

Zone 2 Leiomyosarcoma of Inferior Vena Cava: Our Case Experience with Radical Resection, IVC Reconstruction, Adjuvant Radiotherapy and Outcome

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Abstract

Leiomyosarcoma of Inferior vena cava (IVC) is a rare tumor; this along with delay in diagnosis, radical nature of treatment contributes for poor survival with high morbidity and mortality. We report a case of 62 year old lady who had only pain in right flank as her presenting complaints. On investigations she was found to have Segment 2 IVC tumor.

She underwent radical excision of the IVC mass with right nephrectomy and of right caudate lobe liver resection. We could achieve complete tumor clearance with this radical surgery. She recovered uneventfully from the surgery and later subjected to adjuvant therapy. In the literature, overall 5 year survival after radical resection of IVC. leiomyosarcoma is from 33 to 53.4%. Neoadjuvant or adjuvant therapy can aid in improving survival in these patients but radical resection with multi-disciplinary team approach till date, remains the backbone of treatment in IVC leiomyosarcomas.

Keywords: *Leiomyosarcoma; Inferior Vena Cava*

Abbreviations

STS: Soft tissue sarcoma; IVC: Inferior Vena Cava

Introduction

Leiomyosarcoma of Inferior vena cava (IVC) is a rare tumor; this along with delay in diagnosis, radical nature of treatment contributes for poor survival with high morbidity and mortality.

Case Summary

Sixty-two years lady without any known co-morbidity, presented with continuous, dull aching and non-radiating pain in right lumbar region of five to six months duration. She did not give history of loss of weight and appetite. She also did not give any history of lower limb swelling or pain. Initially, intensity of pain was low not interfering in her daily routine activities but in last one month it has increased and

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hence she got herself investigated. Her Complete blood count, Liver function test and renal function tests were within normal limits. Her transabdominal ultrasonography (USG) showed 5 x 6 cm mass near the right renal hilum extending into the IVC medially and superiorly abutting right lobe of liver. There was no liver metastasis and no free fluid with normal left kidney.

Patient was referred to our institute at this stage. Contrast enhanced computerized tomography (CECT) scan of abdomen was done, which showed a well-defined heterogeneously enhancing 7.6 x 3.6 x 3.5 cm mass lesion centered within the lumen of IVC (Figure 1). Proximally mass was 4.6 cm caudal to hepatic vein-IVC confluence and distally it was 0.5 cm from the left renal vein insertion into the IVC. Anteriorly the mass was infiltrating into the inferior most aspect of caudate lobe of liver and abutting second part of duodenum with maintained fat plain. Posteromedial it was abutting the right crus of diaphragm and coeliac ganglion and postero-laterally it was infiltrating into the upper pole cortex of right kidney and right suprarenal gland (Figure 2). There were 3 renal arteries on right side, out of which proximal two arteries traversing through the tumor. There were multiple leino-renal collaterals communicating with proximal left renal vein.



Figure 1: Coronal section showing the IVC lesion (Segment 2) (yellow arrow).



Figure 2: Transverse section showing IVC lesion invading the right renal cortex and renal hilum (black arrow).

USG guided fine needle aspiration biopsy (FNAB) was done which showed spindle cell tumor and immunohistochemistry (IHC) suggestive of leiomyosarcoma of IVC or retroperitoneum [CD10 positive, Mib 15- 20%. AE 1/AE 3 positive, focal H-caldesmon positive, diffusely positive for SMA (Smooth muscle actin) and negative for DOG1/c-KIT/S 100p/desmin and paired box gene-8 (PAX8)].

To rule out distant metastasis fludeoxyglucose (FDG) positron-emission tomography scan (PET) scan was done, which showed metabolically active IVC lesion and ruled out distant metastasis.

Based up on above imaging and FNAB we made a differential diagnosis of leiomyosarcoma or sarcoid sarcoma arising either from IVC or retroperitoneum.

Patient was otherwise in good health, nutritionally well-built and her Karnofsky performance score was 90 and Eastern Cooperative Oncology Group (ECOG) score was 1. A multidisciplinary team approach used wherein a hepatobiliary surgeon, urologist, vascular surgeon, oncologist, onco-pathologist and intensivist were included and a decision of upfront radical surgery was taken.

An upper midline incision with lateral curved extension into the right lumbar region at the level of umbilicus was taken. Right lobe of liver was mobilized to expose the whole retro-hepatic IVC. The mass was arising from IVC invading the right caudate lobe throughout its length up to 2 cm below the hepatic venous insertion and till junction of two iliac veins below. Right renal hilum and adrenal gland were inseparable from the tumor. Right caudate lobe resected and IVC was dissected off liver parenchyma till the hepatic venous insertion above. The right kidney along with the perinephric tissue, the adrenal glands, the proximal ureter, along with the right renal vein and renal artery was excised en-bloc with IVC. We clamped the stump of left renal vein for sixty minutes and urine output was monitored over this clamp time which was 100 ml. IVC was reconstructed with polytetrafluoroethylene (PTFE) graft of 2.5 x 25 cm with end to end anastomosis from distal to hepatic venous insertion in superior portion to proximal portion of IVC bifurcation in the inferior portion. In view of good urine output even after clamping left renal vein and multiple lienorenal collaterals in the proximal part, left renal vein was not reconstructed into IVC graft (Figure 3). Unfractionated heparin 5000 IU was used intraoperatively and low molecular weight heparin (LMWH) was in the perioperative period.

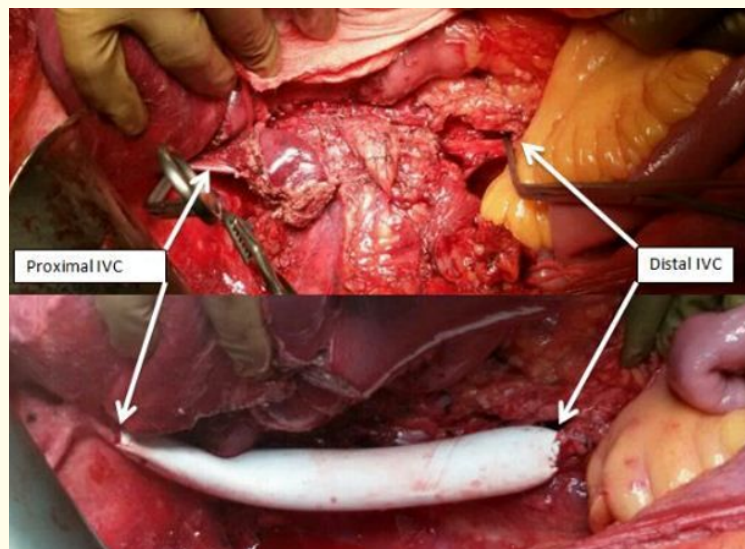


Figure 3: Intraoperative view of repaired IVC using PTFE graft.

Post operatively patient was managed in intensive care and was hemodynamically stable with normal urine output and no pedal oedema.

Before shifting out of ICU, Color Doppler was done to evaluate the status of the PTFE graft which showed a low flow in the PTFE graft without any thrombosis, with normal flow patterns in the proximal part of the graft and hepatic veins. An IVC angiography revealed a narrow anastomotic junction in the distal segment with low flow in the distal part of the graft with normal flow in proximal part without any intraluminal thrombosis. There were multiple para-spinal collaterals present. Because of low flow in the graft LMWH was later switched over to warfarin.

The histopathology showed tumor arising from the muscle coat of IVC and composed of bundle of spindle shaped cells along with baton shaped nuclei (Figure 4) exhibiting 6-7 mitoses/10 hpf. Tumor extends into surrounding adipose tissue, involves the external surface of kidney with adrenal and the liver parenchyma. No vascular or perineural invasion noted. No lymph nodal spread seen in the 14 dissected nodes and all the margins were free of tumor. The IHC on tumor cells stain positively with Desmin, myogenin, SMA and CD10 were consistent with leiomyosarcoma of IVC origin (Figure 4). Post operatively patient recovered without any complications and was discharged from hospital on day seven.

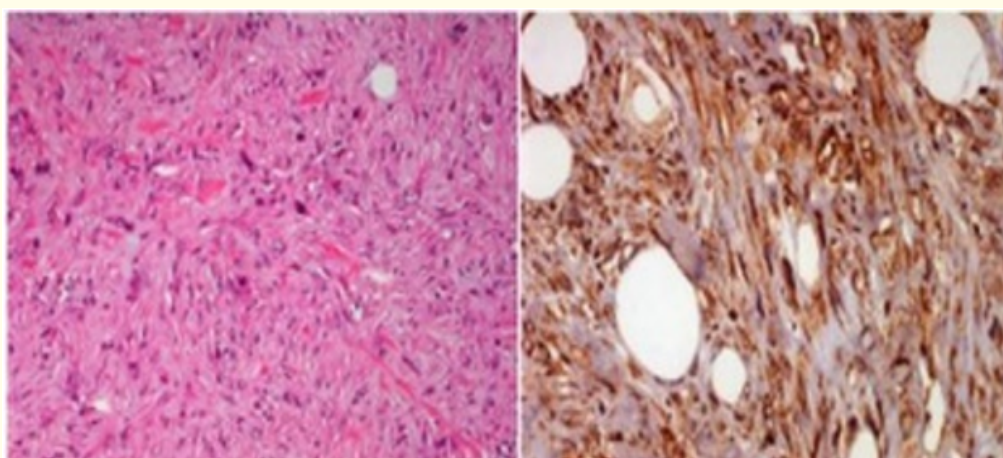


Figure 4: Histopathology tumor shows interlacing fascicles of spindle shaped cells showing marked nuclear pleomorphism with mitotic activity and is diffusely positive for Desmin.

Follow up

She underwent adjuvant radiotherapy after complete healing of wounds. At 6, 12 and 18 months follow up CECT abdomen which showed no recurrence of disease and patent PTFE graft flow. Renal function test is normal and there is no pedal oedema. There is no change of her routine functional ability in life. Her compliance towards follow up is good.

Discussion

About 1% of all adult malignancies are accounted by soft tissue sarcoma (STS) [1]. Commonest locations of STS are extremities 43%, viscera 19%, 15% in retroperitoneum, 10% in trunk and 9% in Head and neck region.

Leiomyosarcoma a form of STS is considered as the rare primary malignant tumor of IVC and is listed as rare disease by National organisation for rare disorder (NORD) [2].

Kulaylat., *et al.* have given a classification of IVC STS based on its location [3]. The classification defines segment 1 as involvement of infrarenal portion of IVC, segment 2 as inter and suprarenal up to the main hepatic veins but not involving the hepatic veins and segment 3 as suprahepatic with or without involving the hepatic veins/intracardiac extension. Commonest of these is segment 2 leiomyosarcoma [3,4]. Segment 2 and 3 type of tumor are the most difficult to manage operatively because of the adjacent organ involvement and complexities in vascular anatomy at this locations [5]. But prognosis of tumor involving middle IVC is better (Segment 2) as compared to other types [6].

Patients presenting symptoms are pain in right lumbar region; pain is mostly dull nonspecific and misleading which contribute to the delayed diagnosis and treatment. Abdominal ultrasound is the initial non-specific investigation for the non-specific clinical symptoms, but contrast-enhanced computerized tomography (CECT) is needed to stage the tumor, check for operability and plan surgical resection. Transesophageal echocardiography is needed in patients where intracardiac extension is suspected [5]. Other symptoms along with or without pain are Budd-Chiari syndrome with hepatomegaly, ascites with or without associated jaundice [5].

The visceral and retroperitoneal STS gets commonly metastasize to liver while the STS from other location gets metastasize to lung, hence a positron emission tomography (PET)/CT scan may be helpful in staging the disease [1]. In cases of diagnostic dilemma fine needle aspiration cytology or a biopsy is necessary. The tract of biopsy may warrant excision during definitive surgery; though there can be difference of opinion in this regard. Histological analysis is done using FNCLCC (Fédération Nationale des Centres de Lutte Contre le Cancer) grading system which is intern based on tumor differentiation, mitotic count and percentage of tumor necrosis [1].

Oedema of Lower extremities can be inconsistent as mentioned in their original article by Kieffer E., *et al* [5]. This clinical finding can be explained by the fact that chronic and slow IVC obstruction opens up the paraspinal and abdominal wall collaterals which shunt blood from lower IVC to the systemic circulation, which was the finding in our case too. It is of utmost important to consider and have detailed anatomical information of collaterals as it would be extremely crucial in planning surgical resection and vascular reconstruction. Also mentioned by Tameo., *et al.* we can measure the renal vein pressure can be measured before and after clamping the renal vein to see how well the clamping is tolerated [6]. In our case we clamped the left renal vein stump close to the IVC after resection of tumor en-bloc and measured urine output from that time onwards which was adequate also there was no gross congestion of left kidney as we had the proximal collaterals which where draining the left renal vein. In the absence of such collaterals the left renal vein should be inserted in the PTFE graft that is used to reconstruct the IVC.

Currently, for patients with no metastasis in initial presentation, optimal initial treatment strategy would be radical excision with adjuvant chemotherapy/radiotherapy. Mingoli A., *et al.* [7] in their series of 218 patients had a better 5 year survival rate of 49.4% and 29.5% 10 year survival in patients which underwent radical tumor resection. Other series with fairly large number of patients and satisfactory follow-up given by Hines., *et al.* [8], Hollenbeck., *et al.* [4] and Kieffer E., *et al.* [5] after radical resection for intent to cure had actuarial survival rates at 5 years of 53.3%, 33% and 34.8% respectively.

Hines OJ., *et al.* [8] in their series have mentioned regarding increase in the overall survival after receiving adjuvant radiation therapy, especially in segment 2 type of IVC leiomyosarcoma. Although chemotherapy and radiotherapy as neoadjuvant and adjuvant has being tried before but it failed to show any major survival benefit. NCCN guidelines favors radiotherapy in R1 resections and to continue it post operatively with an increase of 10 -16 Gy. In case of R0 resection radiotherapy is reserved for high grade tumors, very close resection margins and larger tumors [1,9].

Overall survival in Leiomyosarcoma is very poor, with newer techniques and advances in vascular, oncosurgery, chemotherapy (anthracycline/ifosfamide, Gemcitabine and docetaxel, trabectedin or dacarbazine-containing regimens) and radiotherapy may have shown helped prolonging the 5 year survival but not very significantly [1,5,7,10]. The group of patients with upper part of IVC involvement, lower limb oedema on presentation, intraluminal tumor growth, complete IVC occlusion and Budd-Chiari syndrome had significantly poor overall survival rates [7]. In our patient, none of these signs and symptoms was present.

Recently Roland., *et al.* [10] in their retrospective analysis had discussed regarding expression of β -catenin and its negative impact on disease free survival and patients with higher expression of insulin like growth factor-receptor (IGF-1R) had shorter duration for distant recurrence. This points our attention towards the fact that a molecular variable also has a major impact on outcome of the disease and its natural course.

Conclusion

Upfront radical resection is one of the main components in optimal care in IVC Leiomyosarcoma till date with good survival benefits as seen in our case. After the development of lienorenal collaterals we can avoid reconstructing the left renal vein into the PTFE or Neo-IVC graft. In our case paraspinal collaterals served to drain blood by skipping the IVC; which may also explain no pedal oedema and low flow in the PTFE graft. Obtaining a detailed venous anatomy pertaining to segment two of IVC is warranted with a venogram to view the status of collaterals which may impact in planning the procedure especially in vascular reconstruction.

Conflict of Interests

No conflict of interest.

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