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Leiomyosarcoma of the Inferior Vena Cava Presenting as Deep Vein Thrombosis

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ABSTRACT

Leiomyosarcoma of the inferior vena cava is a rare smooth muscle sarcoma with a variable presentation. We report a case of inferior vena cava leiomyosarcoma with the sole presenting symptom of lower extremity edema, with an initial diagnosis of deep venous thrombosis. Further evaluation with a venogram and computed tomography scan of the patient's abdomen and pelvis revealed a wall-adherent filling defect and soft tissue mass and subsequent biopsy revealed leiomyosarcoma of her inferior vena cava. Our patient was treated with a thrombectomy and excision of her tumor and was then provided chemotherapy as an outpatient with resolution of her symptoms. Such a case demonstrates a rare underlying etiology of the common presenting symptom of lower extremity edema.

Introduction

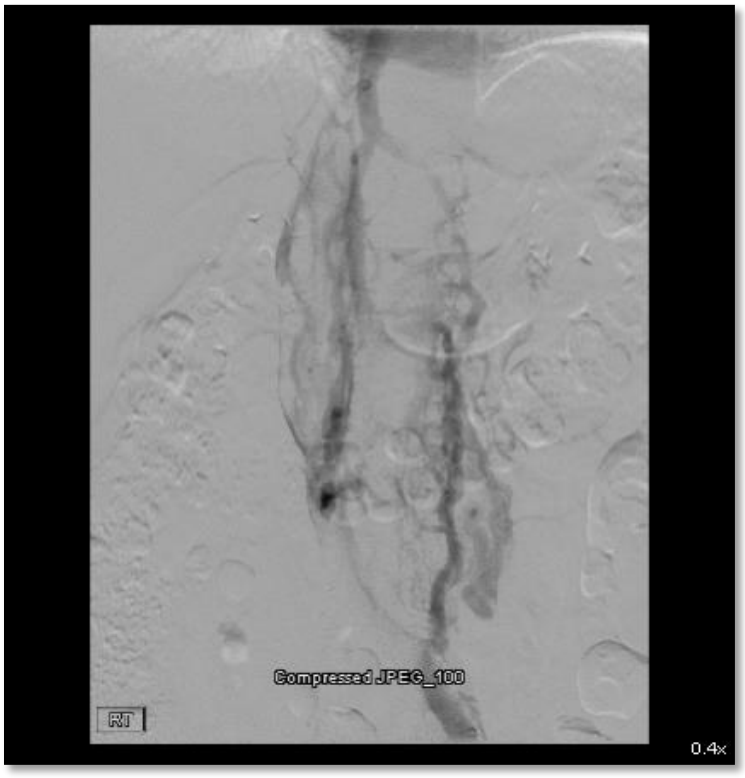
Leiomyosarcomas are soft-tissue sarcomas of smooth muscle and are the most common sarcomas of large blood vessels. While leiomyosarcomas as a whole are one of the most frequent soft tissue sarcomas, inferior vena cava (IVC) leiomyosarcomas are rare, causing less than 0.5% of adult soft tissue sarcomas.[1,2] The presenting symptoms are commonly varied and vague, including abdominal distention, lower extremity swelling, dyspnea, and weight loss. Deep venous thrombosis (DVT) has commonly been described in patients with leiomyosarcoma of the inferior vena cava.[3] Although leiomyosarcoma is a rare cause of lower extremity DVT due to its low prevalence, DVTs often occur in leiomyosarcomas of blood vessels because their location increases thrombosis risk. Due to often nonspecific signs and symptoms, there is often a delay in diagnosis and treatment. Surgical resection remains the only cure, however, many patients present with advanced disease and metastasis at the time of diagnosis and are not eligible for surgery.[3,4] Therefore, in cases with additional abnormalities in the appearance of a DVT, imaging or biopsy is recommended. Prompt evaluation, diagnosis, and treatment are critical and improve overall outcomes for patients with leiomyosarcoma of the IVC.

Case presentation

A 58-year-old female with a history of chronic venous insufficiency presented to her primary care physician with worsening bilateral lower extremity edema. She was initially treated with compression stockings but had no improvement after four months, so she was referred to a vascular surgeon for a superficial venous ablation of her right leg due to the persistence of her symptoms. Lower extremity venous Doppler ultrasounds performed at that time revealed no DVT. However, a week after her venous ablations, she began to develop significantly worsening right lower extremity edema for which she sought additional treatment. A subsequent right lower extremity ultrasound showed an extensive DVT of the common femoral and deep femoral vein, for which the patient was hospitalized, started on intravenous heparin, and then discharged after two days on apixaban.

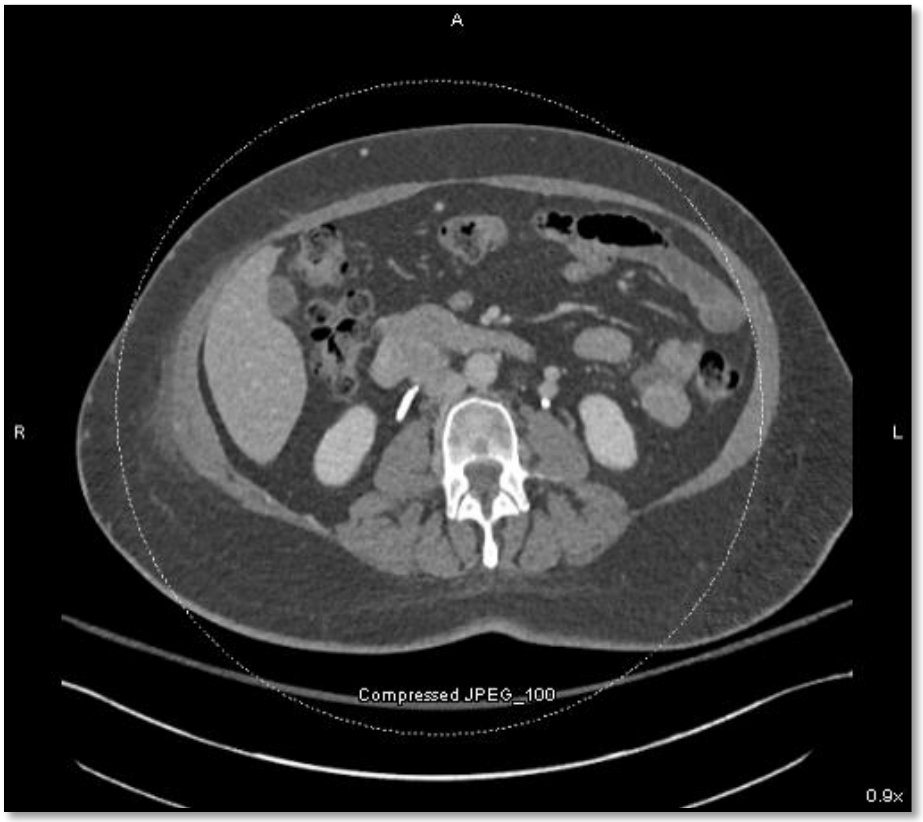
After a week of apixaban, the swelling had worsened and the patient was referred for a thrombectomy by interventional radiology. A venogram performed during this procedure showed chronic thrombosis of the IVC and iliocaval segment as well as a large, wall-adherent, filling defect in the juxtarenal IVC extending to the intrahepatic IVC. Given these abnormal findings, the patient received a computed tomography (CT) scan of her abdomen and pelvis with contrast which revealed a lobulated soft tissue mass at the level of the 2nd/3rd portion of the duodenum concerning for IVC sarcoma. The scan also revealed a thrombus distending the intrahepatic portion of the IVC consistent with tumor thrombus and chronic thrombosis of the infrarenal IVC involving several associated right-sided veins. An inpatient biopsy performed the following day was diagnostic for leiomyosarcoma.

Image 1



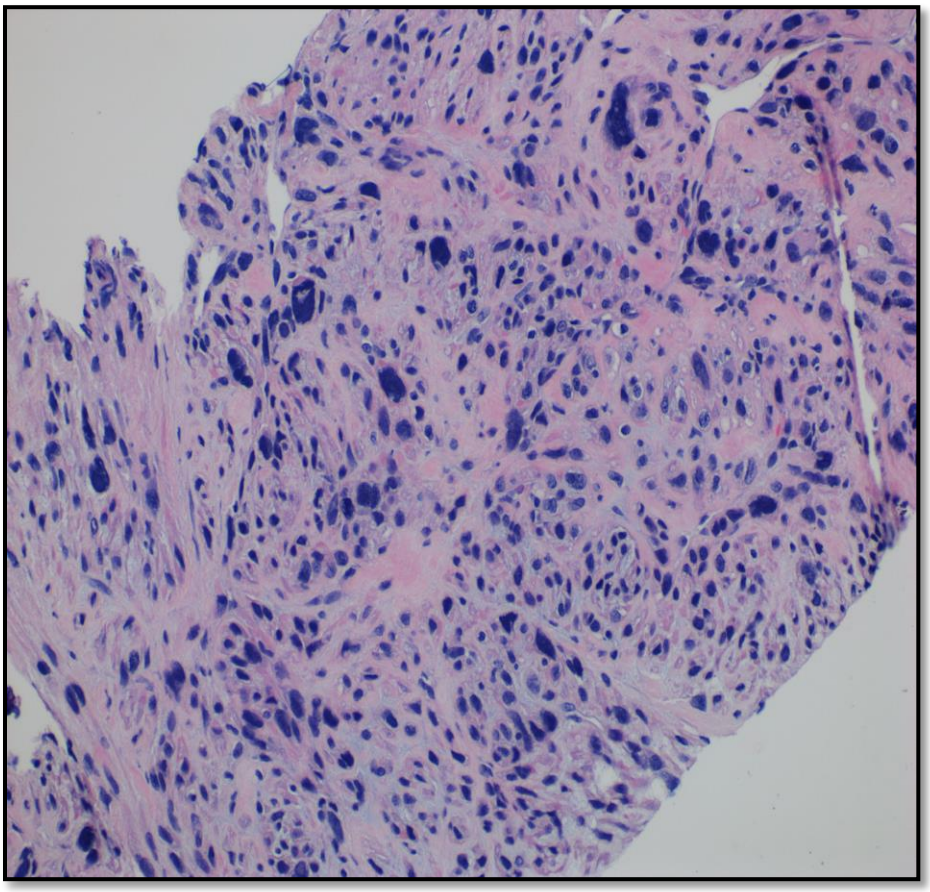
Venogram showing a filling defect in what appears to be a chronically occluded intrahepatic IVC

Image 2



Late phase venous coronal CT images showing a low attenuation mass in the IVC.

Image 3:



The H&E section shows spindle cell proliferation with marked nuclear pleomorphism. There are many cells with very large, irregular hyper chromatic nuclei (see above figure). Mitosis rate was low. Immunohistochemical staining performed on sections of this biopsy show the tumor to be strongly and diffusely positive for design and vimentin, and negative for S100, CD117, DOG1 and CD34 consistent with leiomyosarcoma.

The patient was discharged and referred to a surgeon who performed an exploratory laparotomy with right retroperitoneal sarcoma excision including complete thrombectomy of her IVC tumor thrombus and repair of the IVC. The patient tolerated the procedure well and pathology confirmed a high-grade leiomyosarcoma of the IVC which extended to the margins. The patient's right lower extremity edema greatly improved post-operatively, and she was discharged on apixaban. She was then referred to oncology for initiation of chemotherapy on discharge and was treated with six cycles of adjuvant doxorubicin and dacarbazine.

Discussion

Leiomyosarcomas are malignancies of smooth muscle cells that can arise almost anywhere in the body. They are a common cause of soft tissue and abdomino-pelvic sarcomas, the most common cause of uterine sarcoma, and the most common sarcoma of large blood vessels.[4] However, the overall incidence of IVC leiomyosarcoma is low, with fewer than 300 cases arising from the IVC reported in the literature before the twenty-first century.[1,5] While uncommon in all populations, IVC leiomyosarcomas present more commonly in women with an approximately 3:1 ratio and

are most common in the fifth and sixth decades of life.[1] There are few clear predisposing conditions or risk factors.[3] Initial symptoms are often vague and nonspecific such as fatigue, abdominal bloating, or weight loss. Most reports currently found in the literature describe initial symptoms of abdominal pain or distension, lower extremity edema, and back pain.[6,7,8] Symptoms may also include a palpable abdominal mass, nephrotic syndrome (if the renal vein is affected), Budd-Chiari syndrome (if the hepatic vein is affected), and edema. These tumors also have an increased risk of causing venous thromboembolism through the stasis of blood flow, which likely occurred in this patient. Despite an extensive review of the literature, we were unable to find another case of a patient presenting with only lower extremity edema found to have a DVT along with IVC leiomyosarcoma.[9, 10]

Although differences in presentation may be related to the location of the tumor itself, the severity of symptoms often worsens with disease progression and many patients have advanced disease at the time of diagnosis with further evaluation and diagnosis only initiated after symptoms become more severe. Due to the rarity of IVC leiomyosarcoma, there is no standard work-up or staging process.[1,2] Leiomyosarcoma of the IVC is typically discovered initially through abdominal imaging with CT, magnetic resonance imaging (MRI), or ultrasound and then confirmed with biopsy (often CT-guided given these tumors can present in locations that are technically difficult to reach).[5,11] MRI may be more accurate than CT for diagnosis, however, imaging with CT or MRI is most commonly performed.[12] CT scans can reveal the location of the tumor arising from the IVC and can demonstrate features suggestive of malignancy such as heterogeneous and lobulated appearance as was seen with our patient. MRI with contrast can further help differentiate a mass from a thrombus in the vessel.[13] The mainstays of treatment include surgical excision, sometimes followed by radiation and/or chemotherapy.[5] Surgical excision of the tumor without invasion or metastasis is the only cure, however, most tumors have significant growth at the time of presentation. Metastases are common, especially to the liver, lungs, and bone.[14]

Chemotherapy is most commonly adjuvant, with neoadjuvant chemotherapy more common in inoperable cases. Most chemotherapy regimens are doxorubicin-based, with doxorubicin plus dacarbazine found to have improved overall survival compared to other regimens.[6,15] These tumors portend a poor prognosis, even in comparison to other leiomyosarcomas.[16,17] The prognosis depends on the extent of tumor invasion and histopathological features with an overall 5-year survival of between 30-66%.[10] However, although recurrence rates are high regardless of tumor characteristics, larger tumor size and resection with positive margins are associated with disease free survival. In addition, tumors in the middle segment of the IVC are associated with the highest survival rates most likely because tumors located in this region can compress the surrounding structures including the liver, pancreas, intestines, and kidneys leading to symptoms that prompt earlier evaluation.[16] Therefore, the time to diagnosis and treatment is of critical importance.

Conclusion

Although it is rare, IVC leiomyosarcoma is a detrimental cause of lower extremity edema and DVT. Lower extremity swelling is a common complaint and while further evaluation is not indicated for every patient, it should be considered in those who do not respond appropriately to treatment especially if they have additional persistent symptoms such as abdominal pain, back pain, or generalized edema. In cases of unprovoked DVT, providers should maintain a high index of suspicion for malignancy and should consider performing further evaluation with imaging in addition to age-appropriate cancer screening if indicated based on the clinical presentation. If imaging reveals that a thrombus appears to have an unusual morphology, leiomyosarcomas or other malignancies should be considered and a prompt biopsy should be performed to confirm the diagnosis. Such actions allow for earlier diagnosis, referral, and treatment.

Conflicts of Interest Statement:

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