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Diagnosis and management of inferior vena cava leiomyosarcoma: review of the literature with a case presentation

İnferior vena kava leiomiyosarkomda tanı ve tedavi: Literatür derlemesiyle birlikte bir olgu sunumu

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Inferior vena cava (IVC) leiomyosarcoma is a rare clinical entity. The best treatment for this rare tumor is complete surgical resection of the tumor and consequently resection of IVC leading to the need for venous reconstruction. Ligation of IVC after resection or reconstruction including primary repair, patch repair or tube grafting with synthetic or biological materials are available. As the current knowledge of IVC sarcomas is based primarily on case reports and small case series, it is of utmost importance to report individual cases. In this article, we report a 69-year-old female with IVC leiomyosarcoma who underwent reconstruction with a Dacron tube graft in the light of clinical characteristics of the disease from diagnosis to treatment along with a detailed review of the literature data.

Key words: Inferior vena cava; leiomyosarcoma; vascular tumor.

İnferior vena kava (İVK) leiomyosarkomu, nadir görülen bir hastalıktır. Bu nadir tümörün en iyi tedavisi, tümörün tamamen cerrahi rezeksiyonu ve dolayısıyla venöz rekonstrüksiyon ihtiyacı doğuran İVK'nin rezeksiyonudur. Rezeksiyon sonrası İVK'nin bağlanması veya primer onarım, yama ile onarım veya sentetik ya da biyolojik materyallerle tüp greft konulması gibi farklı rekonstrüksiyon yöntemleri mevcuttur. İnferior vena kava leiomyosarkomlarına ilişkin mevcut bilgiler olgu sunumları ve küçük olgu serilerine ait olduğu için, olgu sunumlarının bildirilmesi önemlidir. Bu yazıda, İVK leiomyosarkomu olan ve Dacron tüp greft ile rekonstrüksiyon uygulanan 69 yaşında kadın bir olgu, İVK leiomyosarkomalarının tanıdan tedaviye klinik özellikleri, literatür verileri eşliğinde incelenerek sunuldu.

Anahtar sözcükler: İnferior vena kava; leiomyosarkom; vasküler tümör.

Inferior vena cava (IVC) leiomyosarcoma is a rare clinical disease. The first case was described from an autopsy performed by Perl in 1871,[1] and since that time, only a few hundred cases have been reported.[2] In 1992, the International Registry of IVC leiomyosarcomas was established to study the pathogenesis and natural history of this tumor and a total of 218 cases were collected at that time.[3] In a comprehensive review of the literature after 1992, another study was comprised of 211 cases, regarding that approximately 418 total cases of IVC leiomyosarcoma were reported in the literature.[4] This low number emphasizes the importance of the need to report individual cases. The best treatment for this rare condition is complete surgical resection of the tumor with subsequent resection of the IVC because of the need for venous flow continuity. Ligation of the IVC after resection or the use of different methods of reconstruction, such as primary repair, patch repair, or tube grafting with synthetic or biological materials, have been suggested. In this report, we review the literature and also present a case of IVC leiomyosarcoma that was surgically resected and reconstructed with a Dacron tube graft.

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REVIEW

Tumors of the IVC are rare and often malignant and can be either primary or secondary in origin. Primary tumors originate from within the vessel wall while secondary tumors originate in the adjacent tissue and surround, compress, or invade the IVC.[2] The most common primary vascular tumor is leiomyosarcoma, a tumor of mesenchymal origin that develops from the smooth muscular fibers of the tunica media.[5] Primary vascular leiomyosarcomas account for 2% of all leiomyosarcomas, with the most common site being the IVC.[6,7] Inferior vena cava leiomyosarcoma is quite a rare tumor, at present slightly more than 400 patients have been enrolled.[8]

Presentation

Leiomyosarcomas of the IVC occur predominantly in females and are seen more frequently in the sixth decade of life.[3,7] They may present with a myriad of symptoms, but this depends on the level of the tumor. In addition, patients may appear asymptomatic due to the slow tumor growth that often occurs with incidental diagnoses. Cardiac arrhythmias, syncope, and pulmonary embolism can be seen at the suprahepatic level, (segment III-upper) and Budd-Chiari syndrome, ascites, nonspecific abdominal pain, biliary symptoms, nausea, renal insufficiency, and nephrotic syndrome can be seen at the suprarenal level (segment II-middle). Moreover, dilated veins on the abdominal wall, palpable mass, abdominal pain, deep venous thrombosis (DVT), and lower extremity edema can be seen at the infrarenal level(segment I-lower) involvement.[2,9] Additional nonspecific symptoms may include fever, weakness, anorexia, nausea, vomiting, night sweat, and dyspnea, some of which may be a result of metastasis.[2,10] These symptoms usually develop at a late stage due to the tumor growth which delays the diagnosis and worsens the prognosis. The tumor spreads locally to the liver, pancreas, and the porta hepatis, and distant metastasis usually occurs in the liver, lungs, and lymph nodes (LNs).

Diagnosis

Since the tumor grows slowly and remains asymptomatic for a prolonged period of time, discovery is made incidentally in 10.5% of patients and at the autopsy in 33%.[5,11] Diagnosis is often via computed tomography (CT) or magnetic resonance imaging (MRI), which typically shows an abdominal mass involving the IVC which extends to the surrounding tissue and possible localized spreading or distant metastasis. Additionally, an abdominal ultrasonography (USG) can provide valuable information about vena cava patency and intraluminal tumor thrombosis but only if adequate visualization is achieved. Furthermore, explorative material can be obtained using USG for histological diagnosis. Another helpful diagnostic tool is cavography, which can detect a filling defect or compression and deviation of the IVC due to intraluminal or extraluminal growth.[12] It is also useful for locating tumors with intraluminal growth because it is possible to perform a transluminal biopsy via this type of angiography. The use of cavography is also important in cases of IVC occlusion in order to demonstrate collateral flow and plan the appropriate surgical strategy.[2,10] Confirmation of the diagnosis is done via a histopathological examination after intravenous, fluoroscopic CT, a duplex-guided biopsy, or usually after surgical resection,[9] as was performed in our case.

Differential diagnosis of IVC leiomyosarcoma includes malignant tumors of the kidneys, as they can have metastatic cavoatrial involvement. The most common type is renal cell carcinoma. Furthermore, the tumor thrombus penetrates the IVC through the renal vein in 4-10% of patients suffering from this type of kidney cancer. Caval resection in conjunction with a thrombectomy is reported to prolong survival in these patients, and cardiopulmonary bypass (CPB) may also be beneficial.[13,14]

Grading and classification

Histological grading and classification has been done by various authors, but no standardization exists at the moment. Anatomical classification of the IVC into three segments is common, but in the literature, this has been carried out using different names. Mingoli et al.[3] described the following three regions within the IVC for tumor involvement: *(i)* the lower segment (infrarenal) (37%), *(ii)* the middle segment (from the hepatic veins to the renal veins) (44%), and *(iii)* the upper segment (from the right atrium to the hepatic veins) (20%).[3,9,15] Similarly, according to Kulaylat,[5] primary tumors of the IVC occur in three different segments: segment I (below the inflow of the renal veins), segment II (from the inflow of the renal veins to the inflow of the hepatic veins, excluded), and segment III (from the inflow of the liver veins up to the right atrium). The authors found that segment II was more often involved (46%) than segment I (38%) or segment III (16%).[5,7] Kieffer et al.[16] also divided the IVC into three segments: the suprahepatic IVC (between the hepatic veins and the right atrium), the suprarenal IVC (between the renal and hepatic veins), and the infrarenal segment (between the confluence of the common iliac veins and renal veins).[2]

Histopathological grading has also been recommended based on the mitotic count. These tumors are typically positive for smooth muscle antibodies (SMAs), vimentin and h-caldesmon, and desmin positivity ranges between 50-80%.[4]

Clinical staging has been suggested as being either occlusive (presenting with a mass, edema, or thrombophlebitis), nonocclusive (asymptomatic or an incidental finding), or terminal (distant metastasis).[9]

Prognosis

Inferior vena cava leiomyosarcoma has a poor prognosis with surgical resection playing a critical role in patient survival. The risk of death is higher for proximal segment disease and is the lowest for middle segmental involvement. In addition, lower limb edema, Budd-Chiari syndrome, intraluminal tumor growth, and IVC occlusion were also determined to be risk factors for increased death.[3,15]

Perioperative mortality ranges from 0-20% in the literature,[17] and the five-year survival rate varies from 33% in one study[18] to 56%[17] in another. Furthermore, Mann et al.[17] calculated the overall survival rate and five-year disease-free survival rate as 56% and 37%, respectively. Meanwhile, the tumor recurrence rate has been reported to be as high as 67% (local recurrence 33% and distant recurrence 48%),[18] with rates of 59%,[17] 53%,[3] and 40%[4] having been reported in other series.

Treatment

Managing IVC leiomyosarcomas is challenging because the primary treatment is complete surgical resection of the tumor with the involved IVC, which leads to the necessity of IVC reconstruction for venous continuity. The goal is to achieve local control, maintain venous return, and prevent recurrence.[13] Complete surgical resection plays a definitive role in patient survival, whereas adjuvant therapy has an unclear role, as neither chemotherapy nor radiotherapy have proven to be effective.[3,16]

Surgical resection was first reported in 1928 by Melchior.[7] Surgical management includes ligation of the IVC, primary or patch repair, and segmental replacement with tube grafting. Ligation after resection has also been suggested by some authors, but reconstruction of the IVC seems to be the most common approach.

A limited resection of the caval wall can be repaired by a simple suture, or patch grafting may be performed to prevent a possible narrowing of the lumen. Several prosthetic or biological materials have been recommended for the reconstruction of the IVC after resection. Autografts like pericardium, peritoneofascial grafts composed of the peritoneum and posterior rectus fascia, or autogeneous vein grafts (mainly the vena saphena manga); or prosthetic grafts made of polytetrafluoroethylene (PTFE), Teflon, or Dacron can be used for patch angioplasty.[13,21] Ringed PTFE prostheses are the preferred grafts for caval replacement rather than biological grafts.[7] Bovine pericardial grafts,[10] fresh IVC allografts,[13] and banked venous homografts[21] have also been mentioned as other options for the reconstruction of the IVC.

Different surgical techniques for tumors involving the renal veins also have been advocated by some. The left renal vein can be ligated because of the existence of important venous collaterals (lumbal, gonadic, and adrenal veins), and these collaterals are generally sufficient for satisfactory venous return without the occurrence of renal insufficiency. Since there are no effective collaterals, right renal venous flow should be conserved. This can be done by the reimplantation of the right renal vein on the vena cava or caval graft or by renal autotransplantation in the right iliac fossa.[7,21]

The use of extracorporeal circulation and veno-venous bypass techniques have also been described in the literature for tumors in the middle and upper part of the IVC.[7,22] Superior vena cava (SVC) leiomyosarcoma is extremely rare and the replacement of the SVC with a bovine pericardial prosthesis using femoro-femoral bypass on a beating heart have been reported.[6]

Although various options exist for reconstructing the IVC, some authors have questioned whether there is an actual need for reconstruction.[23] They concluded that lower extremity edema after ligation of the IVC is well tolerated and that reconstruction is not necessary for tumors below the level of the hepatic veins. On the other hand, graft replacement avoids complications of IVC ligation like DVT, ascites, lower extremity edema, and renal dysfunction.[12] Other authors have also suggested that when the IVC ligation rather than reconstruction is performed, thrombus may form in the blind portion of the IVC and may even extend above the hepatic vein, resulting in Budd-Chiari syndrome.[13] Therefore, it is recommended that an incompletely occluded IVC with insufficient collateralization should be replaced with a prosthesis, whereas a completely occluded IVC that does not involve renal veins inflows and which is richly collateralized can be ligated without functional impairment.[7]

Performing surgery to create an arteriovenous fistula (AVF) either between the aorta and IVC or iliac

vein or between the femoral vessels[9] has also been recommended in order to boost flow velocity, which would then improve the patency of the IVC graft. Proponents of this procedure state that it would make long-term anticoagulation therapy unnecessary.[7,24] However, AVFs are known to be related to complications such as limb edema and high-flow cardiac failure.[9,11]

The role of adjuvant chemotherapy and radiotherapy is not clear and remains controversial at the present time. Preoperative.[15,23] and intraoperative.[16] radiation therapy may have some beneficial effects, such as improving local control. Furthermore, some reports have suggested that radical resection followed by adjuvant chemotherapy should be considered as the optimal therapeutic strategy,[12,24] and others have advocated the possible role of radiotherapy.[15,16,23] However, all of these recommendations need further confirmation since the results may vary according to the individuals involved in the case.

Follow-up

Follow-up of patients operated on for IVC leiomyosarcoma should continue because of slow tumor growth and the possibility of the tumors returning since recurrent tumors can be operated with good long-term results.[11] Postoperative anticoagulation therapy is controversial, but some have recommended this treatment option for six months postoperatively in order to allow for good re-endotelization of the prosthesis. At that time antiaggregant prophylaxis can be substituted.[7]

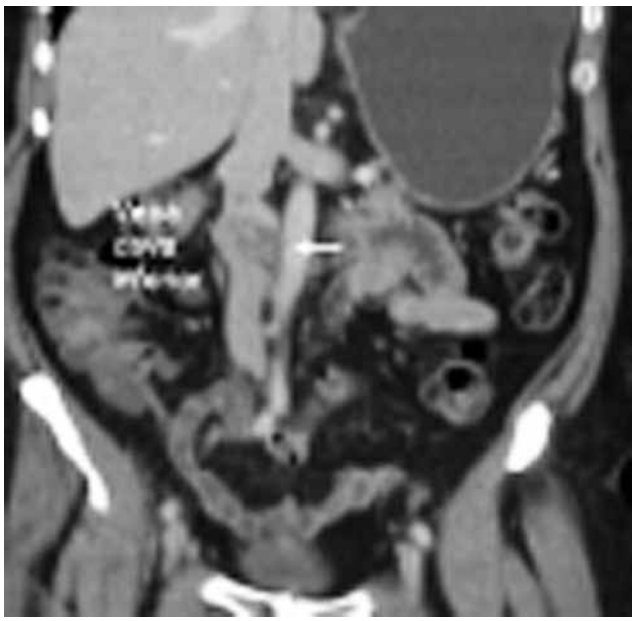

Figure 1. Magnetic resonance imaging demonstrating the solid mass located at the lumen of the inferior vena cava.

The rarity of IVC leiomyosarcomas limits randomized trials, so obtaining information concerning this disease is dependent on case reports, case series, and retrospective review studies. With that in mind, we also present our own experience involving an IVC leiomyosarcoma reconstructed with a Dacron tube graft, which provided good patency one year after the operation.

A 69-year-old female was admitted to the cardiovascular clinic with shortness of breath, pain in her left leg, and bilateral leg edema. A physical examination revealed no signs of an abdominal mass or tenderness, but bilateral leg edema was detected. Routine laboratory tests that included cancer markers were all within normal limits, and echocardiography revealed normal left ventricular function. However, an abdominal CT scan showed a solid, vascular, lobulated mass, extending extraluminally and measuring 5 cm in diameter including the 5 cm segment in the infrarenal region of the IVC. This finding led to the diagnosis of leiomyosarcoma (Figure 1). However, no thrombosis in the IVC was detected, and there were no signs of pulmonary embolism or distant metastases. After evaluating all of the available information, surgery was planned.

The IVC was explored through a median sternotomy incision, and a macroscopic examination revealed an irregular, surfaced, solid mass protruding from the vessel wall in the infrarenal level of the IVC. A longitudinal venotomy showed intraluminal tumor growth that was almost obstructing the lumen of the IVC. In the posterior area of the IVC, the tumor appeared to have moved outside of the IVC toward the

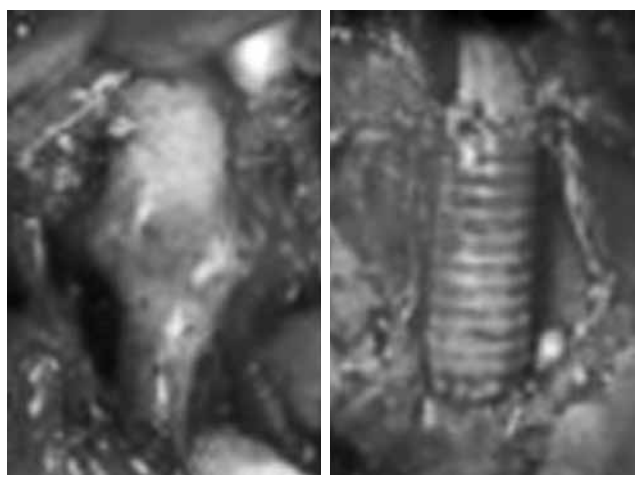

Figure 2. Intraoperative image of the inferior vena cava leiomyosarcoma before and after reconstruction with a Dacron tube graft.

columna vertebralis and fatty tissue. The tumor was then resected along with the vessel wall to provide tumor-free surgical margins. Next, the IVC was resected segmentally, and a 20 mm Dacron tube graft was anastomosed in an end-to-end fashion (Figure 2). Since the caval clamp time was about 25 minutes, a caval shunt was considered unnecessary during the venous reconstruction. The early postoperative course was normal, and the patient was discharged on the postoperative sixth day without any complications. A histopathological examination revealed a high-grade intimal leiomyosarcoma, and an immunohistochemical study showed that the tumor was strongly and diffusely positive for smooth muscle activity, focally positive for desmin, and negative for the S-100 protein. The macroscopic and microscopic analysis of the specimen identified a leiomyosarcoma arising from the IVC. The patient was given low-dose aspirin and warfarin at discharge to maintain graft patency, and she was referred to the oncology department for further therapy. Radiotherapy (RT) was given for one and a half months after the operation, but chemotherapy was not performed. A follow-up CT scan showed no local recurrence or distant metastasis with a patent graft at twelve months postoperatively.

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