.8 minutes, the mean anesthesia duration was 441 ± 19.4 minutes. The mean intraoperative blood loss was 520.0 ± 103.6 mL, the mean cold ischemia time for the kidney was 99 ± 12.4 minutes. The kidney warm ischemia time did not exceed 10 minutes for all

the cases. There were no intraoperative complications. The general intraoperative parameters are presented in the Table.

Table. Characteristics of extracorporeal surgical interventions

Criterion	Group of patients (n = 7)
Tumor weight (mean ± standard deviation), kg	9.6 ± 1.14
The tumor size, according to the planned morphological study findings (mean ± standard deviation), cm	35.6 ± 7.0 x 37.2 ± 5.5
Heterotopic autotransplantation, n (%)	5 (71%)
Results of fast-track cytology study of the tumor, n Liposarcoma Leiomyosarcoma Malignant Peripheral Nerve Sheath Tumors (MPNST)	 5 1 1
Results of fast-track cytology of the specimen from the isolated kidney surface, n Tumor cells found: leiomyosarcoma, liposarcoma Tumor cells not found	 2 5
Stenting of the reimplanted ureter, n	5
Adrenalectomy, n	6th
Simultaneous surgical procedure, n Hysterectomy Cholecystectomy	 1 1
Method of constructing vascular anastomoses, n IIA[1] + RA [2] , EIV [3] + RV [4] EIA [5] + RA, EIV + RV IIA + RA, CIV [6] + RV Renal artery allografting, n Microvascular reconstruction of renal vessels, n	5 1 2 1 1 2
Technique of ureterocystoanastomosis construction, n Starzl Witzel-Sampson-Lich	5 1 4

Note: [1]IIA: internal iliac artery; [2]RA: renal artery; [3]EIV: external iliac vein; [4]RV: renal vein; [5]EIA: external iliac artery; [6]CIV: common iliac vein.

Postoperative complications were revealed in 3 patients (60%), as classified according to the International Clavien-Dindo Classification of Surgical Complications. Grade II complication developed in one case: that was the bleeding (coagulopathy) diagnosed in the graft bed and controlled conservatively. Grade III complications developed in 2 cases. In one case, it was Grade IIIa complication, namely a urinary leak due to the partial incompetence of ureterocystoanastomosis that was diagnosed by the check MSCT of abdominal organs and small pelvis on the 8th day. The leak was drained under the CT guidance. The other case was Grade IIIb complication, namely the bleeding from the suspensory ligament of ovary that required a relaparotomy on the 1st day after the surgery; the final hemostasis was achieved by additional ligation of the ovarian vessels. The mean length of stay for the patients in the Intensive Care Unit postoperatively was 6.4 ± 2.3 days, the mean postoperative hospital stay was 24.6 ± 11.4 days. All patients underwent a complex urological and oncologic examination during follow-up at 1, 3, and 6 months after the surgery, and later on, once every 6 months during the following 2 years. An out-patient routine examination included laboratory and instrumental tests to evaluate the function of the reimplanted and healthy kidneys and to exclude the tumour disease progression (the development of distant metastases, locoregional recurrence). All the patients were alive, with no signs of the disease recurrence at 40, 28, 24, 10, and 4 months after the surgery.

Thus, the presented clinical observations demonstrate the feasibility of "kidney-preserving" surgical interventions for the removal of giant retroperitoneal sarcomas using extracorporeal and transplantation

technologies, provided no true tumor growth present in the kidney structures.

The authors state there is no conflict of interests to declare

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