Observational Study

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Surgical management strategy for leiomyosarcoma of Zone I-II inferior *vena cava*

A case series

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Abstract

Objectives: Leiomyosarcoma of inferior *vena cava* (IVC) is a rare clinical entity with severe vascular involvement. Surgical management of leiomyosarcoma is still challenging.

Methods: This a retrospective study of consecutive patients referred to our hospital from January 2017 to June 2019. Depending on the anatomical site of affected IVC, leiomyosarcomas were categorized into zone I-II. The clinical data including baseline information, surgical parameters, peri-operative management, short- and mid-term outcomes were observed.

Results: Four patients with leiomyosarcoma of zone I-III underwent radical resection without intraoperative mortality. Prosthetic grafts were interpositioned in all patients to instruct *vena cava.* Renal vein reconstruction was perfumed in two patients due to involvement to renal veins. Median blood loss was 450 mL (200–600 mL), median operative time was 215 minutes (150–240 minutes). No Clavien-Dindo IIIa or higher complication was observed. No organ dysfunction and recurrence were observed with median follow-up of 25.5 months.

Conclusions: Curative resection of zone I-II leiomyosarcoma is associated with longer survival in selected cases, *en-bloc* resection with complex vascular reconstruction could be considered.

Abbreviations: CT = computed tomography, DFS = disease free survival, IVC = inferior vena cava, OS = overall survival.

Keywords: leiomyosarcoma, morbidity, outcome, radical resection, vascular reconstruction

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AT and TT contributed to this work equally.

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1. Introduction

Leiomyosarcoma is a malignant mesenchymal tumor originating from smooth muscle of gastrointestinal and vascular wall and accounts for 5%-10% of soft tissue tumors.[1] Primary leiomyosarcomas is originated from inferior *vena cava* (IVC) wall and presents as a very rare clinical entity.[2] It grows slow and insidiously without significant symptoms at early stage; thus, it is extensively advanced with multi-organ and vascular involvement when the diagnosis of leiomyosarcoma is confirmed.[3,4] With the advancement of surgical oncology and its adjuncts, radical resection has become the only curative option considering poor clinical efficacy of chemo and radio-therapy.[5] Renal vein involvement is common for IVC leiomyosarcoma of zone I-II and require nephrectomy or renal vein reconstruction.[5–7]*En bloc* resection of affected kidney may facilitate surgical process but compromise postoperative renal function, therefore, kidney preserving renal vein reconstruction is theoretically acceptable. This study analyzed the technical features, short- and mid-term results of radical resection of zone I-II leiomyosarcoma.

2. Methods

From January 2017 to June 2019, a total of six patients with leiomyosarcoma of IVC underwent surgical treatment at our medical center, Xinjiang Medical University, and medical reports were retained. During the period, five patients with IVC leiomyosarcoma were treated in our center, among them, four patients were categorized into zone I-II leiomyosarcoma and underwent radical resection. The remaining one patient was II-III leiomyosarcoma and underwent *ex vivo* Liver resection and autotransplantation with atrial reconstruction.[3] The detailed baseline information and clinical characteristics of these four patients are given in Table 1.

2.1. Ethical review

This study was approved by the institutional ethical committee of 1st afflicted hospital of Xinjiang Medical University and conducted in accordance with Helsinki Declaration. Informed of consents were obtained from all patients or their legal custodies.

2.2. Preoperative assessment

Both imaging and functional evaluation were carried out prior surgery. Preoperative thoracoabdominal CT scan, abdominal MRI and three-dimensional reconstruction were examined to assess the size, site, involvement, severity and metastatic status of the tumor. Ultrasonography on both lower extremities were routinely performed to rule out deep venous thrombosis. 2 patients underwent preoperative phlebography to further assess the extension of tumor in *vena cava* (Fig. 1). Cardio-pulmonary functions were assessed with electrocardiogram, echocardiogram and lung function test before surgery. Considering the possible renal vascular involvement, renal dynamic imaging was routinely carried out to precisely assess preoperative renal function. Leiomyosarcomas were categorized according to their anatomical site, zone I refers to the section of IVC from lower than bilateral renal veins level, zone I refers to IVC section between renal veins and hepatic veins, and zone III refers to IVC section above hepatic veins level (Fig. 2)

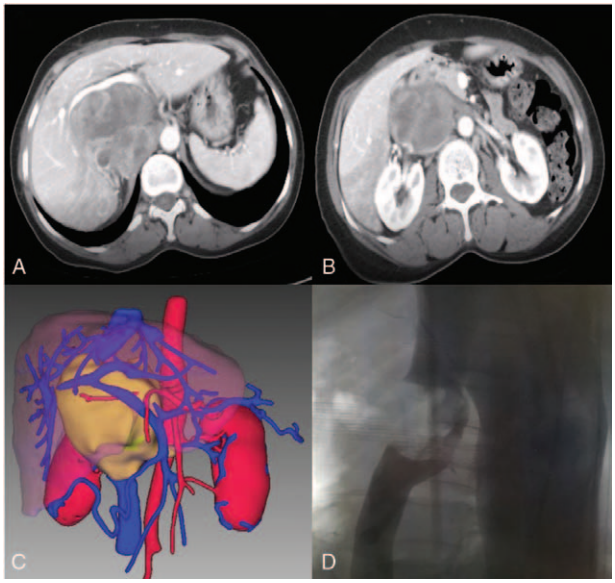

Figure 1. Preoperative assessment of Leiomyosarcoma. A, CT scan shows the giant tumor originating from retro-hepatic *vena cava* in Case 4; B, CT scan shows bilateral kidney vein involvement in Case 4; C, three-dimensional computed tomography showed the extension of the tumor in Case 4; D, Phlebography shows the retro-hepatic vena cava involvement in Case 4.

2.3. Surgical planning

After multidisciplinary team discussion including Transplant Surgeon, Oncologist, Anesthesiologist, Nephrologist, and radiologist, surgical resection with vascular reconstruction with prosthetic graft was decided. Considering the renal vein involvement in 2 patients, renal venoplasty was planned with unilateral nephrectomy as an alternative.

2.4. Surgery

After successful induction of general anesthesia, laparotomy was performed via abdominal midline incision. Any possible intra-abdominal metastasis was ruled out by palpation and intraoperative ultrasonography. Lateral peritoneum was excised with "Kocher" maneuver and infra-hepatic IVC was exposed by pulling

Table 1

Preoperative characteristics of leiomyosarcoma patients.

Case	Sex	Age	Symptom	Zone	Tumor size	Surgical approach
1	Female	42	Back pain	II	5 *3*2 cm^3	Abdominal approach
2	Female	47	Back pain	II	10*6*5 cm^3	Abdominal approach
3	Female	45	Back pain, leg edema	I-II	8*4*4 cm^3	Abdominal approach
4	Female	38	Back pain	I-II	9*5*4 cm^3	Abdominal approach

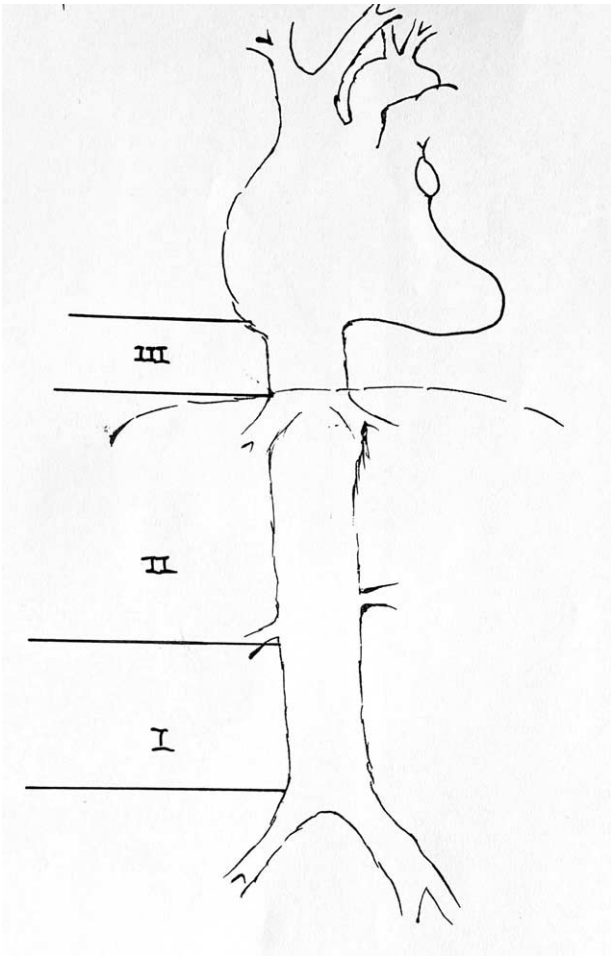

Figure 2. Anatomical categorization of leiomyosarcoma of IVC origin.

descending duodenum centrally. The extension of tumor was then reassessed with direct vision. Individualized vascular reconstruction was planned and performed according to the tumor involvement of each patient (Fig. 3) Since the tumor cephalad into retro-hepatic vein, right lobe of liver was mobilized and retro-hepatic vena cava was exposed. Short hepatic veins and right adrenal veins were dissected and suture closed. Distal part of *IVC* was carefully dissected and suspend. By this time, proximal and distal IVC were ready for clamping and dissection of tumor since the tumor was above the level of bilateral veins in patient 1 and 2. For patient 3 and 4, dissection was proceeded laterally, since the tumor invaded the renal veins. Kidney preserving renal vein reconstruction was considered and the tumor was carefully dissected towards lateral or bilateral hilum. Unaffected section of renal vein was confirmed and suspended for further reconstruction. Tumor was further disconnected to retroperitoneal tissues with no accessory injuries. Proximal and distal part of IVC were consecutively clamped in all patients, right renal vein in patient 3 and bilateral renal veins in patient 4. Prosthetic graft was interpositioned in all patients for reconstruction of IVC and the venous blood flow was restored thereafter in patients 1 and 2. For patient 3, an opening on the right side of the prosthetic graft was taken and the stump of right renal vein was sutured with 5-0 prolene in running fashion. Leiomyosarcoma was extended near to inferior and superior renal vein confluence in patient 4, therefore, a cone pipe was prepared with prosthetic graft as left renal vein and sutured to IVC prosthetic graft on bench. Furthermore, an opening was excised for the right renal vein reconstruction (Fig. 4). After the completion of bench venoplasty, the vascular graft was then sutured to superior and inferior stump of the IVC. Right renal vein was anastomosed to IVC prosthetic graft, while left renal vein anastomosed to cone pipe prosthetic graft. Clamps were removed after the successful vascular reconstruction and systematic flow and renal flow were restored. Sutured site was critically examined for possible bleeding and soft tissue bleeding was cauterized or suture ligated. Resected specimens were sent to pathology and one abdominal drainage tube was placed to surgical area.

2.5. Postoperative management and follow-up observations

After the operation, the patient was sent back to general ward with no intensive care unit after surgery needed. A dose of 40 mg low molecular weight heparin sodium was injected from postoperative day two. While, prophylactic dose of 10 mg oral rivaroxaban tablet was administered after discharge for 3-month. Short-term (<90 days) and mid-term postoperative complications were

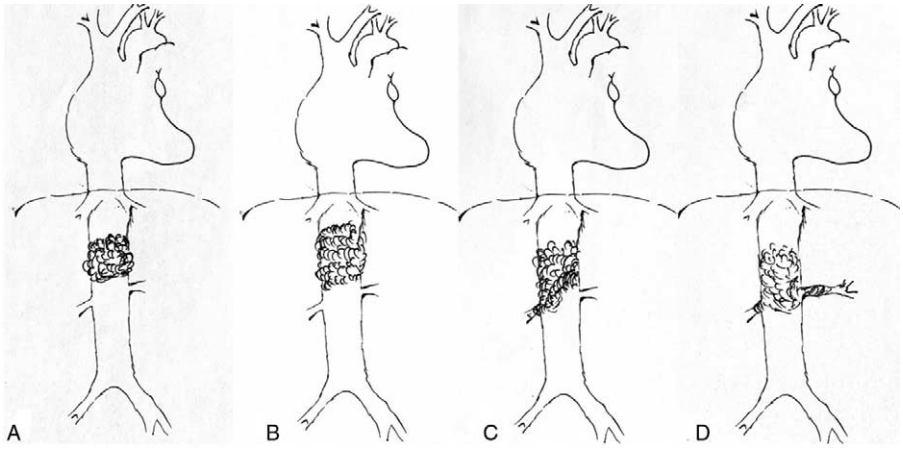

Figure 3. Schematic involvement of leiomyosarcoma in separate cases. A, tumor involvement in Case 1; B, tumor involvement in Case 2; C, tumor involvement in Case 3; A, tumor involvement in Case 4.

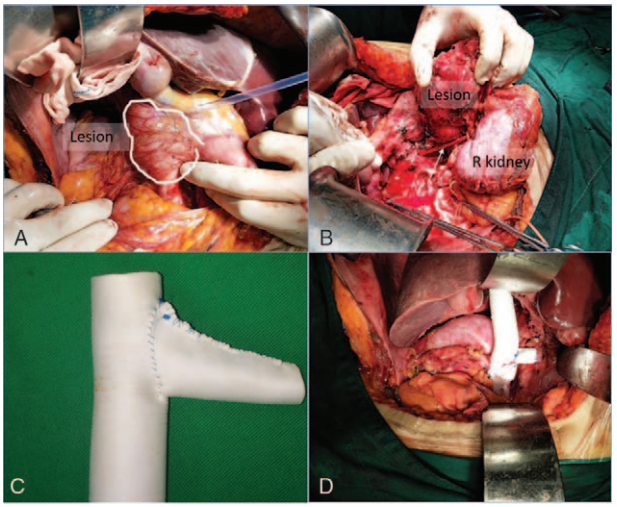

Figure 4. Surgical resection of leiomyosarcoma and vascular reconstruction. A, laparotomy showed giant tumor of IVC origin; B, Tumor with renal vein involvement (white arrow shows renal artery); C, Prosthetic graft reconstruction on bench; D, IVC replacement with bilateral renal vein reconstruction.

identified and cured. All subjects were followed every 3–6 months after discharge for general status, kidney function, quality of life, vascular patency and possible recurrence.

2.6. Statistical analysis

Descriptive statistics were calculated and numeric data were presented as median with the actual range of data, the SPSS statistical package 17.0 was used. Difference is significant when p value is less than 0.05.

3. Results

Four female patients with zone I-II leiomyosarcoma with mean age of 43 years (38–47 years) successfully underwent radical resection. All patients complained about back pain and leg edema was shown in patient 3. Radical resection of leiomyosarcomas were achieved through abdominal approach with no need for veno-venous bypass. The IVC was resected and reconstructed using prosthetic in all patients. Right renal and bilateral renal veins reconstruction were performed in patient 2 and 3 respectively. The median volume of intraoperative bleeding was 450 mL (200–600 mL), median operative time was 215 minutes (150–240 minutes) and median postoperative hospital stays 8 days (5–10 days).

Postoperative pathology showed leiomyosarcoma with mean size of 8 cm * 4.5 cm * 3.75 cm. No Clavien-Dindo IIIa or higher complication occurred after surgery. Vascular patency was confirmed by ultrasound and CT scan 3 months after surgery. Right renal vein thrombosis was developed in Case 4 with normal kidney function confirmed by liver function test and dynamic renal imaging. Continuous oral rivaroxaban tablet was administered. No recurrence was found in all patients with the median 25.5 months follow-up (21–30 months). Neither chemotherapy nor radiotherapy was given to all patients (Table 2).

4. Discussion

Leiomyosarcoma of IVC origin is a rare malignant tumor with slow and insidious growth. It is more frequently reported in middle aged females.[5] At the early stage, specific symptoms and clinical sings are lacking and early diagnosis is hard to achieve.[8] The clinical symptoms and surgical decision-making process are closely related with anatomical site, size and area of involvement. Oppression by giant tumor and / or returning obstacles of venous flow are the main causes of symptoms including back pain, abdominal lump, leg edema and sometimes hepatomegaly and ascites. When the leiomyosarcoma affects heaptocaval region, Budd-Chiari syndrome could develop as clinical symptoms.[9,10] Due to the lack of specific tumor marker, some patients with early leiomyosarcoma could be presented with varicose vein of lower limb, deep venous thrombosis or ascites, therefore these conditions should be cautiously taken with further investigation with CT, MRI scan and ultrasonography required to rule out the possibility of leiomyosarcoma.[11]

For patients who are tolerable to general anesthesia and with no remote organ metastasis, R0 surgical resection is vital important and provide long-term survival. Usually, multidisciplinary team discussion is helpful for preoperative evaluation, surgical planning and perioperative management.[12] The indication for IVC and other vascular reconstruction after radical resection should be based upon the size, tumor extension, defect of IVC and preparation for vascular substitutes. In most cases, IVC should be reconstructed to restore the venous flow. However, in cases with confirmed rich collateral circulation, IVC could be resected without reconstruction.[7,13] The presence of rich collateral circulations could be confirmed based upon patients clinical symptoms such as swelling, renal function and digital subtraction angiography (DSA). Several vascular substitutes such as PTFE prosthetic graft,[14] iliac vein, jugular vein,[15] great saphenous vein, cryopreserved vessel[6] and parietal peritoneum[16] are reported with their inherent pros and cons. In current study, we have used prosthetic graft both for IVC and renal vein, patency of the vascular graft was confirmed by postoperative ultrasound and no postoperative infection occurred.

Mutli-organ resection provided better long-term survival in patients with IVC leiomyosarcoma. However, multi-organ resection might result in organ dysfunction with impaired

Table 2

Clinical outcomes of leiomyosarcoma patients.

Case	IVC replacement	Renal vein reconstruction	Blood loss (ml)	Blood transfusion	R0 resection	Operative time (min)	Complication	Follow-up (months)	Recurrence	Current status
1	PTFE graft	No	200	No	Yes	150	No	30	No	Alive
2	PTFE graft	No	600	No	Yes	200	No	26	No	Alive
3	PTFE graft	Right renal vein	400	No	Yes	230	No	25	No	Alive
4	PTFE graft	Bilateral vein	500	No	Yes	240	Right renal vein thrombosis	21	No	Alive

IVC = Inferior *vena cava*, PTFE = Polytetrafluoroethylene.

quality of life.[7,17] In this study, we have performed kidney preserving resection by complex reconstruction and patients recovered with normal renal function. Nephrectomy and kidney autotransplantation should be reserved only for patients without possibility for renal vascular reconstruction.

Recurrence is common even after radical resection, the tumor size, multi-organ resection are the risk factors for disease recurrence. The reported cumulative 5-year overall survival (OS) rate and 5-year disease-free survival (DFS) were 55% and 5% respectively.[5,17,12,18] Postoperative recurrence does not preclude re-resection of the leiomyosarcoma.[3] No randomized clinical trial evaluates the clinical efficacy of neoadjuvant chemo- or radiotherapy. Despite of practice of chemotherapy in some selected patients, its benefits should be cautiously taken with recommendation evidence is 2B.[19] Neoadjuvant radiotherapy may help to reduce the size of tumor, increase the resectibility and control tumor growth. However, no confirmed data support the benefits of radiotherapy as a treatment modality.[20]

This study has some limitations that need to be addressed. First, this study reports the experience of IVC leiomyosarcoma which is rarely seen in clinical practice, thus explaining the small number of patients. Then, this is a retrospective analysis of surgically resection leiomyosarcoma patients with no control. In these advanced cases, radical resection with vascular reconstruction could be valuable option. with no control group. Finally, the post-operative follow-up time is relatively short and the clinical outcomes is needed to be evaluated.

5. Conclusions

Curative resection of zone I-II leiomyosarcoma is associated with longer survival in selected cases, *en-bloc* resection with complex vascular reconstruction could be considered.

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Author contributions

LB conceived the study and critically reviewed the manuscript. TT, AT, XF and TL collected data and performed analysis and contributed to the writing of the manuscript. SA and performed the literature research and analysis. AA, NA, JW and JMZ contributed to the discussion and approval of the manuscript. All authors have read and approved the final version of the manuscript.

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