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Leiomyosarcoma of the Inferior Vena Cava in an HIV-Positive Adult Patient: A Case Report and Review of the Literature

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Data Collection B
Statistical Analysis C
Data Interpretation D
Manuscript Preparation E
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Funds Collection G

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Conflict of interest: None declared

Patient: Female, 64
Final Diagnosis: IVC leiomyosarcoma
Symptoms: Back pain • leg pain • leg swelling
Medication: —
Clinical Procedure: IVC filter placement • CT-guided IVC mass biopsy
Specialty: Oncology

Objective: Rare disease

Background: Leiomyosarcoma is the most common primary malignancy of the inferior vena cava (IVC), and represents approximately 10% of primary retroperitoneal sarcomas. Leiomyosarcoma presents with non-specific symptoms, including abdominal pain or back pain. There is an increased incidence in immunosuppressed individuals.

Case Report: An unusual presentation of IVC leiomyosarcoma is reported in a 46-year-old female patient infected with human immunodeficiency virus (HIV) who was on highly active antiretroviral therapy (HAART) and who had a normal CD4 count of 934, who presented with back pain. Magnetic resonance imaging (MRI) of the lumbar spine showed a mass of the IVC. Initial computed tomography (CT)-guided biopsy of the IVC mass was non-diagnostic. An IVC filter was inserted, and the patient was discharged home, but 20 days later, she returned to the hospital with worsening right flank pain. Laboratory tests showed acute renal failure, and a repeat CT scan showed IVC thrombus extending 5 cm superiorly. When compared with the previous CT, there was an extension of thrombus into both renal veins. Histopathology of a transjugular needle core biopsy showed a moderately differentiated leiomyosarcoma. The patient was transferred to a multidisciplinary sarcoma center for surgical resection, chemotherapy, and radiation therapy.

Conclusions: This report is of a rare case of IVC leiomyosarcoma in a middle-aged HIV-positive woman with a normal CD4 count. Leiomyosarcoma of the IVC is extremely rare, is often detected when advanced, and has a poor prognosis. This case report describes the clinical, imaging, surgical and histopathological findings of leiomyosarcoma of the IVC.

MeSH Keywords: CD4 Lymphocyte Count • Epstein-Barr Virus Infections • HIV • Leiomyosarcoma • Vena Cava, Inferior

Full-text PDF: https://www.amjcaserep.com/abstract/index/idArt/905787

Background

Leiomyosarcoma of the inferior vena cava (IVC) is the most common primary tumor of vena cava and is a very rare malignancy with a few hundred of cases reported worldwide [1,2]. Recently, there have been several case reports on this condition that have demonstrated the challenges of the diagnosis of primary leiomyosarcoma of the IVC. However, the management of this tumor remains controversial [1–3].

Leiomyosarcoma of the IVC occurs more commonly in women, with a prevalence ratio of women to men of approximately 3.5: 1, and with a median age at presentation of 54-years-old [1,3]. Due to the nature of this tumor and its location, symptoms are usually nonspecific, and primary leiomyosarcoma of the IVC may be under-detected for several years before the diagnosis is made. Symptoms may be vague and include weight loss, fatigue, abdominal pain, back or flank pain, as well as lower extremity pain and swelling. In some cases, leiomyosarcoma of the IVC can present with Budd-Chiari syndrome with of abdominal distention, hepatomegaly, ascites, and jaundice [2,4].

Imaging studies using computed tomography (CT) and magnetic resonance imaging (MRI) have been the mainstay of diagnosis of leiomyosarcoma of the IVC. Additional diagnostic modalities may include cavography, ultrasound (US), and echocardiography (ECG) may be needed for preoperative patient workup.

The prognosis of leiomyosarcoma of the IVC is often determined by tumor size, location, differentiation (grade), stage, and the extent of surgical resection required, as chemotherapy and radiation are usually not effective. Patients with leiomyosarcoma of the IVC who are treated with complete surgical resection have a significantly better prognosis and survival compared with other forms of treatment, and the five-year survival rate following surgery has been reported to be approximately 50% [2,5].

Case Report

A 46-year-old female African American presented to the emergency department with a ten-day history of constant back pain (4/10 in severity), radiating to both legs, accelerated by activity and alleviated by rest, associated with lower extremity swelling. About one week before admission, the patient had fallen on a staircase, and although she had sustained no bruises or fractures, she noticed increased intensity of her pain and worsening of the leg swelling which forced her to seek medical attention.

The patients had a past medical history of hypertension, non-insulin dependent diabetes mellitus (NIDDM), who was infected with human immunodeficiency virus (HIV) who was on highly active antiretroviral therapy (HAART) and who had a normal CD4 count of 934 and an undetectable viral load. She had been HIV-positive since 2009, had a history of intravenous drug abuse, and had a previous laminectomy for lumbar spine disc herniation in 2010.

The patient was a current smoker of half a pack of cigarettes per day for 34 years, she was sexually active and used barrier contraception, and denied the use of oral contraceptive use in the recent past. The only significant family history was that the patient's mother died from gastric cancer at 65-years-of-age. On admission to hospital, she was hemodynamically stable.

Physical examination showed moderate tenderness of both calves and bilateral non-pitting edema up to her knees. There was no spinal or para-spinal tenderness, straight leg raising test was positive bilaterally, and deep tendon reflexes normal.

Imaging studies included lower extremity Doppler ultrasound, which did not show deep venous thrombosis (DVT). Magnetic resonance imaging (MRI) of the lumbar spine showed old postoperative changes and degenerative changes of the left lamina at L4–L5. An incidental finding from the MRI was a lesion filling and extending the length of the inferior vena cava (IVC) from L2 through to L4 measuring approximately 8 cm in length (superior to inferior) and 2.7 cm in diameter. A contrast-enhanced computed tomography (CT) scan of the abdomen was performed to exclude a vascular tumor (Figure 1). The abdominal CT scan showed an enhancing thrombus in the mid-IVC extending to above the confluence of the renal veins, with expansion into the aortocaval region at its distal portion.

There was a non-enhancing thrombus in the distal IVC and the left and right common iliac veins and non-occlusive thrombus in the left and right external and common femoral veins. A venocavogram was obtained, and the IVC mass was biopsied under CT guidance. An IVC filter was then inserted, and the patient was started on a full dose of anticoagulation with rivaroxaban.

At the request of the patient, she was discharged home with a plan to be followed-up as an outpatient while waiting for her biopsy results. A few days after her hospital discharge, the histopathology finding from the examination of the first needle biopsy was inconclusive.

Twenty days following her hospital discharge, the patient was readmitted to the emergency room with sudden, sharp, non-radiating, severe (9/10), right-sided flank pain, exacerbated by movement. She denied any fever or dysuria and reported that she had stopped taking rivaroxaban ten days before her

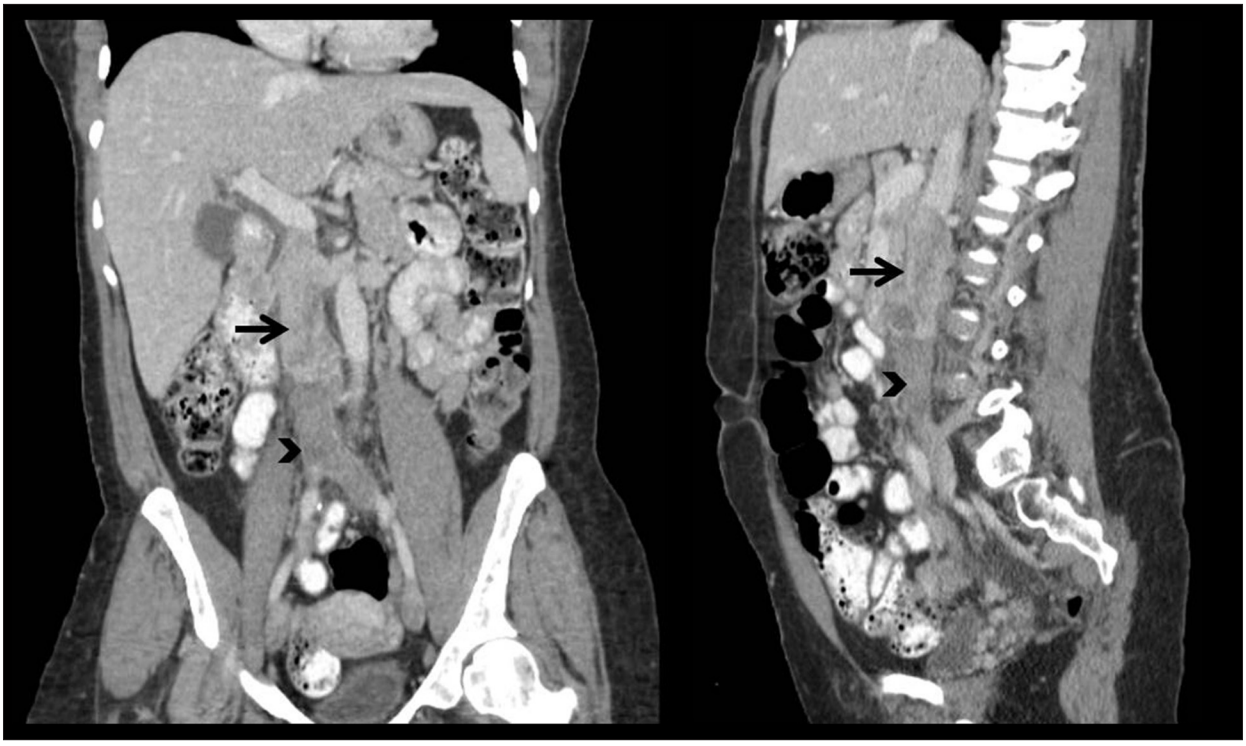

Figure 1. A contrast-enhanced computed tomography (CT) image of the abdomen and pelvis. A contrast-enhanced CT of the abdomen and pelvis shows tumor or thrombus within the mid-inferior vena cava (IVC). Tumor is shown to invade through the wall of the IVC and may be seen to arise from the retroperitoneum. Non-enhancing bland thrombus (arrowhead) is noted inferior to the contrast-enhancing tumor thrombus (arrow) in the distal IVC and in the left and right common iliac veins.

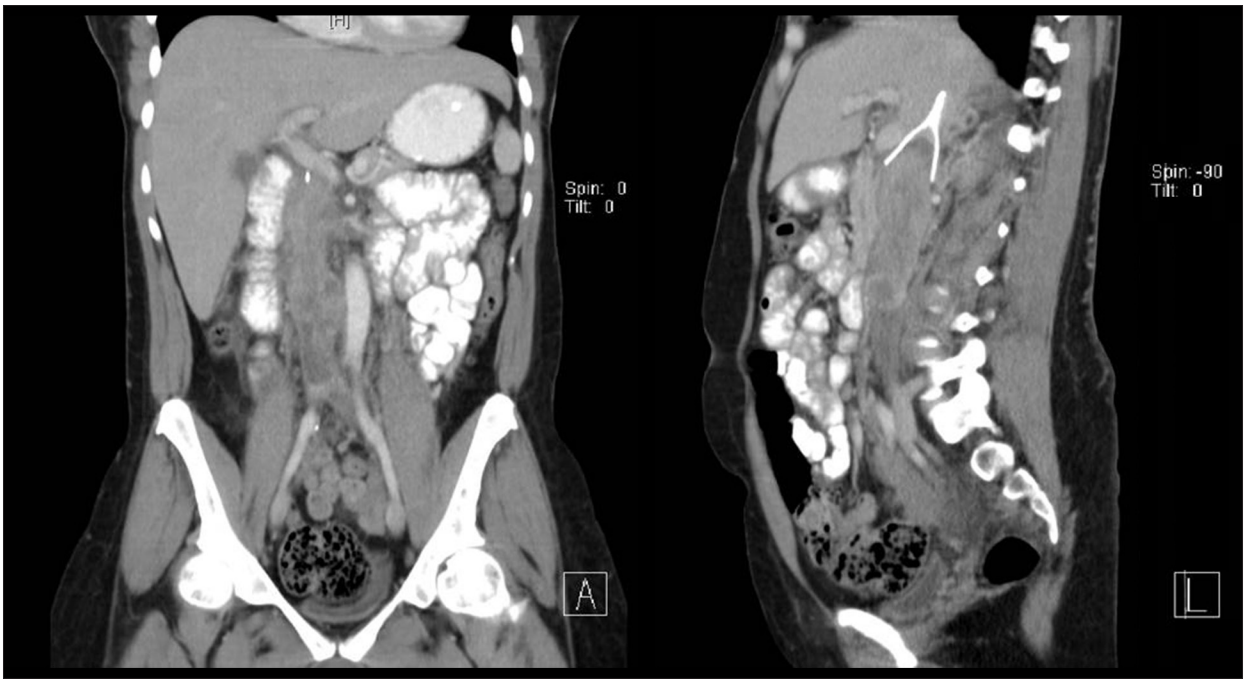

Figure 2. A computed tomography (CT) image of the abdomen and pelvis taken one-month later. One month later, a repeat CT of the abdomen and pelvis without contrast shows extensive thrombosis of the inferior vena cava (IVC) limited superiorly by the suprarenal IVC filter. Thrombus extends about 5 cm superiorly, compared with a previous CT with likely extension into both renal veins. The mass extends outside the wall of the IVC into the aorto-caval space, a few centimeters above the iliac bifurcation.

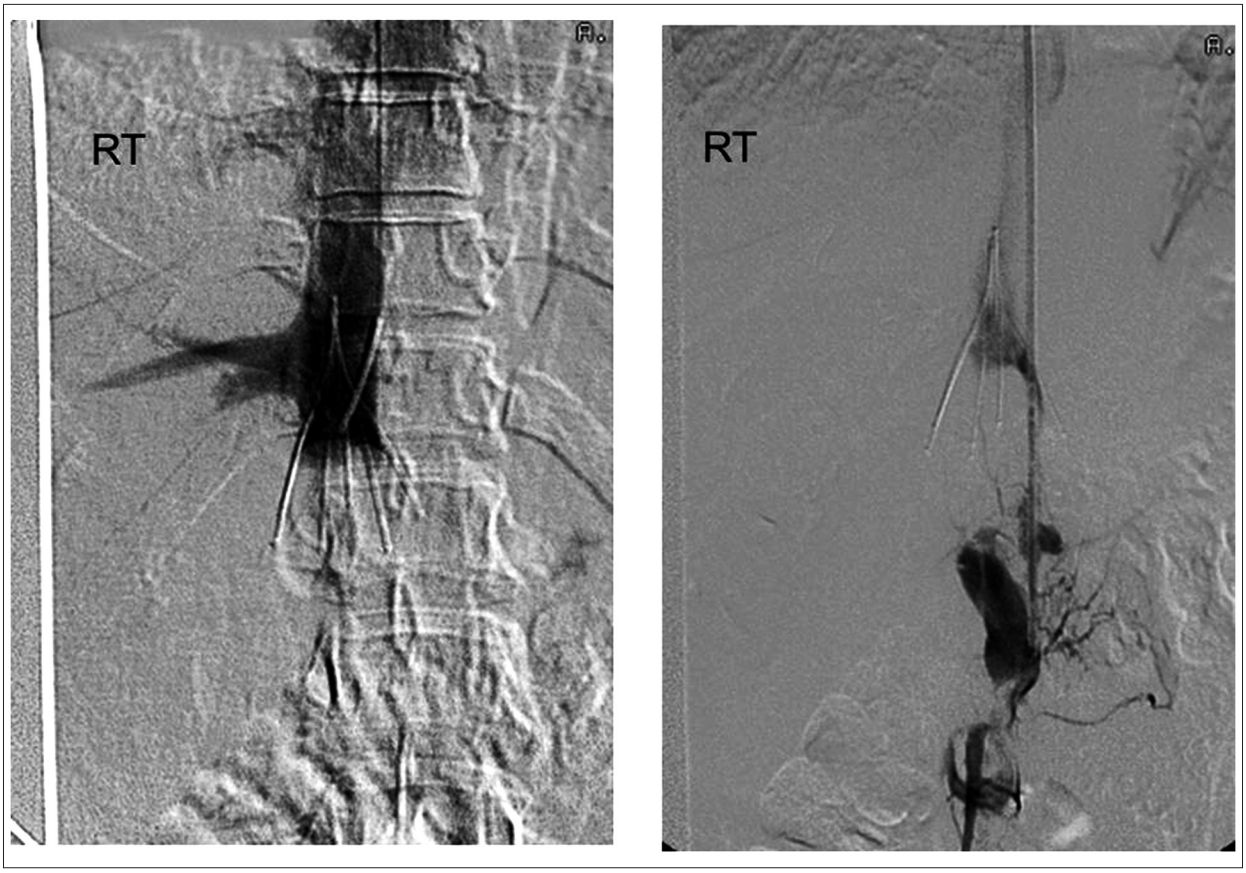

Figure 3. Inferior venocavogram. Inferior venocavogram shows extension of the mass into the inferior vena cava (IVC) filter with a 'reverse meniscus sign' approximately halfway up the filter. The renal veins are not identified in this imaging study and may be partially thrombosed. An inferior right hepatic vein is noted at the level of the upper portion of the filter. A repeat transjugular core biopsy of the IVC mass was then performed.

second hospital admission. Physical examination showed a new finding of right costovertebral angle tenderness (CVAT). Laboratory results showed acute renal failure. A repeat CT of the abdomen and pelvis without contrast showed extensive IVC thrombosis limited superiorly by the suprarenal IVC filter. The IVC thrombus had extended a further 5 cm superiorly when compared with the prior CT and with likely extension into both renal veins (Figure 2). The mass extended outside the wall of the IVC and into the aortocaval space, a few centimeters above the iliac bifurcation. MRI imaging showed a 3.5×2.8×4.0 cm irregularly shaped retroperitoneal contrast-enhancing mass between the distal abdominal aorta and the IVC, which invaded the IVC. A thrombus was also noted in the distal left renal vein. A nephrogram was symmetrical, and no mass in any other organs was identified on CT imaging.

A cavogram was repeated, and a second biopsy was obtained from the mass (Figure 3). This time, the biopsy showed a moderately differentiated leiomyosarcoma (Figure 4). Immunohistochemistry if the tumor tissue showed smooth muscle differentiation of the tumor and established the diagnosis

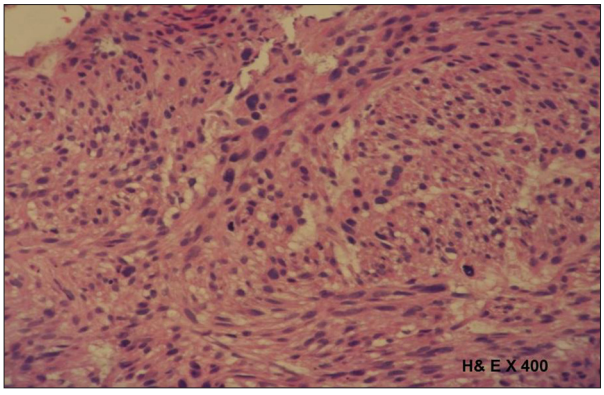

Figure 4. Photomicrograph of the histology of the needle core biopsy of the leiomyosarcoma. Photomicrograph of the needle core biopsy shows a hypercellular spindle cell neoplasm, with cells resembling smooth muscle cells, but with moderate to severe cell pleomorphism, Hematoxylin and eosin (H&E) (Magnification ×400). Immunohistochemistry shows strong positive staining for vimentin, desmin, and smooth-muscle α-actin (SMA). A diagnosis of a moderately differentiated leiomyosarcoma was made.

of leiomyosarcoma of the IVC. *In situ* hybridization for Epstein-Barr virus (EBV) encoded small nuclear RNAs (EBERs) was negative. Cancer staging was performed with a pan CT scan, MRI, and echocardiography, which were negative.

The vascular surgery service was therefore consulted, and the patient was subsequently transferred to another institution for multidisciplinary sarcoma treatments. To date, the patient has survived for five years following her initial diagnosis of primary leiomyosarcoma of the IVC, with no tumor recurrence or functional limitations.

Discussion

Leiomyosarcoma of the inferior vena cava (IVC) is the most common primary malignancy of the IVC and comprises between 5–15% of retroperitoneal soft tissue tumors with only around six hundred cases reported in the literature [2–7]. There has been a previous registry study on leiomyosarcoma of the IVC [2], and some published case series [4–6], but the majority of publications are small case series or case reports [1, 7].

Most of the cases of primary leiomyosarcoma of the IVC occur in women in their 6th decade of life, who present with abdominal pain. Due to its retroperitoneal location, the presentation of leiomyosarcoma of the IVC is usually insidious, and the majority of cases in the published literature were diagnosed at a late stage.

Leiomyosarcoma of the IVC is classified into three groups based on the level of IVC involvement: segment I: infrarenal; segment II; inter-renal and supra-renal, up to but not including the main supra-hepatic veins; segment III: supra-hepatic, up to the right atrium [2,4]. Segment I leiomyosarcoma of the IVC can cause various degrees of lower extremity edema and right upper quadrant abdominal pain, back, or flank pain. Segment II leiomyosarcoma of the IVC can cause right upper quadrant abdominal pain and sometimes causes renovascular hypertension. Segment III leiomyosarcoma of the IVC with hepatic vein involvement can cause Budd-Chiari syndrome with symptoms including abdominal distention, nausea, vomiting, hepatomegaly, ascites, and jaundice [2,4].

Leiomyosarcoma of the IVC usually grows via intraluminal or extraluminal growth and local spread [8,9]. In most cases, imaging studies show an IVC filled with tumor, as well as extraluminal growth in the retroperitoneum. When there is an extraluminal expansion, the diagnosis of leiomyosarcoma of the IVC is often mistaken for primary leiomyosarcoma arising from retroperitoneal smooth muscle, as in our patient. Current literature considers such tumors as leiomyosarcoma of the IVC if there is predominantly intraluminal growth or if the segment of the involved IVC needs to be resected with the extraluminal tumor [8,9].

Imaging methods usually include CT, MRI, cavography, ultrasound, and echocardiography. Contrast-enhanced CT can typically demonstrate a large, lobulated, non-calcified heterogeneous mass with peripheral enhancement. While CT is important to localize the tumor, in the majority of cases of leiomyosarcoma of the IVC, gadolinium-enhanced MRI is needed to evaluate tumor expansion, morphology, and collateral vessels, as well as to distinguish tumor from thrombus, and to establish the staging before surgery [8,9].

The incidence of smooth muscle tumors is increased in immunosuppressed patients, including in patients with human acquired immunodeficiency syndrome (AIDS) and organ transplant recipients, but most of these smooth-muscle tumors have been reported in children [10–12]. Smooth muscle tumors in immunocompromised patients often occur in unusual locations, such as central nervous system, eyes, and skin, and exhibit latent Epstein-Barr virus (EBV) infection [10–12]. These tumors can have incomplete smooth muscle differentiation but show nuclear Epstein-Barr virus (EBV) encoded small nuclear RNAs (EBERs) as a diagnostic feature [13,14]. Latent EBV infection is associated with smooth muscle cell tumors in immunocompromised individuals, but not in immunocompetent individuals [13,14].

EBV-positive leiomyosarcoma has been observed in highly immunocompromised patients [15]. However, three other tumors, Burkitt's lymphoma, Hodgkin's lymphoma, and diffuse large B-cell lymphoma, can occur in either EBV-positive or EBV-negative individuals and are not directly linked to immune deficiency, although all these tumors have an increased incidence in AIDS patients [15]. How the human immune system interacts with EBV and to what extent the failure of controlling viral infection leads to the pathogenesis of leiomyosarcoma of the IVC are still unclear. In our case report, the patient had HIV-infection but was still considered as immunocompetent as the CD4 count was 934 and *in situ* hybridization to detect EBV in the IVC tumor biopsy was negative. Therefore, it is possible that the presentation and characterization of individual cases of leiomyosarcoma of the IVC are determined by the individual's immune state. To our knowledge, this is the first report of a case of leiomyosarcoma of the IVC in an HIV-infected adult patient.

Aggressive surgical resection is the current treatment of choice for primary leiomyosarcoma of the IVC. Complete resection with clear surgical resection margins is feasible in two-thirds of treated patients [5]. The surgical technique used depends on the size and location of the tumor. Mingoli et al. have shown no survival benefits of tangential resection of the IVC

compared with segmental resection, and the preferred technique was reported to be tangential excision followed by patch graft angioplasty [2]. However, reconstruction with an interposition graft should be attempted first, as synthetic patches have a greater risk of thrombosis when compared with autologous vein grafts [16]. Palliative surgical re-resection should be attempted if possible, but the long-term outcome of surgery for IVC leiomyosarcoma has been unsatisfactory, as the reported survival rates at five years and ten years were only 49.4% and 29.5%, respectively; the cancer-free survival rates at five-years and ten-years were only 31.4% and 7.4%, respectively [2]. However, these data probably were not accurate because approximately half of the patients in this study were lost to follow-up. In the three series with sufficient populations and satisfactory follow-up, five-year survival rates after radical resection were 53.3% [5], 33% [6], and 34.8% [4], respectively.

There are controversial reports on the role of neoadjuvant and adjuvant therapy for leiomyosarcoma of the IVC. While some studies advocate postoperative chemotherapy and concomitant radiation therapy [5] and demonstrate prolonged disease-free interval with pre-and postoperative chemotherapy, and independent of radiation therapy [17], other studies show no benefit from postoperative chemotherapy and radiation and recommend neoadjuvant therapy for high-risk leiomyosarcoma [18].

Recently, manipulation of immune checkpoint inhibitors, such as CTLA4 or PD-1 with targeted antibodies has recently emerged as an effective anticancer strategy in many malignancies, and in a recent case series study reduced disease progression and improved disease stability were observed in patients with metastatic or unresectable leiomyosarcoma treated with the anti-PD1 therapeutic monoclonal antibody, nivolumab, with or without the tyrosine kinase inhibitor, pazopanib [19].

Conclusions

Leiomyosarcoma of the IVC is a rare and aggressive diagnosis. This case report of a 46-year-old HIV-infected female patient with a CD4 count of 934, suffering from back pain and lower extremity edema, and diagnosed with EBV-negative leiomyosarcoma of the IVC by transjugular core needle biopsy. The patient underwent surgical resection, chemotherapy, and radiation therapy. To date, the patient has survived approximately five years following her initial diagnosis, with no cancer recurrence or functional limitations. Treatment of leiomyosarcoma of the IVC is surgical resection, but adjuvant chemotherapy and radiation, as well as new targeted cancer therapies are all options to be considered, given the poor prognosis for leiomyosarcoma of the IVC.

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