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REVIEW

Current update on IVC leiomyosarcoma

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Abstract

Primary leiomyosarcoma of the inferior vena cava (IVC) is a rare soft tissue sarcoma associated with poor prognosis. Patients are often asymptomatic or present with nonspecific abdominal symptoms, which delays initial diagnosis and contributes to poor oncologic outcome. Key imaging modalities include ultrasonography (US), computed tomography (CT), and magnetic resonance imaging (MRI). Characteristic imaging features include imperceptible caval lumen, dilation of the IVC, heterogeneous enhancement of the tumor, and development of extensive collateral circulation. Surgical resection is the mainstay of treatment, while chemotherapy and/or radiation may serve as therapy adjuncts. This article reviews the pathology, clinical findings, imaging features and management of IVC leiomyosarcoma.

Keywords Leiomyosarcoma · Inferior vena cava · Retroperitoneal · Computed tomography · Magnetic resonance imaging

Abbreviations

IVC Inferior vena cava
US Ultrasonography
CT Computed tomography
MRI Magnetic resonance imaging

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Background

Primary leiomyosarcoma of the inferior vena cava (IVC) is a very rare mesenchymal tumor associated with extremely poor prognosis [1]. It accounts for less than 1 in 100,000 of all adult malignancies and approximately 0.5% of adult soft tissue sarcomas [2–4]. Notably, approximately less than 450 cases are described in the literature [3]. However, these tumors are the most common primary tumors of the IVC [4]. IVC leiomyosarcoma predominantly occurs in females with female/male ratio of approximately 3:1 [2]. These tumors tend to be more common in the fifth or sixth decades of life, although any age group may be affected. These slow-growing tumors can arise in any vein, but usually develop in the IVC and accounts for 50% of all venous leiomyosarcomas [5].

IVC leiomyosarcomas are classified according to the IVC segment involved: lower segment, middle segment, and upper segment, with the middle segment being the most commonly affected segment [5]. IVC leiomyosarcomas are associated with three tumor growth patterns: extraluminal (62%), intraluminal (5%), and combined extraluminal and intraluminal (33%) [4].

Patients may be asymptomatic or present with nonspecific symptoms, including malaise, weight loss, nausea, vomiting, and abdominal pain [1, 4]. Due to its silent or nonspecific presentation, the disease is frequently diagnosed at an advanced stage, and patients have poor long-term prognoses given subsequent local recurrence and metastases. Various

imaging modalities, including ultrasonography (US), computed tomography (CT), and magnetic resonance imaging (MRI), play vital roles in the diagnosis and follow-up of this disease which can help guide management. This article reviews the pathology, clinical findings, imaging features, and management of IVC leiomyosarcoma.

Pathology and immunohistochemistry

On a macroscopic level, leiomyosarcomas are usually well-circumscribed, gray-to-white fleshy masses that may demonstrate hemorrhage, necrosis, or cystic changes [4]. Extraluminal IVC leiomyosarcomas often achieve a large size (greater than 10 cm) in the retroperitoneal space before resulting in symptoms. Because of its extent, their pseudocapsules often contain tumor cells. Conversely, intraluminal IVC leiomyosarcomas are often small and firmly attached to the vessel wall. Due to their small size, they do not generally demonstrate hemorrhage or necrosis. Combined extraluminal and intraluminal IVC leiomyosarcomas demonstrate characteristics of each subtype [4]. Microscopically, leiomyosarcomas have atypical interlaced patterns with bundles of spindle-shaped cells with elongated nuclei [4]. The neoplastic cells are immunopositive for smooth muscle actin, caldesmon, and desmin. Sometimes, they may express positive vimentin and epithelial membrane antigens [6]. Moderate or poor tumor differentiation in combination with location of the disease are major factors in determining patient prognoses [1, 7]. In particular, cases with upper segment with right atrial involvement, predominant intraluminal growth pattern, and compromised liver function are associated with poor prognoses [7].

Interestingly, several immunohistochemical biomarkers are associated with tumor recurrence and disease-specific survival. β-catenin is a downstream signaling protein in the Wnt pathway involved in oncogenesis, and high expression of cytoplasmic β-catenin in vascular leiomyosarcomas ($p = 0.06$) is associated with higher distant recurrence and lower survival [8]. Also, high expression of IGF-1R in vascular leiomyosarcomas ($p = 0.04$) is associated with lower time to distant recurrence and lower survival [8]. Additionally, mutations in the Pten gene are frequently reported in leiomyosarcomas, as Pten loss results in dysregulation of phosphatidylinositol 3-kinase (PI3K), hyperactivation of Akt, increased cellular proliferation, inhibition of apoptosis, defective double strand break repair. Immunohistochemical analysis of the PI3K/Akt pathway may help guide management decisions; in the setting of Pten-altered leiomyosarcoma, poly ADP-ribose polymerase (PARP) inhibitors and mammalian target of rapamycin (mTOR) inhibitors can be potentially used [9].

Clinical features

The clinical presentation depends on the location, growth pattern, and segment involvement of the IVC leiomyosarcoma. IVC leiomyosarcoma in the upper segment, also known as infrarenal involvement (from the iliac veins up to the renal veins), may manifest as Budd-Chiari syndrome due to the hepatic vein outflow obstruction. IVC leiomyosarcoma in the middle segment (from the renal veins to the hepatic veins) may present as nephrotic syndrome and right upper quadrant pain, due to obstruction of the renal vein drainage. IVC leiomyosarcoma in the lower segment (from the hepatic veins to the right atrium) can manifest as lower extremity edema, due to inflow obstruction. Unfortunately, common presenting symptoms are nonspecific and include abdominal pain, weight loss, abdominal mass, nausea, and vomiting, which may delay diagnosis [4]. Intraluminal leiomyosarcomas are more likely to cause symptoms earlier than those that are purely extraluminal. Tumor fragments may dislodge from the primary retroperitoneal tumor and embolize into the pulmonary arteries or even into the right atrium resulting in pulmonary emboli, tricuspid valve impairment, and cardiac arrhythmia. IVC venous outflow obstruction could also potentially result in hepatic and renal failure.

Imaging features

Various imaging modalities can be utilized to diagnosis, staging, and surveillance of IVC leiomyosarcomas (Fig. 1). Due to their nonspecific clinical presentations, US and CT are often the first imaging modalities used in their work-up. IVC leiomyosarcomas are often unexpected findings on imaging. CT is very helpful in identifying the tumor origin, invasion, and metastases in IVC leiomyosarcomas (Figs. 2, 3). MRI serves as a useful imaging adjunct in characterizing adjacent invasion and tumor thrombosis (Fig. 4) [10].

US may be used to evaluate the IVC; however, sonographic features of IVC leiomyosarcoma are nonspecific. Tumor is often heterogeneously hypoechoic on grayscale US (Fig. 1). Doppler US may demonstrate absent or abnormal flow in the IVC due to the intraluminal tumor. However, tumoral vascularity may be present on color Doppler. Due to central obstruction in the IVC, Doppler evaluation of the lower extremities may show abnormal Doppler waveform with reversal of flow. Large intraluminal tumors tend to become more heterogeneous and can extend into the hepatic veins and heart [4]. When the tumor is solely extraluminal, the tumor's solid components

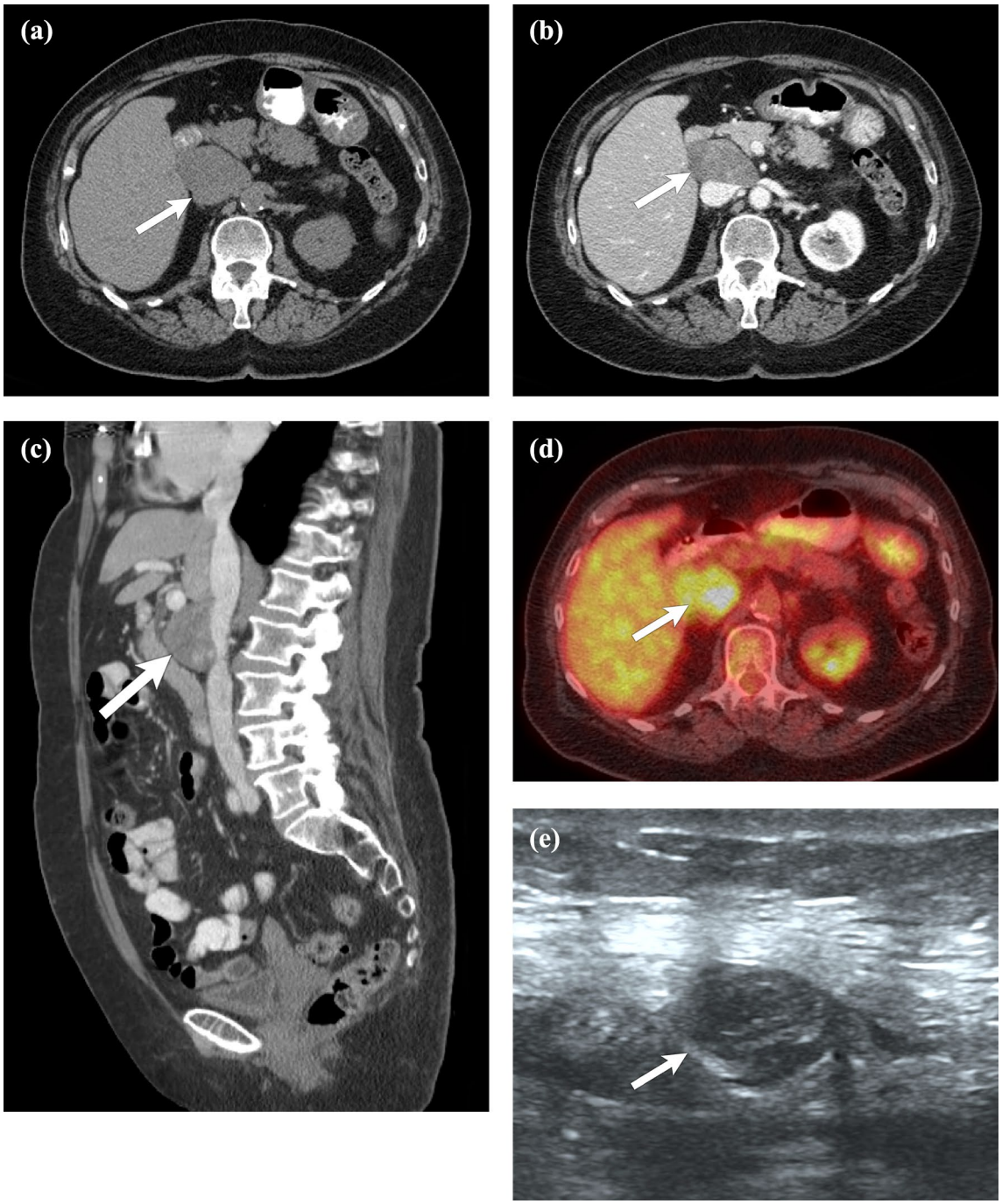

Fig. 1 A 79-year-old female with extraluminal IVC leiomyosarcoma. **a** Axial non-contrast CT and **b** intravenous contrast-enhanced CT in the portal venous phase shows a heterogeneous mass (arrow) arising from the wall of the IVC. **c** Sagittal reformat CT image shows the tumor (arrow) and its relationship to the anterior wall of the IVC. **d** Axial fused PET/CT image shows the tumor (arrow) to be FDG avid. **e** Intra-operative ultrasound shows the heterogeneous hypoechoic tumor (arrow) arising from the wall of the IVC

are usually isoechoic to liver and may contain internal cystic spaces. Combined intra- and extraluminal extension is inadequately evaluated with this imaging modality due to poor mural definition. Unfortunately, limitations also include operator dependence and artifacts from overlying bowel gas and patient's body habitus [11]. In the operative setting, US has been used to examine the surrounding vasculature, including venous shunts, and determine the safety of clamping and resecting the IVC [12]. It has also been used to demonstrate adequate venous flow following IVC reconstruction [13].

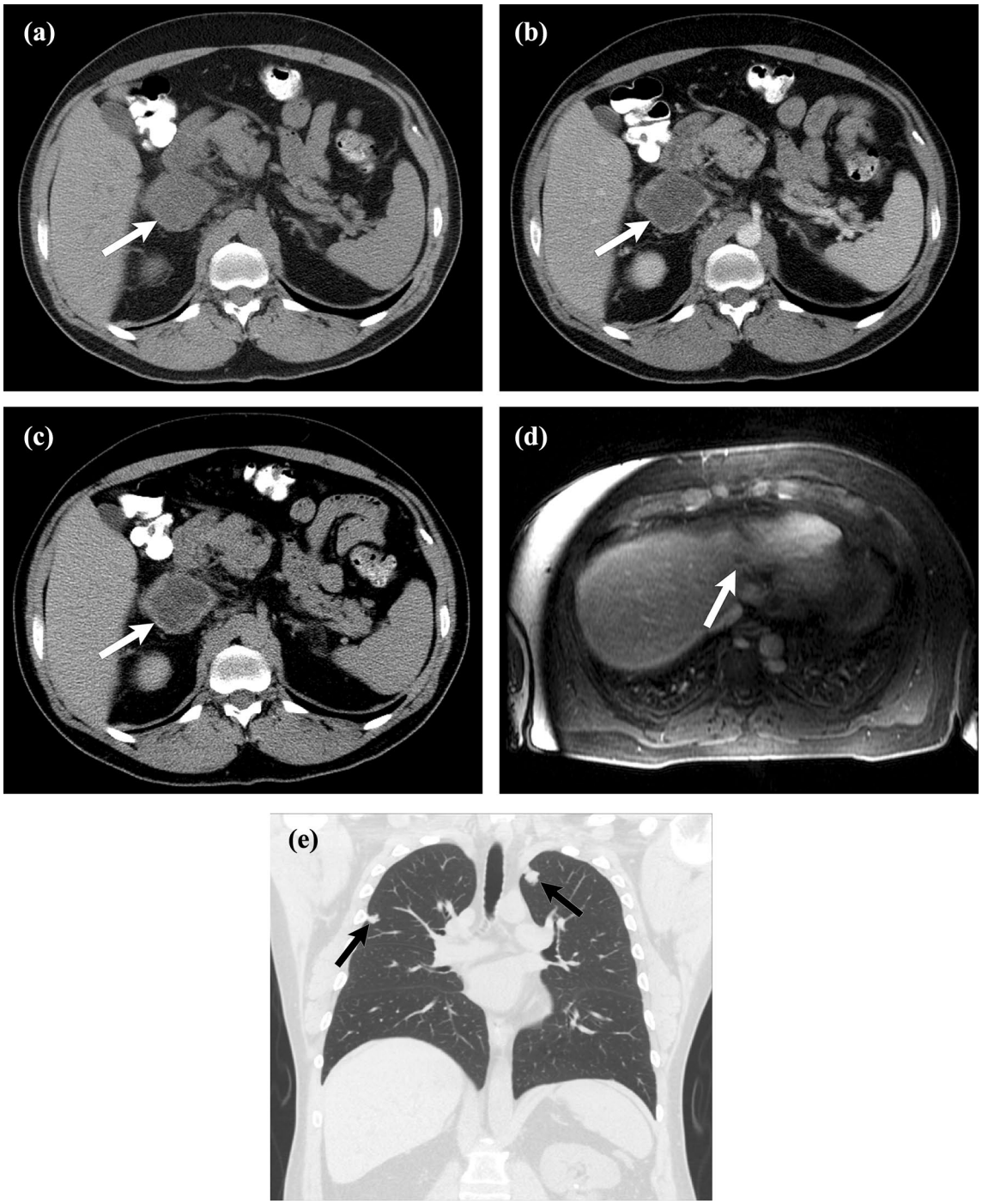

Fig. 2 A 48-year-old male with intraluminal IVC leiomyosarcoma. **a** Axial non-contrast, **b** portal venous phase and **s** delayed phase CT image of the upper abdomen shows an expanded IVC with heterogeneous tumor (arrow). Note the heterogeneously enhancing solid components at the peripheral aspect of the intraluminal tumor, while the central portions are necrotic. Patient underwent chemotherapy followed by surgical resection. Follow-up was performed with MR of the abdomen and the pelvis and CT of the chest. **d** Axial T1-weighted, fat-suppressed post-contrast fast spin echo MR image shows a small subtle ring enhancing lesion (arrow) in the left hepatic lobe which was biopsy-confirmed to be metastasis. Patient underwent embolization of the liver metastasis. **e** Coronal CT chest in lung windows demonstrates multiple bilateral pulmonary nodules (arrows). CT-guided lung biopsy-confirmed pulmonary metastases

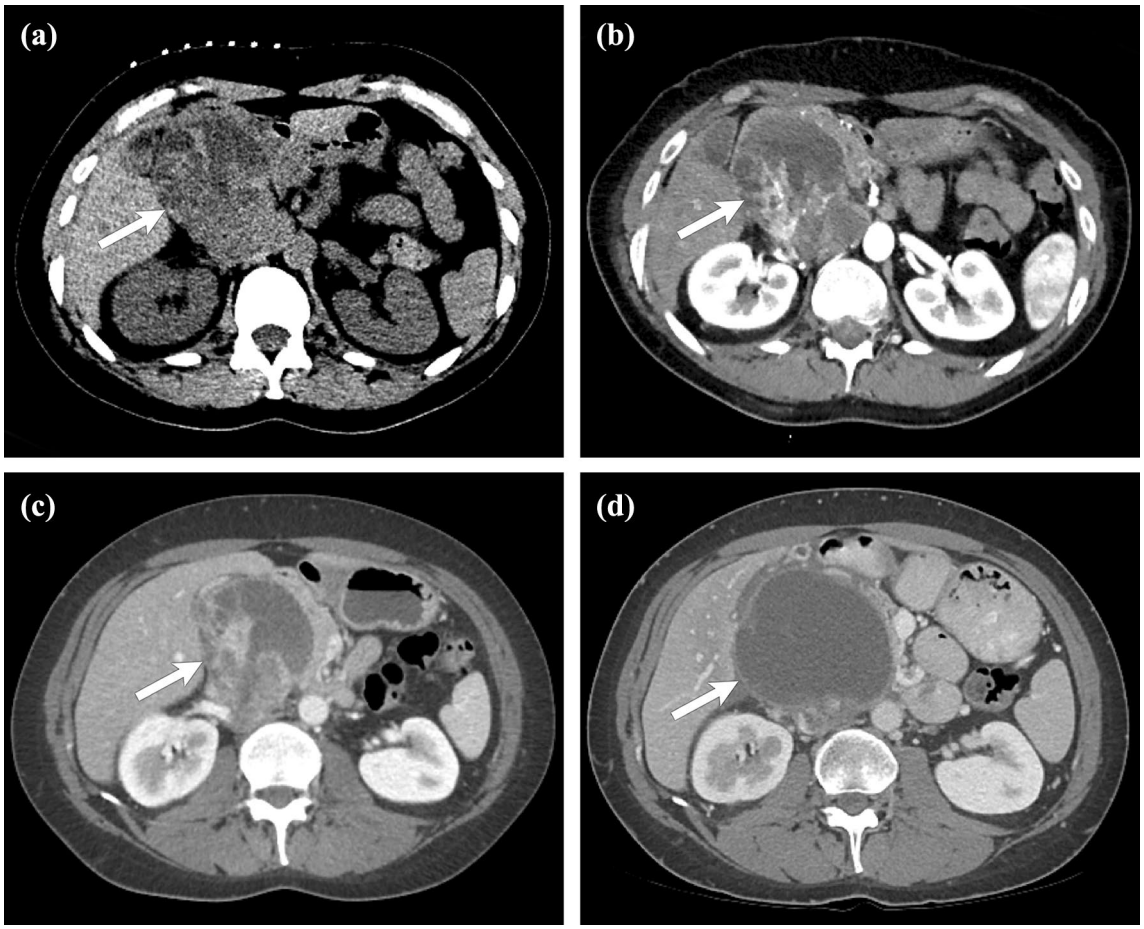

Fig. 3 A 42-year-old female with mixed intraluminal and extraluminal IVC leiomyosarcoma. **a** Axial non-contrast, **b** arterial phase and **c** portal venous phase CT image of the upper abdomen shows a large heterogeneously enhancing tumor (arrow) arising from the IVC. Note that the IVC is expanded due to the intraluminal component of the tumor, but the tumor has extended beyond the confines of the IVC, infiltrating into the adjacent retroperitoneal space. Patient received chemotherapy with doxorubicin and dacarbazine, followed by radiotherapy (50.4 Gy in 28 fractions). **d** Axial CT post chemo-radiotherapy demonstrates excellent response to therapy. The tumor (arrow) is now markedly hypodense, consistent with response to therapy

CT serves as the workhorse in oncologic imaging given tis various advantages, including excellent spatial resolution and ready availability. To the authors' knowledge, there is no standard CT protocol for imaging IVC leiomyosarcoma, owing to the rarity of this tumor. However, a useful CT protocol for IVC assessment would include pre-contrast CT and intravenous contrast-enhanced CT images acquired in the arterial, portal venous and delayed phases (Figs. 1, 2, 3). Acquisition of arterial phase images may allow better assessment of the relationship of the tumor to the adjacent major arterial structures for preoperative planning and also help in the detection of hypervascular metastases. Portal venous phase (60 s post intravenous contrast administration) images demonstrate better opacification of the IVC and contrast enhancement in the IVC [11, 14]. However, there is denser contrast enhancement in the renal and suprarenal IVC than the infrarenal IVC in the portal venous phase; ideally, delaying this phase to 70–90 s after contrast administration achieves uniform contrast enhancement in the IVC [14, 15]. Multiplanar CT with sagittal and coronal reconstructions help reveal the craniocaudal extent of IVC involvement (Figs. 1, 5). Common CT features include an irregularly distended IVC filled with a complex, lobulated, heterogeneously enhancing soft tissue mass (Figs. 1, 2, 3, 5). Tumor heterogeneity occurs due to internal hemorrhage and necrosis, and areas of recent hemorrhage may demonstrate increased attenuation on CT [16]. The tumor's primary growth pattern can be defined, as intraluminal involvement is suggested by an irregularly enhancing intraluminal mass obstructing and extending along the IVC course (Fig. 2). A potential diagnostic conundrum may occur with differentiating IVC leiomyosarcomas with extraluminal growth pattern versus other venous retroperitoneal leiomyosarcomas. Extraluminal tumor is often larger than 10 cm and demonstrates

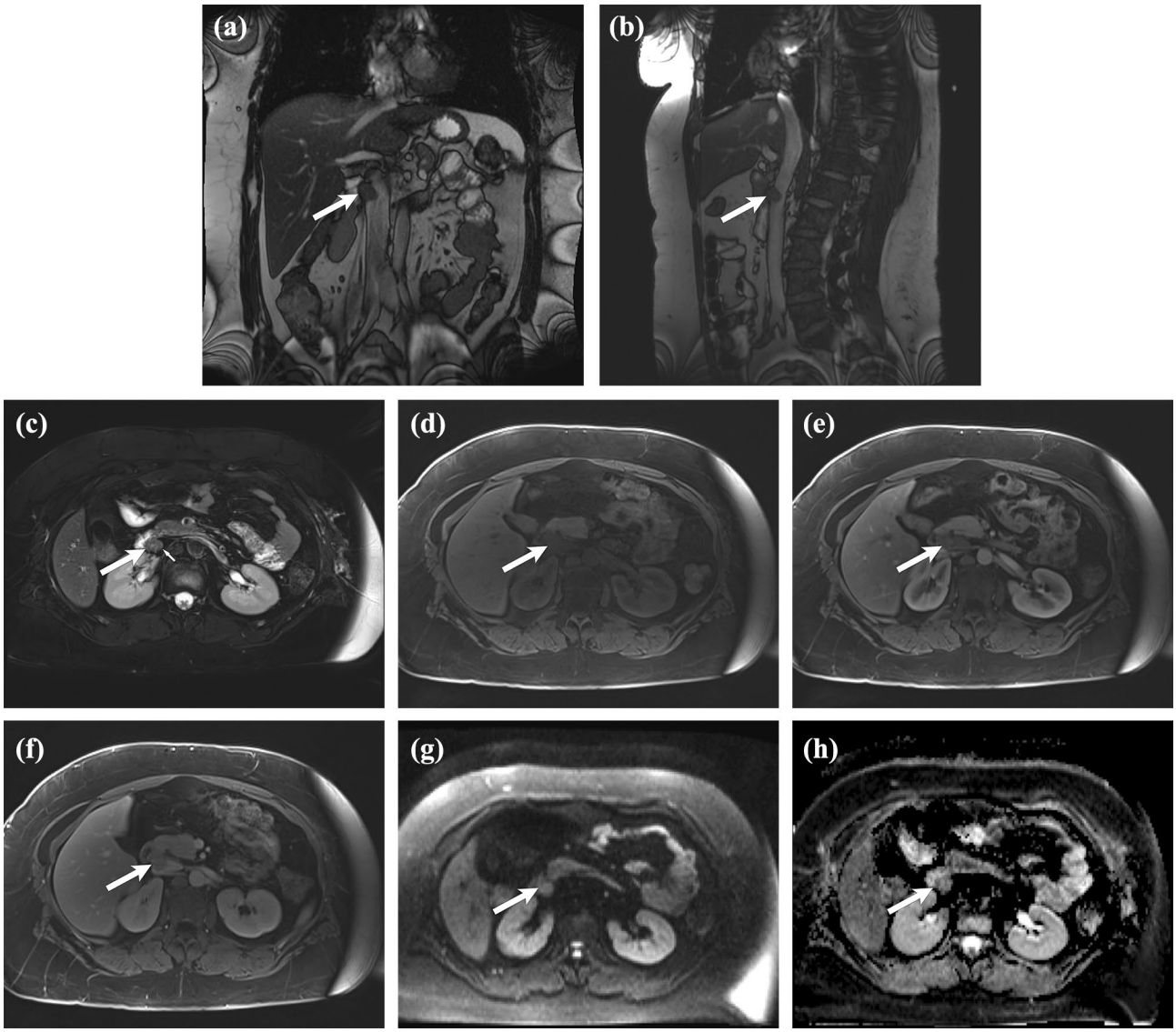

Fig. 4 A 31-year-old female with IVC leiomyosarcoma. **a** Coronal and **b** Sagittal True fast imaging with steady state precession (True-FISP) MR images show a 2 cm mass (arrow) arising from the IVC. **c** Axial T2-weighted fat-suppressed MR image shows a mass (large arrow) with intermediate signal intensity arising from the IVC. Note the flow void within the normal portions of the IVC (small arrow). The tumor is difficult to delineate from the normal flow void on the noncontract images, and can be easily misdiagnosed on the non-contrast images. **d** Axial T1-weighted fat-suppressed 3D gradient echo pre-contrast MR image shows the tumor (arrow) arising from the IVC. **e** Intravenous gadolinium-enhanced portal venous phase and **f** delayed phase MR images of the abdomen show the heterogeneously enhancing IVC leiomyosarcoma (arrow). **g** Axial diffusion weighted image with B value 500 and **h** ADC map shows restricted diffusion within the tumor (arrow)

varying degrees of internal necrosis. An especially helpful imaging feature is an imperceptible IVC at the point of maximal contact with the mass, which elucidates its site of origin as the IVC rather the retroperitoneum; this has a sensitivity and specificity of 75% and 100%, respectively [17]. Conversely, a mass compressing the IVC suggests that the mass' origin is outside of the IVC. Additionally, extraluminal involvement typically follows tissue planes of least resistance and displaces adjacent organs [4, 16]. Combined extra- and intraluminal involvement demonstrates patterns of both extra- and intraluminal growth, and its appearance depends on the relative size of each component (Fig. 3) [4].

Abdominal MRI serves as a useful adjunct for IVC leiomyosarcoma evaluation (Figs. 4,6,7). Standard MR sequences for abdominal imaging should be obtained, including In- and Opposed-Phase T1-Weighted Gradient-Recalled Echo (GRE), T2-Weighted Turbo Spin Echo (TSE) and Fast Spin Echo (FSE), and Volume Interpolated T1-Weighted Fat-Suppressed Unenhanced T1-weighted imaging, gadolinium-enhanced dynamic 3D

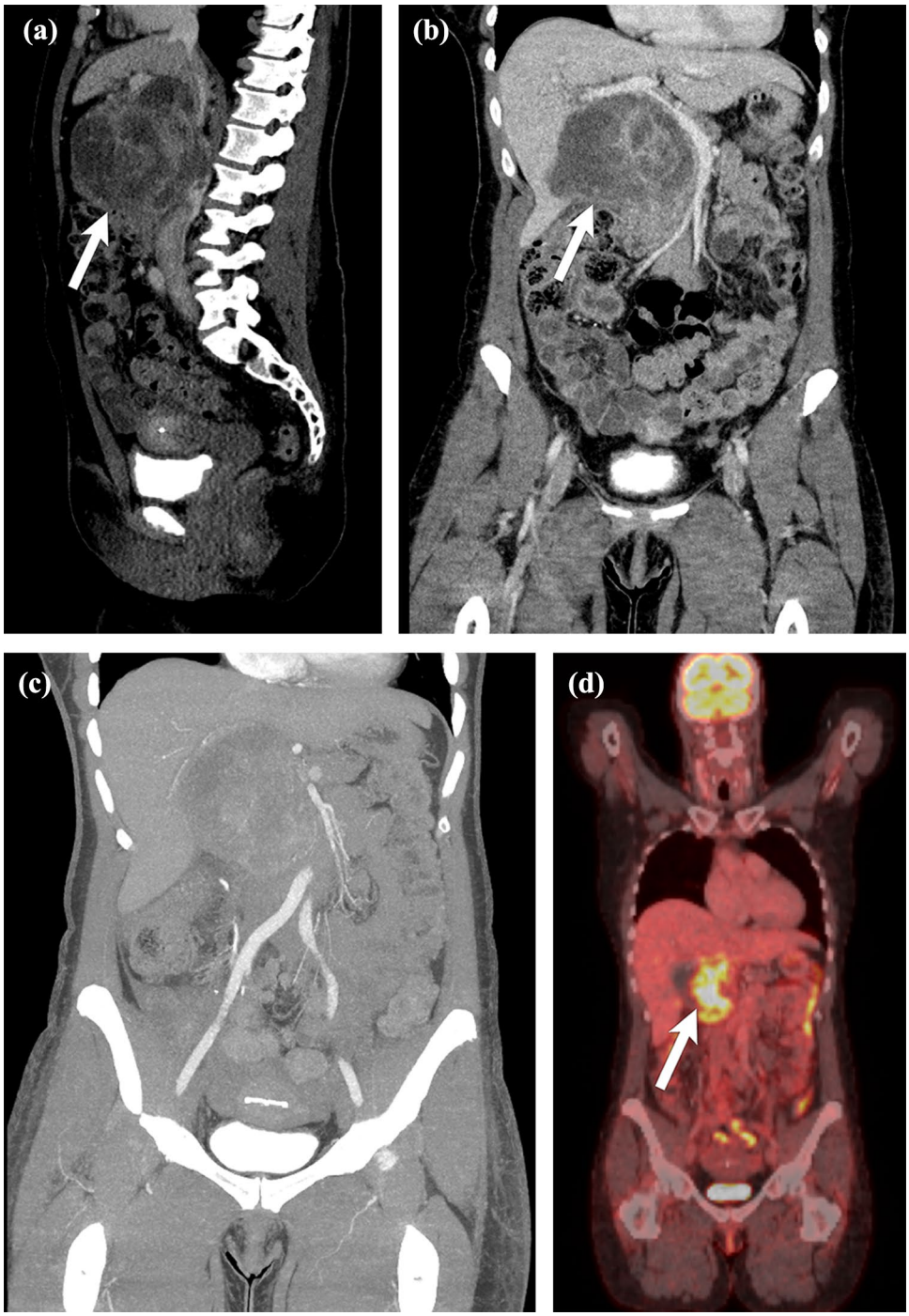

Fig. 5 A 46-year-old female with IVC leiomyosarcoma. **a** Sagittal reformat CT and **b** coronal reformat CT in portal venous phase shows a large heterogeneously enhancing IVC leiomyosarcoma (arrow). **c** Coronal MIP image of CT angiogram shows the tumor's relationship to the adjacent major vascular structures, which may be helpful in surgical planning. **d** Coronal fused PET/CT image shows the solid components of the tumor (arrow) to be markedly FDG avid, while the necrotic portions of the tumor are non-FDG avid

GRE sequences and diffusion weighted imaging. Balanced steady-state-free-procession techniques may be helpful in delineating intraluminal filling defects, as this yields excellent contrast between vessel and soft tissues [11]. Suggested CT and MR imaging sequences are summarized in Table 1. The role of MR angiogram and venogram in IVC leiomyosarcoma has not been elucidated, but may be potentially helpful, especially for evaluation of the tumors' intraluminal component.

On abdominal MRI, the mass typically demonstrates T1 hypo- or isointense signal relative to muscle, T2 iso- or hyperintense signal relative to muscle, and heterogeneous enhancement on post-contrast T1-weighted images (Figa. 4, 7) [4, 18, 19]. The tumor does not demonstrate internal fat or calcifications. Prominent collateral circulation may be seen around the lesion, especially in slow-growing tumors. These tumors typically demonstrate restricted diffusion (Fig. 4). Given the rarity of this tumor, there are no large-scale

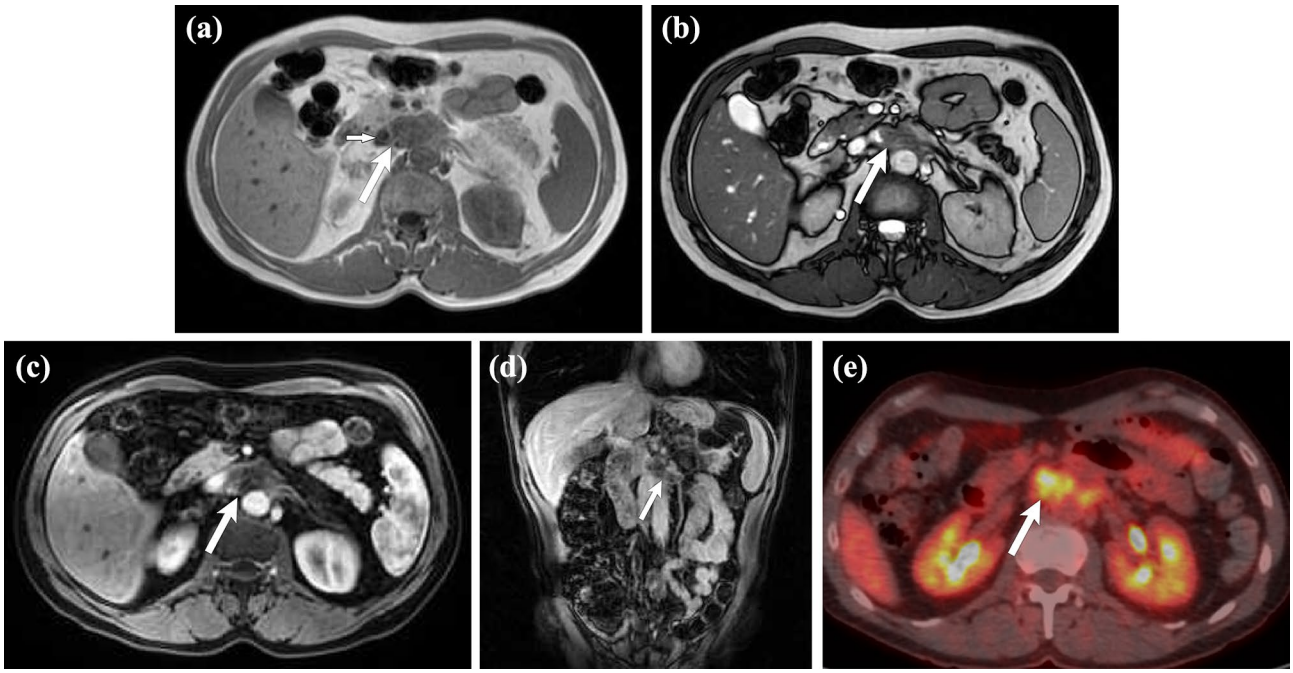

Fig. 6 A 66-year-old male with left renal vein leiomyosarcoma. **a** Axial T1-weighted MR image of the abdomen shows the tumor (long arrow) involving the left renal vein. Note the normal flow void in the IVC (small arrow). **b** Axial true fast imaging with steady state precession (TrueFISP) MR image of the abdomen shows the tumor involving the left renal vein. **c** Axial T1-weighted post gadolinium-enhanced MR image in the portal venous phase and **d** coronal T1-weighted post gadolinium-enhanced MR image in the equilibrium phase shows the heterogeneously enhancing hypovascular tumor (arrow). **e** Axial fused PET/CT image shows that the tumor (arrow) is FDG avid

studies that have directly compared the accuracy of CT and MRI in the diagnosis and staging of IVC leiomyosarcoma. However, given its superior soft tissue resolution, MRI can be helpful in detecting involvement of adjacent structures [20]. Additionally, contrast-enhanced MR venography can serve as pre-operative tool by defining the tumor's growth, morphology, extent, and collateral vessels while also differentiating tumor from non-neoplastic IVC thrombus [21]. Features that suggest IVC leiomyosarcoma rather than thrombus include enlarged IVC, increased T2 signal, and enhancement. Since both IVC leiomyosarcoma and thrombus can demonstrate restricted diffusion, evaluation of the other sequences would be essential [22]. Similar to CT, MRI can depict the tumor's primary growth pattern. Intraluminal involvement is suggested with patent blood vessels that demonstrate signal void on spin echo sequences and enhance less than tumor. Extraluminal involvement is depicted by organ displacement and heterogeneous signal characteristics depending on the degree of internal necrosis [4].

In preoperative imaging, it is important to report the tumor size, location, relationship to surrounding structures such as visceral involvement, extent of IVC involvement, and relationship to renal and retrohepatic veins, and any intraluminal component (Fig. 8). Additionally, lumbar vessels and collateral veins in the retroperitoneum should be defined as these can contribute to significant blood loss during surgery [23].

Hematogenous metastases occur frequently, and the disease may subsequently metastasize through the lymphatics. Liver, lungs, and lymph nodes are common areas of metastases in late stages (Fig. 2) [10]. Metastases typically demonstrate similar imaging features as the IVC leiomyosarcoma on MRI: T1 hypointense signal and T2 hyperintense signal [16].

The role of 18F-fluorodeoxyglucose (FDG) Positron Emission Tomography/Computed Tomography (PET/CT) in the diagnosis and management of IVC leiomyosarcoma is not yet clear [1]; however, it may be potentially helpful for evaluating extent of disease spread, especially in advanced stage disease (Figa. 1, 5).

Following surgery, systemic therapy, and/or radiation therapy, CT and MRI serve as the key imaging modalities for surveillance. Decreased enhancement, size, and apparent diffusion coefficient (ADC) values may suggest response to therapy. However, new enhancement may reflect progression or recurrence. This should be cautiously interpreted as this may be related to disrupted blood vessels. This can be clarified with MRI, which would demonstrate hemorrhagic products with decreased ADC values [23].

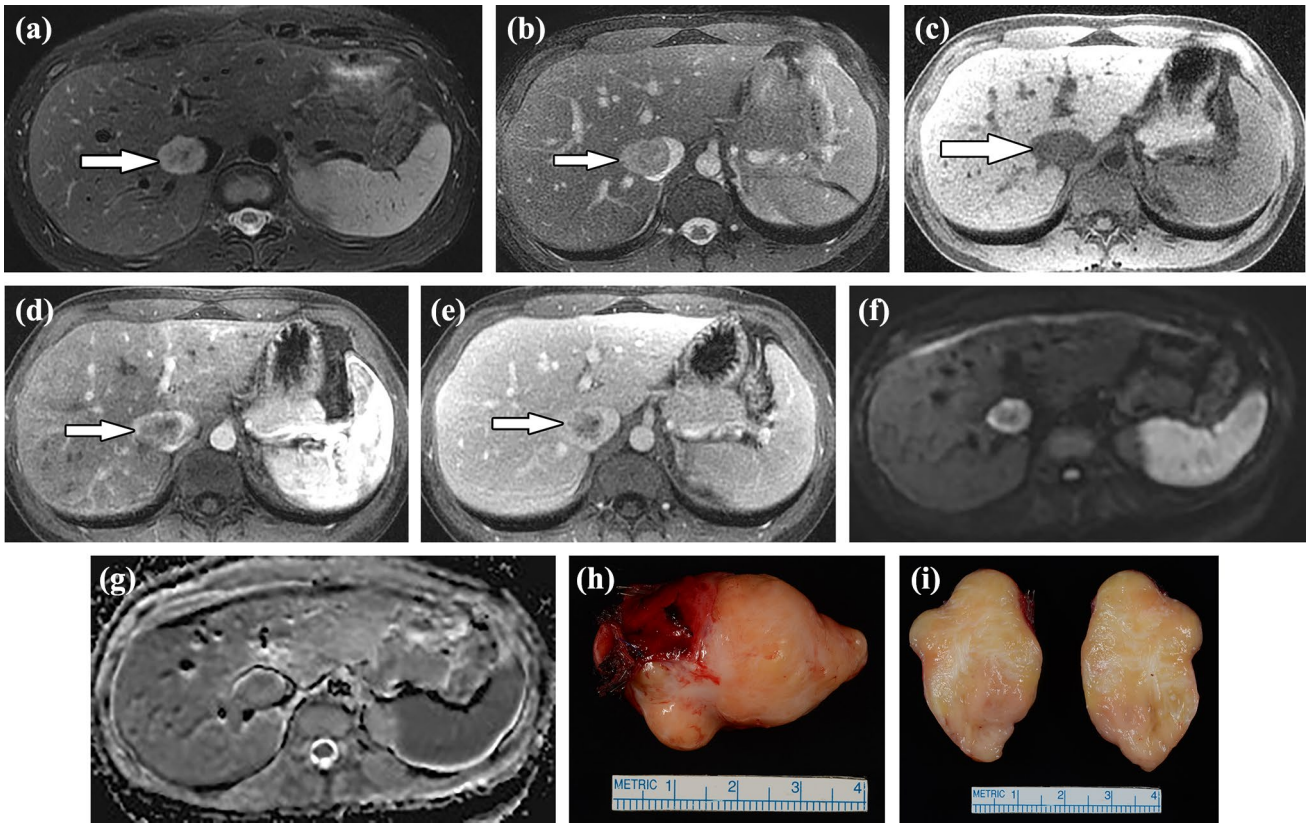

Fig. 7 MR imaging features of Intraluminal IVC leiomyosarcoma. **a** Axial T2-weighted MR image and **b** Axial FIESTA (Fast Imaging Employing Steady-state Acquisition) MR image of the abdomen shows the tumor (arrow) involving the IVC. **c** Axial T1-weighted pre-contrast image shows T1-isointense tumor (arrow). Note that the tumor can be very difficult to see on the non-contrast image, and may be mistaken for enlarged IVC. **d** Axial T1-weighted post gadolinium-enhanced MR image in the arterial phase and **e** Axial T1-weighted post gadolinium-enhanced MR image in the portal venous phase shows the heterogeneously enhancing intraluminal tumor (arrow). **f** Axial diffusion weighted image with B value 800 and **g** ADC map shows restricted diffusion within the tumor. Patient underwent curative surgical resection. **h** Gross macroscopic image shows a lobulated, multinodular mass. **i** Macroscopic cut surface image shows the soft, fleshy nature of the tumor

Table 1 CT and MR imaging sequences to evaluate IVC leiomyosarcoma

CT	MRI
Pre-contrast	In- and Opposed-phase T1-weighted Gradient-Recalled Echo (GRE) imaging
Arterial phase	T2-weighted Turbo Spin Echo (TSE) and Fast Spin Echo (FSE) imaging
Venous phase	Volume Interpolated T1-weighted fat-suppressed unenhanced T1-weighted imaging
Delayed phase	Gadolinium-enhanced dynamic 3D GRE imaging
	Diffusion weighted imaging
	± Balanced steady-state-free-precession

In summary, the important imaging characteristics of IVC leiomyosarcoma include imperceptible caval lumen, dilation of the IVC, heterogeneous enhancement of the tumor, and development of extensive collateral circulation due to its slow growth (Table 2) [17, 24]. However, while imaging features are helpful, biopsy is necessary for definitive diagnosis [1, 10].

Differential diagnoses

It is important to distinguish primary IVC leiomyosarcoma from a wide variety of tumors invading the IVC and also primary retroperitoneal neoplasms as this will dictate management.

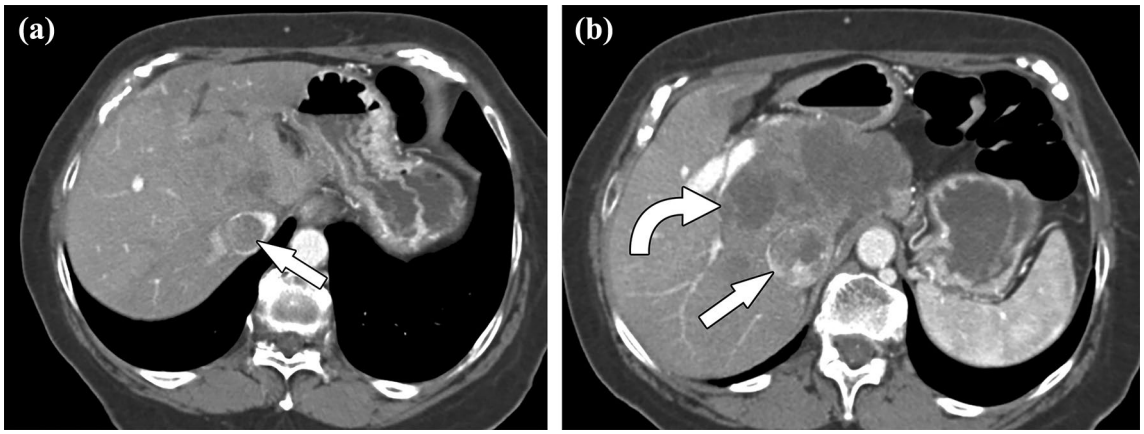

Fig. 8 IVC leiomyosarcoma with hepatic metastasis. Axial CT images **a**, **b** shows predominantly intraluminal IVC leiomyosarcoma (arrows). Hepatic metastatic involvement (curved arrow in **b**) secondary to direct tumor invasion is also seen

Table 2 Summary of key imaging features

CT	US	MRI
Imperceptible caval lumen Dilation of IVC Complex, lobulated mass with heterogeneous enhancement Extensive collateral vessels	Absent or abnormal flow in IVC secondary to intraluminal mass	T1: isointense T2: iso- or hyperintense Heterogeneous enhancement Diffusion restriction Extensive collateral vessels

Various tumors that are uncommonly associated with IVC invasion and/or tumor thrombi include renal cell carcinoma, adrenal carcinoma and hepatocellular carcinoma. Tumor thrombi can be differentiated from bland thrombus by the expansion of the IVC lumen and enhancement of the thrombus [11, 21]. Renal cell carcinoma is the most common malignancy that extends into the IVC, and imaging typically shows a heterogeneously enhancing renal mass extending through the renal vein and into the IVC in 4%–10% of cases [11]. Adrenal cortical carcinoma is an aggressive disease that has a bimodal distribution and can be functional in 62% of cases. Imaging shows a heterogenous mass replacing the adrenal gland, displacing surrounding structures and extending into the IVC in 30% of cases. This tumor can also show associated calcifications, which is not seen in IVC leiomyosarcoma [11]. Hepatocellular carcinoma is associated with tumor thrombi in the portal venous system extending into the hepatic veins and IVC in 4%–5.9% of patients and can also possibly involve the right atrium [11]. Tumors that are rarely associated with IVC invasion include urothelial carcinoma, Wilms tumor, and nonseminomatous testicular carcinoma. Urothelial carcinoma demonstrates filling defects in the renal collecting system and the IVC and/or renal vein. Wilms tumor presents in the pediatric age group with a mixed solid and cystic renal mass that can extend into the IVC in 4%–8% of cases [11]. Nonseminomatous testicular carcinoma often demonstrates bulky retroperitoneal lymphadenopathy and may be associated with tumor invasion through the IVC.

Primary retroperitoneal neoplasms are important differential considerations for IVC leiomyosarcoma, including retroperitoneal leiomyosarcomas, leiomyomas, adipocytic tumors, fibroblastic tumors, neurogenic tumors, rhabdomyosarcoma, and cystic tumors, as prognosis and management can differ[18, 19]. Retroperitoneal leiomyosarcomas are large, heterogeneous masses with similar pattern of spread compared to IVC leiomyosarcomas [25]; differentiating them by imaging features such as imperceptible IVC help delineate their site of origin. Benign leiomyomas are often seen in women of reproductive age and demonstrate a decreased T2 signal, variable enhancement on MRI, and no restricted diffusion. Adipocytic tumors, including the various types of liposarcoma, usually demonstrate internal fat on CT and MRI, contrasting with IVC leiomyosarcoma [18]; they may demonstrate restricted diffusion. Fibroblastic tumors, including solitary fibrous tumor, appear heterogeneous and highly vascular with prominent collateral vessels on CT and flow voids on MRI; myxofibrosarcomas may show the "tail" sign on fat-suppressed contrast-enhanced T1-weighted MRI secondary to the curvilinear tumoral fascial projections extending from the mass epicenter [18]; they may demonstrate restricted diffusion. Various neurogenic tumors, such as neurofibromas, typically show the

target sign: peripheral signal hyperintensity with central signal hypointensity and no restricted diffusion; malignant peripheral nerve sheath tumors are more likely to present as large ill-defined masses with internal heterogeneity, necrosis and/or hemorrhage with restricted diffusion [18]. Rhabdomyosarcomas have a heterogeneous, nonspecific infiltrative appearance with necrosis and restricted diffusion and are often seen in children. Cystic lesions, such as lymphatic malformations and cystic teratomas, are often seen in children and can be distinguished from IVC leiomyosarcoma as cysts are not a predominant feature of IVC leiomyosarcoma [18].

Management

Given the rarity of the tumor, there is a limited data to drive optimal oncologic management; however, multidisciplinary approach is generally recommended [3, 5, 12]. Surgical resection of the primary tumor is considered the only potential curative treatment, allowing for 5- and 10-year survival rates of 49.4% and 29.5%, respectively [26]. Surgical approach usually depends on the location and extent of the tumor with an abdominal approach typically sufficient for lower segment IVC leiomyosarcoma. Upper and middle segment IVC leiomyosarcoma might necessitate sternotomy as well and possibly cardiopulmonary bypass in the most superior tumors with right atrial extension [3, 27]. IVC reconstruction can be accomplished using IVC ligation, primary repair, patch angioplasty, or interposition graft using polyetrafluoroethylene (PTFE) or homografts [3]. Anticoagulation therapy can be given prophylactically or long-term following IVC reconstruction. However, there are currently no guidelines regarding anticoagulation management, and their use remains at the discretion of the surgeon [2, 28]. One study reported creating an arteriovenous fistula to ensure patency of the PTFE, which would eliminate the need for long-term anticoagulation [29]. Reconstruction might not be needed in cases of IVC leiomyosarcoma with extraluminal growth pattern [5]. En bloc resection of adjacent structures such as the right kidney, adrenal gland, or the gallbladder might be needed for improved outcomes [5]. Postoperative complications occur in 18%–30% of patients and commonly include lower extremity edema and renal failure [30]. Lower segment IVC leiomyosarcoma is associated with lower incidence of postoperative complications, compared to higher segment tumor [3]. Additionally, surgical resection of metastatic disease such as pulmonary metastasectomy or liver resection should be considered in patients with advanced disease as it boosts the overall survival [31]. IVC stenting may be an option for providing symptomatic relief in patients presenting with debilitating symptoms (such as lower extremity edema, pelvic pain and ascites), associated with malignant IVC vascular occlusion.

The role of neoadjuvant or adjuvant treatment is still unclear. Neoadjuvant chemotherapy and radiation therapy may be required prior to surgical resection in borderline unresectable tumors (e.g., tumor abutting 180 degrees circumferentially around the abdominal aorta and superior mesenteric artery) to reduce tumor size and increase resectability rate [3, 32]. Chemotherapy agents that have been utilized include a combination of dacarbazine, doxorubicin, cyclophosphamide, and ifosfamide/cisplatin [33]. However, there is no standard chemotherapeutic regimen, and management may vary according to patient characteristics [5]. Adjuvant radiation therapy may be considered in patients with microscopically positive margins as it decreases the risk of local recurrence [3]. With increased understanding of the tumor biology of the IVC leiomyosarcomas, molecularly targeted therapies may be potential therapeutic options in the future. The use of insulin-like growth factor-1 receptor (IGF-1R) antibody blockade, mTOR blockade, and PARP inhibitors in the management of soft tissue sarcomas and leiomyosarcomas are currently under investigation [8, 9].

Prognosis

Patients with IVC leiomyosarcoma have a reported 5-year disease-free survival of 6% and overall survival of 55%, although these statistics are inherently limited due to disease rarity [30]. The main predictors of survival in patients with IVC leiomyosarcoma are curative radical resection, margin status, tumor size and the absence of metastatic disease at the time of surgery [3, 30]. Negative surgical margin is associated with 3- and 5-year-survival of 76% and 68%, respectively; in contrast, the 3- and 5-year-survival rate is reported to be 0% in patients with positive margins [3]. Additionally, middle segment IVC leiomyosarcoma is associated with better prognosis, which is assumed to be due to the earlier presentation of this group as tumor expansion causes compression of multiple surrounding abdominal organs [30]. Unlike other sarcomas, histologic grades are not reported to significantly alter the prognosis in IVC leiomyosarcoma, which might reflect the aggressive nature of IVC leiomyosarcomas, regardless of the grade [30]. Tumor involvement of the upper segment of the IVC, intraluminal tumor growth, IVC occlusion, leg edema, and Budd-Chiari syndrome are factors associated with poor prognosis and increased postoperative mortality [7, 34]. Most patients with IVC leiomyosarcoma develop recurrence after surgery with a 5-year disease-free-survival of 6%-44% and 5-year overall survival of 33%-67% [30, 31]. Time to recurrence is an important prognostic factor. IVC leiomyosarcoma tends to recur distally more than locally (37% vs 16%). Patients who develop recurrence may be considered for salvage resection (3).

Conclusion

IVC leiomyosarcoma is a rare, aggressive retroperitoneal malignancy. Clinical symptoms are often nonspecific and may contribute to delay in the diagnosis. Imaging, especially CT and MRI, play a critical role in the diagnosis, staging and follow-up of this tumor. Awareness of the multimodality imaging features of IVC leiomyosarcoma and its differential diagnoses can help guide optimal patient management. However, histopathology may be required for definitive diagnosis. Aggressive surgical resection is essential for curative treatment, while chemotherapy and/or radiation may further aid management of this rare sarcoma.

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