Nonseminomatous Germ Cell Testicular Tumour With Metastatic Retroperitoneal Lymphadenopathy Presenting As Severe Backache Due To IVC Thrombosis

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Abstract — IVC thrombosis is often under-recognized. Malignancy can cause spontaneous IVC thrombosis due to its prothrombotic potential. Malignant tumors can compress, adhere or infiltrate the IVC wall causing endothelial damage with subsequent thrombosis. Retroperitoneal lymphadenopathy can cause compressive distortion of IVC causing venous stasis and turbulent flow. Metastatic retroperitoneal lymphadenopathy from testicular tumor is a rare cause of IVC invasion with resultant IVC thrombosis which can rarely present as backache. High index of suspicion is needed to detect primary testicular tumor in cases of IVC thrombosis, especially in young individuals.

A 26-year-old male patient presented with lower back ache, weight loss and fever. MRI Lumbosacral spine done outside showed a soft tissue signal intensity retroperitoneal mass in aortocaval region compressing IVC. Ultrasound (done outside) revealed mild right sided hydrourteronephrosis secondary to a lobulated heterogeneous mass in inter-aortocaval region encasing right ureter and invading IVC causing thrombosis. Contrast enhanced Computerized axial tomography of abdomen showed a heterogeneously enhancing lobulated mass with multiple internal calcifications, in inter-aortocaval region at L3-4 level invading the IVC causing IVC thrombosis. Both tumor thrombus and bland thrombus were present. The right testis showed a subtle 10x10 mm hypodense lesion with peripheral calcification. DW-MRI showed diffusion restriction in retroperitoneal mass and the IVC tumor thrombus. Possibility of primary testicular tumor with metastatic retroperitoneal lymphadenopathy causing IVC invasion with resultant thrombosis was considered which was confirmed on histopathological examination.

Index Terms — IVC thrombosis; non-seminomatous germ cell tumor; retroperitoneal lymphadenopathy; Testicular tumour.

I. CASE REPORT

A 26 years old male patient presented with lower back ache, weight loss and fever. MRI Lumbosacral spine (Fig. 1) done in an outside center showed a soft tissue signal intensity retroperitoneal mass in aorto-caval region compressing IVC- likely lymph nodal mass.

Ultrasound (USG) Abdomen showed mild hydrenephrosis in right kidney and mild hydroureter in upper portion. A lobulated mixed echoic mass of size 84x76x57 mm noted in retroperitoneum in inter-aortocaval region proximal to level of aortic bifurcation extending to pre-aortic and pre-caval region (Fig. 2 A-B). It showed few echoreflective foci of calcification. It appeared to be encasing/ involving adjoining right ureter causing mild hydrenephrosis and proximal hydroureter. The mass was invading adjoining IVC causing IVC thrombosis. The thrombus extended proximally upto level of renal veins. Distally the thrombus extended into common iliac veins.
right external iliac vein and right common femoral vein. USG of right testis (Fig. 2 C-D) showed a well-defined mixed echoic solid mass measuring 18 (length) x14 (antero-posterior) x15 (transverse) mm showing peripheral echoreflective calcification in its posterior portion.

Fig. 2. Ultrasound abdomen Longitudinal (A) and transverse (B) sections showing fairly well defined solid mass of heterogeneous echotexture in retroperitoneum just proximal to level of aortic bifurcation compressing and displacing IVC towards the right, invading IVC with resultant IVC thrombosis. Ultrasound of right testis, longitudinal (C) and transverse (D) sections showing a well-defined mixed echoic, predominantly hypoechoic solid mass in right testis with peripheral echoreflective calcification.

CT Abdomen and pelvis (Figures 3-6) showed a fairly well defined lobulated soft tissue density mass measuring 77 (length) x56 (antero-posterior) x69 (transverse) mm in retroperitoneum in inter-aortocaval region at L3-4 level. It appeared heterogeneous in density on plain study and showed heterogeneous post contrast enhancement. Multiple small hyperdense foci suggestive of calcification were noted within the mass. The mass was extending in pre-aortic and precaval region and was causing spaying of adjoining aorta and IVC which were displaced laterally by the mass. Fat plane between the mass and right anterolateral margin of adjoining aorta was obscured. IMA was displaced towards the left by the mass with obscuration of the intervening fat planes. Fat planes between the mass and adjoining IVC was obscured. Intraluminal filling defect measuring approx. 77 (length) x22 (antero-posterior) x24 (transverse) mm was noted in adjoining IVC extending proximally up to opening of bilateral renal veins in IVC showing heterogeneous post contrast enhancement. This was likely to represent tumor thrombus. IVC distal to tumor thrombus showed hypodense filling defect extending into both the common iliac veins, right external iliac vein, right internal iliac vein and right common femoral vein in upper right thigh suggestive of bland thrombosis. No extension of thrombus was noted in renal veins. Rest of intrahepatic IVC, hepatic, supra-hepatic portion of IVC appeared normal. The mass was also compressing and encasing the adjoining right ureter with resultant proximal mild hydroureteronephrosis with delayed appearance of nephrogram and no excretion of contrast in PC system in delayed phase. Few subcentimeter sized enhancing lymph nodes were noted in para-aortic, paracaval, inter-aorto-caval region.

Liver and both adrenal glands appear normal. No hepatic/adrenal metastasis was noted. A subtle well defined hypodense lesion measuring approx. 10x10 mm with peripheral calcification was noted in right testis.

Possibility of primary testicular tumor with metastatic retroperitoneal lymphadenopathy causing IVC invasion with resultant IVC thrombosis involvement of adjoining right ureter with proximal right hydroureteronephrosis was considered.

Fig. 3. Plain CT scan of abdomen (A-D) shows a fairly well defined lobulated soft tissue density mass in retroperitoneum in inter-aortocaval region at L3-4 level. It shows multiple small hyperdense foci suggestive of calcification were noted within the mass. Right kidney shows mild hydrenephrosis due to ureteric compression.

Fig. 4. Contrast enhanced axial CT scan of abdomen (A-D) shows a fairly well defined heterogeneously enhancing lobulated soft tissue density mass in retroperitoneum in inter-aortocaval region at L3-4 level. Right kidney shows mild hydrenephrosis due to ureteric compression. Filling defect noted in IVC due to thrombosis.
Fig. 5. Contrast enhanced CT scan of abdomen coronal images (A-B) shows a fairly well defined heterogeneously enhancing lobulated soft tissue density mass in retroperitoneum in inter-aortocaval region at L3-4 level causing mass effect on both aorta and IVC. Filling defect noted in IVC due to thrombosis extending proximally upto infrahepatic portion of IVC and inferiorly into bilateral common iliac veins.

Fig. 6. Contrast enhanced CT scan of abdomen sagittal images (A-B) shows a fairly well defined heterogeneously enhancing lobulated soft tissue density mass in retroperitoneum in inter-aortocaval region at L3-4 level causing mass effect on both aorta and IVC. Filling defect noted in IVC due to thrombosis extending proximally upto infrahepatic portion of IVC and inferiorly into bilateral common iliac veins.

MRI of abdomen (Fig. 7-10) showed a fairly well defined lobulated soft tissue intensity mass in retroperitoneum in inter-aortocaval region at L3-4 level appearing isointense to muscle on T1WI and heterogeneously hyperintense on T2WI with IVC thrombosis extending proximally upto infra-hepatic portion appearing hyperintense on both T1 and T2WI. Right kidney shows mild hydronephrosis due to compression and encasement of adjoining right ureter. Diffusion restriction (Fig. 11) was noted in retroperitoneal mass with low ADC values suggestive of neoplastic etiology. IVC thrombus also showed restricted diffusion with low ADC value suggestive of tumor thrombus. Thrombus in distal portion of right external iliac vein and right common femoral vein did not show restricted diffusion on DWI- likely to be bland thrombus.

Fig. 7. MRI Abdomen Axial T1 (A-D) shows a fairly well defined lobulated soft tissue intensity mass in retroperitoneum in inter-aortocaval region at L3-4 level appearing isointense to muscle with IVC thrombosis appearing hyperintense.

Fig. 8. MRI Abdomen Axial T2 (A-C) shows a fairly well defined lobulated soft tissue intensity mass in retroperitoneum in inter-aortocaval region at L3-4 level appearing heterogeneously hyperintense with IVC thrombosis appearing hyperintense.
Figure 9 - MRI Abdomen Axial T2 (A-C) shows IVC thrombosis and mild hydronephrosis in right kidney due to ureteric compression.

Fig. 10. MRI Abdomen Axial T2 (A-C) shows a fairly well defined lobulated soft tissue intensity mass in retroperitoneum in inter-aortocaval region at L3-4 level appearing heterogeneously hyperintense with IVC thrombosis extending to bilateral common iliac veins appearing hyperintense.

Fig. 11. MRI Abdomen Diffusion weighted imaging (A-D) - Retroperitoneal mass showing restricted diffusion on DWI (C) with low ADC value (D). IVC thrombus showing restricted diffusion on DWI (A, C) with low ADC value (B, D).

Whole body 18FDG PET-CT scan (Fig. 12) showed a well-defined heterogeneously enhancing FDG avid (SUV max 16.61) retroperitoneal mass measuring 8.41(SI) x 5.24 (AP) x 7.39 (TR) cm. retroperitoneal mass encasing aorta and IVC inferior to the levels of renal veins. Tumor thrombosis of infrarenal IVC was noted. Non FDG avid thrombosis of bilateral common iliac veins, right external iliac vein, right internal iliac vein, right common femoral vein and right superficial femoral vein was also noted.

Trucut biopsy of retroperitoneal mass and IVC thrombus was done. Trucutbiopsy cores from both the sites showed metastatic deposits of non seminomatous malignant germ cell tumor with tumor cells arranged in tubules, glands and focal retiform pattern. Cells showed large irregular vesicular nuclei and prominent pink nucleoli. Focal areas of necrosis were seen. No evidence of undifferentiated cells or heterogeneous elements seen. Findings were suggestive of metastatic deposits of non seminomatous malignant germ cell tumor (predominantly yolk sac tumor component).

AFP was 8052 IU/mL (normal range in men is 0.5-5.5 IU/mL). S. LDH was 320 IU/L. (normal 80-230 IU/L). Beta-HCG was <5 mIU/mL i.e. normal.

Patient underwent right orchidectomy followed by chemotherapy. Histopathology confirmed non-seminomatous germ cell tumor.

Fig. 12. PET CT showing FDG avid retroperitoneal mass in aorto-caval region and tumoral thrombus in infra-renal IVC.

II. INTRODUCTION

IVC thrombosis often goes undetected. Symptoms and signs are related to etiology. These range from no symptoms to cardiovascular collapse due to pulmonary embolism. Lower back pain, painful lower limb swelling, fever, dilatation of cutaneous abdominal veins and rise of inflammatory markers suggest IVC thrombosis [1].

Incidence of abdominal venous thrombosis is 1.3:1 in oncology patients undergoing cross sectional imaging. In decreasing order of frequency, IVC, renal veins and portal venous system are involved. The prevalence of thrombosis is higher in renal cell carcinoma (RCC) as compared to retroperitoneal, hepatocellular carcinoma (HCC) and metastatic liver tumors. Bland/ benign thrombosis of IVC
occurs secondary to DVT of affected lower limbs and is often associated with risk factors like hypercoagulability, immobility and trauma [2].

Due to aggressive behavior, abdominal tumors adjacent to IVC can invade IVC. These are renal angiomyolipoma which has aggressive evolution, renal cell carcinoma, pheochromocytoma, adrenal carcinoma, hepatocellular carcinoma, leiomyosarcoma of IVC and rarely Para neoplastic hypercoagulable state. It can occur secondary to deep vein thrombosis affecting lower limb in patients receiving long term oral contraceptives, patients with antiphospholipid syndrome, various coagulopathies and vasculitis [3].

Tumour thrombus in the IVC is a rare complication of testicular Ca. It needs appropriate treatment with surgery and chemotherapy [4]. IVC involvement in 2 autopsy series of patients with testicular germ cell tumour was 3% and 11% of patient [5, [6]. 4 cases of IVC invasion were found in 650 patients with testicular carcinoma in whom 397 patients had retroperitoneal disease [7].

### III. DISCUSSION

IVC thrombosis can be congenital or acquired. There is high incidence of thrombophilia in congenital IVC anomalies (like prothrombin gene mutation, protein C and S deficiency, activated protein C resistance, antithrombin deficiency and dysfibrinogenemia), Hence thrombophilia screening is must in patients with IVC anomalies. This occurs due to interaction between stasis and hypercoagulability [1]. Acquired IVC thrombosis occurs due to spontaneous thrombosis in normal vessel, thrombosis secondary to external vascular compression or due to pathological changes in the vessel wall [8]. Spontaneous IVC thrombosis in malignancy occurs due to prothrombotic potential of the tumor with radiotherapy and chemotherapy treatment which enhance the risk of thrombosis. Malignant tumors can compress, adhere or infiltrate the IVC wall causing endothelial damage with subsequent thrombosis. IVC thrombosis can occur secondary to abdominal trauma causing endothelial injury due to direct vessel wall injury, compression or shearing forces or intrinsic compression from adjacent hematoma. Retroperitoneal lymphadenopathy can cause compressive distortion of IVC causing venous stasis and turbulent flow [1].

IVC thrombosis in testicular tumour occurs by 2 mechanisms [4]:

A) Direct invasion of the spermatic vein and then of IVC. Hence IVC invasion is more frequent in right testicular tumour due to direct insertion of right gonadal vein into IVC.

B) Metastatic retro peritoneal lymph nodes by lymphatic spread causing Direct IVC invasion, due to development of lymphatic- venous shunting. Hence bulky metastatic retroperitoneal lymphadenopathy in testicular tumour is a major risk for IVC tumour thrombus.

IVC thrombosis can be acute or chronic. Acute IVC thrombosis can present with lower back ache and buttck pain, cauda equina symptoms and sciatica type pain. Chest pain with breathlessness can occur if there is pulmonary embolism. Patients can present with bilateral lower limb swelling with dilatation of superficial veins. Isolated thrombosis of IVC without involvement of the iliac and femoral veins can develop collaterals along the posterior abdominal wall. If iliac or femoral veins are involved, dilated veins can appear on abdominal wall between the groin and axillae. Ascites can also develop.

Chronic IVC thrombosis occurs due to slow progressive thrombosis and can cause dull aching pain in lower limbs with symptoms of venous claudication, lower limb swelling and discomfort. These are increased by exercise and relieved by rest and elevation.

IVC thrombus can be diagnosed by ultrasound, Doppler, CT scan and MRI [9]. Duplex ultrasound is a non-invasive accurate first line investigative modality. Normally IVC shows continuous waveform with respiratory variations. These become pulsatile as IVC empties into the right atrium, with IVC thrombosis, the waveform appears monophasic. Limitations of Duplex USG are operator dependence, limitations due to overlying bowel gas and body habitus, difficulty in assessing venous compressibility. It can detect adjoining retroperitoneum, renal or adrenal mass. Dynamic CT study is non-invasive, rapid test which can detect and assess the thrombus extent along with detecting the cause of thrombosis. Both bland and tumour thrombus are seen as filling defect in IVC. Malignant thrombus shows enhancement within the filling defect and can detect contiguous adjacent mass. If adjacent tumor is not seen, then the enhancing intraluminal tumor thrombus is due to IVC leiomyosarcoma. Bland thrombus shows lack of enhancement and absence of any adjoining mass.MRI lacks radiation and is replacing CT as optimal non-invasive imaging tool. It can detect IVC anomalies, accurately delineate the proximal and distal extent of thrombus and its age. It can also detect morphological changes in thrombus after therapy. Availability, cost and risk of nephrogenic systemic fibrosis are the disadvantages [9].

Tumour thrombus should be differentiated from bland (benign) thrombus. Tumour thrombus will show enhancement after contrast administration like retroperitoneal mass or primary tumour. A bland thrombus will show lack of enhancement. A tumour thrombus will be FDG avid on PET CT as it is metabolically active due to trace uptake. A bland thrombus will be non-FDG avid on PET CT. On diffusion weighted MRI, the thrombus will show restricted diffusion with low ADC values [3], [18]. F FDG PET CT scan can differentiate between hyper-metabolic tumoral thrombosis and non-hyper-metabolic bland thrombosis on IVC. This helps in preventing unnecessary long-term anticoagulation treatment as tumoral thrombus does not require long term anticoagulation [10].

DW-MRI with quantification of apparent diffusion coefficients (ADC) can differentiate between malignant and bland IVC thrombosis without use of IV contrast. Malignant thrombus shows heterogeneous tumor like signal on T2WI with low ADC values. Bland thrombus is iso to hypointense on T2WI and do not show restricted diffusion [2].

Ultrasound can detect size and extent of retro-peritoneal lymph nodes, their internal architecture (presence of necrosis and calcification), and presence of IVC thrombosis. Colour Doppler can be useful in differentiating between
tumour thrombus and bland thrombus. Tumour thrombus will show vascularity while bland thrombus will show lack of vascularity. Both CT and MRI are gold standard for evaluation of retro-peritoneal disease, presence of IVC invasion and detection of IVC thrombosis with sensitivity close to 100% [11]. MRI should be obtained within 1-2 weeks in the post-operative period to rule out remaining thrombus due to aggressive nature of the tumour [12, [13].

Treatment suggested is orchidectomy and chemotherapy, retroperitoneal lymph node dissection and vascular reconstruction [14]. IVC thrombosis has a high risk of pulmonary tumoral embolism leading to death [5]. Pulmonary tumoral embolism can develop despite anticoagulation. Hence a temporary IVC filter prior to orchiectomy and chemotherapy can avoid complication of pulmonary embolism. Chances of pulmonary embolism are high when the tumour thrombus extends to right atrium [15]. In such urgent cases, thrombectomy prior to chemotherapy is needed. Initially chemotherapy followed by surgery with or without IVC filter is performed in patients with IVC thrombus without cardiac involvement. The histopathological composition of intra-luminal IVC thrombus is suggestive of type of testicular carcinoma. Best therapeutic option for such patients is aggressive surgical approach before or after chemotherapy. In majority of cases, the tumour thrombus does not regress completely after chemotherapy. Hence, surgical resection of tumour thrombus is needed.

### IV. LITERATURE REVIEW

<table>
<thead>
<tr>
<th>Author</th>
<th>Year</th>
<th>Age of the patient</th>
<th>Side and type of tumor, age</th>
<th>Metastasis</th>
<th>Treatment administered</th>
</tr>
</thead>
<tbody>
<tr>
<td>Geffen DB et al</td>
<td>1992</td>
<td>34 years</td>
<td>Left mixed seminoma and embryonal cell testicular carcinoma</td>
<td>High volume retroperitoneal disease, visceral metastasis, IVC thrombosis extending into right atrium, pulmonary embolism.</td>
<td>Chemotherapy, Anticoagulants, resection of residual retroperitoneal mass, left radical orchidectomy.</td>
</tr>
<tr>
<td>Fidias P et al</td>
<td>1997</td>
<td>27 years</td>
<td>Right testicular germ cell tumor</td>
<td>Massive retroperitoneal lymphadenopathy, IVC thrombosis, soft tissue neck mass, supraclavicular lymphadenopathy with extension into mediastinum</td>
<td>Anticoagulation, chemotherapy, debulking and resection of retroperitoneal lymph nodal mass, excision of mediastinal mass, right radical inguinal orchidectomy.</td>
</tr>
<tr>
<td>Badawi JK et al</td>
<td>2005</td>
<td>26 years</td>
<td>Right testicular mixed non seminomatous germ cell tumor</td>
<td>IVC thrombosis, retroperitoneal lymphadenopathy.</td>
<td>Right inguinal orchidectomy, retroperitoneal lymphadenectomy, extraction of the IVC thrombus by cavotomy, chemotherapy.</td>
</tr>
<tr>
<td>Kinebuchi Y et al</td>
<td>2007</td>
<td>33 years</td>
<td>Left testicular non seminomatous germ cell tumor</td>
<td>Multiple metasteses in both lungs, retroperitoneal lymph nodes and tumor thrombus in left renal vein extending to the IVC.</td>
<td>Left high inguinal orchidectomy, chemotherapy, Retroperitoneal lymph node dissection.</td>
</tr>
<tr>
<td>Dusaud M et al</td>
<td>2015</td>
<td>45 years</td>
<td>Left testicular non seminomatous germ cell tumor</td>
<td>IVC thrombosis with bilateral pulmonary embolism, retroperitoneal lymph nodes, multiple lung metastases</td>
<td>Radical orchidectomy, chemotherapy, Retroperitoneal lymph node dissection.</td>
</tr>
<tr>
<td>Raup VT et al</td>
<td>2015</td>
<td>34 years</td>
<td>Left regressed testicular seminoma</td>
<td>Metastasis in right kidney. Right renal vein and IVC thrombosis, retroperitoneal lymphadenopathy, left supraclavicular lymphadenopathy.</td>
<td>Left inguinal orchidectomy, chemotherapy, IVC filter cephalad to thrombus.</td>
</tr>
<tr>
<td>Ucer O et al</td>
<td>2016</td>
<td>35 years</td>
<td>Left testicular pure yolk sac carcinoma</td>
<td>Thrombus in left spermatic vein, bilateral external iliac veins and IVC; multiple retroperitoneal lymph nodes, lung metastasis.</td>
<td>Left high inguinal orchidectomy, chemotherapy, anticoagulants, IVC filter.</td>
</tr>
<tr>
<td>Sun C et al</td>
<td>2017</td>
<td>32 years</td>
<td>Left mixed germ cell testicular tumor</td>
<td>IVC thrombosis, retroperitoneal lymph nodes, metastatic mass at the left renal hilum</td>
<td>Left inguinal orchidectomy, Retroperitoneal lymph node dissection, left nephrectomy, IVC thrombectomy.</td>
</tr>
<tr>
<td>Shukla A</td>
<td>2019</td>
<td>28 years</td>
<td>Right testicular pure embryonal carcinoma</td>
<td>Metastasis to duodenum (D2/3) and liver; large retroperitoneal lymph nodes and thrombosis involving right external iliac, right internal iliac, right common iliac veins extending to IVC.</td>
<td>Right orchidectomy, chemotherapy, anticoagulation, thrombectomy.</td>
</tr>
<tr>
<td>Our case</td>
<td>2020</td>
<td>26 years</td>
<td>Right testicular non seminomatous germ cell tumor</td>
<td>Metastatic retroperitoneal lymphadenopathy with IVC thrombosis.</td>
<td>Right orchidectomy, chemotherapy, anticoagulation.</td>
</tr>
</tbody>
</table>
V. CONCLUSION
Metastatic retroperitoneal lymphadenopathy from testicular tumor can rarely invade IVC and cause IVC thrombosis which can rarely present as backache. High index of suspicion is needed to detect primary testicular tumor in cases of IVC thrombosis, especially in young individuals. Comprehensive treatment that is combination of orchectomy, chemotherapy and anticoagulant therapy is usually considered in most of the cases.

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REFERENCES: