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Original Article

Clinical and radiographic profile of intravascular leiomyoma with right heart extension: a report of 3 cases

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Abstract: The aim of this study is to investigate the clinical and radiographic features of intravascular leiomyoma (IVL) with right heart extension. The clinical and radiological data were retrospectively analyzed in 3 cases of histopathologically confirmed IVL with right heart extension. The pertinent literatures were also reviewed. All the three cases were female and had a history of uterine fibroid. The contrast-enhanced computed tomography (CT) scanning revealed a soft tissue density mass in inferior vena cava and right atrium; a mild enhancement during the arterial phase and moderate enhancement during venous phase, with a cord-like vascular shadow; and a clear gap between the mass and the vessel wall. Spiral CT scanning with multiplanner reformation (MPR) reconstruction clearly revealed the morphology, scope and extension pathways of the tumor. The diagnosis of IVL should be considered in female patients with a history of uterine fibroids and a soft tissue density masses in heart and inferior vena in CT scanning.

Keywords: Intravascular leiomyoma, inferior vena, heart, computer tomography

Introduction

Intravascular leiomyoma (IVL) is a benign smooth muscle cell tumor originated from uterine fibroids extending to intrauterine venules or developed from the vascular smooth muscle growing into the pelvic veins and the inferior vena cava. It was firstly reported by Birch-Hirschfield in 1896 [1]. Then, the first case of intracardiac leiomyomatosis (ICL) was reported by Durk in 1907 [2]. The recent studies demonstrated that there were only about 10% of IVL patients had the involvement of the heart or the inferior vena cava [3-5]. The clinical symptoms of IVL are complicated and diverse, or insidious in early stage [6]. The most common clinical symptoms of IVL with right heart extension are similar with the symptoms of inferior vena cava obstruction, which include dizziness, dyspnea, chest tightness, chest pain, palpitations, edema of the lower extremities, or massive abdominal ascites. Furthermore, patients with IVL may have symptoms of breathing difficulties, right heart failure, or even severe cardiac arrest and sudden death due to the outflow tract obstruction in severe cases [6, 7]. Therefore, it is considered a benign but potentially life-threatening tumor. A more important fact is that early diagnosis and timely operation yields a good prognosis. However, due to the infrequency of its occurrence, little is known about the clinical and radiological features of IVL involving the inferior vena cava and the heart. Therefore, it is very difficult to diagnose accurately especially in patients with insidious symptom onset. Moreover, the clinical and imaging features play critical role in the early diagnosis of IVL.

In this study, we reported 3 cases of IVL with heart extension and analyzed the clinical and radiologic features to bring more attention to this disease.

Materials and methods

Patient recruitment and information collection

In this study, we recruited 3 patients who were hospitalized in Jinan Central Hospital and

Table 1. The clinical features of previous cases from literature

Literature	Num of cases	Sex	Age (years)	History of uterine fibroids	Clinical symptoms	Tumor location
Li et al. [6]	7	Female	24-59	Yes	Exertional dyspnea (4 cases); Abdominal discomfort (1 case); Lower limb edema (1 case); No symptoms (1 case).	IVC, RA (6 cases), IVC, RA, RV, PA (1 case)
Fornaris et al. [7]	1	Female	40	Yes	Exertional dyspnea, palpitation.	IVC, RA, RV, PA
Okada et al. [10]	1	Female	81	Yes	Palpitation.	IVC, RA
Huang et al. [14]	3	Female	38-48	Yes	Exertional dyspnea, palpitation (1 case); Exertional dyspnea, lower limb edema (1 case); No symptoms (1 case).	IVC, RA, RV (2 cases), IVC, RA (1case)
Xu et al. [15]	1	Female	41	Yes	Hematemesis.	IVC, RA
Lu et al. [16]	2	Female	50 53	Yes	Exertional dyspnea, palpitation (1 case); Exertional dyspnea, chest pain (1 case).	IVC, RA, RV (1 case), IVC, RA (1 case)
Wang et al. [17]	8	Female	24-59	Yes	Exertional dyspnea (5 cases); Exertional dyspnea, systemic oedema (1 case); Abdominal mass (1 case).	IVC, RA (8 cases)
This paper	3	Female	31-56	Yes	Intermittent syncope (1 case); Chest tightness, chest pain, syncope (1 case); Lower limb weakness (1 case).	IVC, RA, RV, PA (1 case), IVC, RA (2 cases)

Note: IVC: inferior vena cava; RA: right atrium; RV: right ventricle; PA: pulmonary artery.

Wuhan Asia Heart Hospital and underwent tumor resection from September 2008 to December 2015. The diagnosis of IVL involving right heart chambers was confirmed by postoperative pathology in all patients. The complete clinical and radiological data were also recorded. Prior written and informed consent were obtained from every patient and the study was approved by the ethics review board of Jinan Central Hospital. Besides, the pertinent literatures were reviewed to discuss clinicopathological and radiological features of IVL.

CT scanning and imaging analysis

For all patients, the chest or thoracoabdominal contrast-enhanced scans with MPR reconstruction were performed by using 16-slice CT scanner (Toshiba Aquilion 16; Toshiba Medical Systems, Japan) or 64-slice CT system (Brilliance 64, Philips Medical Systems, Cleveland, Ohio). Contrast agent (Ultravist, 300 mgI/ml, 70-100 ml, Schering, Berlin, Germany) were injected through anterior elbow vein at a rate of 3 ml/s using a high-pressure syringe, with the delay times of 25 s and 60 s in arterial and venous phase, respectively. The imaging analysis was conducted by 2 radiologists with more than 10 years' experience. The analysis parameters of imaging features included the lesion location, shape, margin, density, and the homogeneity/heterogeneity of enhancement.

Hematoxylin-eosin staining and immunohistochemistry

The fresh specimens of tumor were obtained after tumor resection and fixed in 10% neutral formalin, followed by routine paraffin-embedding. The sections were stained with hematoxylin-eosin (HE) and evaluated under microscope. For one patient, immunohistochemical analysis was performed to evaluate the expression of CD34, CD68, Ki67, anti-smooth muscle antibodies (SMA), estrogen receptor (ER), progesterone receptor (PR), actin, and S-100.

Results

Clinical characteristics

The three patients were all female, with ages ranged from 31 to 56 years (mean age, 43 years). One patient was hospitalized due to tetraparesis prominent on the lower extremities lasting for one week; the second patient was hospitalized for the symptoms of repeated chest tightness, palpitation, chest pain and shortness of breath for 1 month; while the third patient was hospitalized due to an intermittent syncope for 4 days. The first two patients had undergone the resection of uterine fibroids 1 and 6 years ago, respectively, and the second patient had recurrence of uterine fibroids detected by B-mode ultrasound at admission to

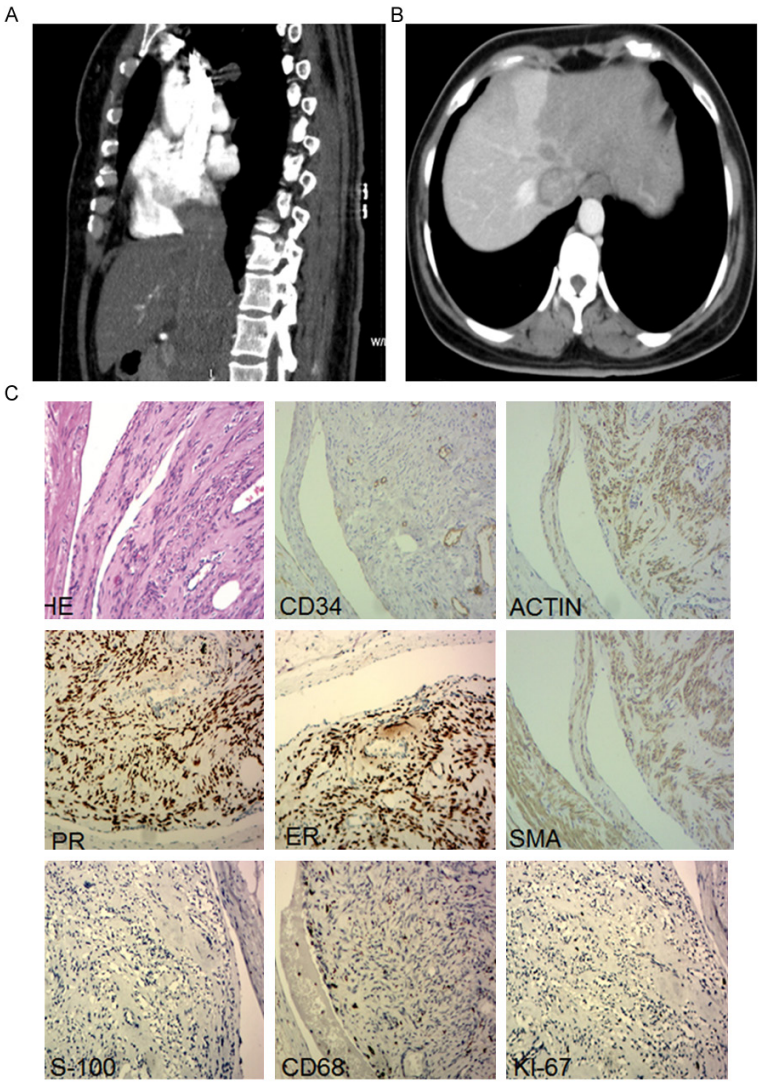

Figure 1. Patient 1 (female, 42 years old). A. In arterial phase, CT with MPR displaying the mass with mild continuous enhancement and vessels inside the mass in right atria, the inferior vena cava and hepatic vein. B. In venous phase, CT scanning showing heterogeneous enhancement of mass, an annular gap between the inferior vena cava wall and the lesion, and low-density drainage region of hepatic vein. C. Tumor cells exhibiting as fusiform leiomyoma with hyaline changes and small vessels in the tumors, and endothelial cells at the edge of the tumors (original magnification ×100, H&E staining). Immunohistochemistry (original magnification ×100): CD34 is positive in vascular endothelial cells and negative in tumor cells. Besides, the tumor cells were stained strongly positively for SMA, ACTIN PR and ER, and negatively for S-100, CD68 and Ki-67.

hospital. The third patient also had uterine fibroids at the time of recruitment. All the patients were examined by echocardiography and contrast-enhanced CT scanning. Two of them were misdiagnosed as cardiac myxoma while the third patient was misdiagnosed as inferior vena cava thrombosis. The misdiagnosis rate was 100%. All patients underwent tumor resection and one patient received emergency heart surgery since the occurrence of sudden cardiac arrest during the waiting period. Finally, all patients had good postoperative outcomes and improved symptoms. One patient was followed up for 18 months and no tumor recurrence was found. The clinical features of previous cases from literature were summarized in **Table 1**.

Radiographic features

All patients were examined by contrast enhanced CT scanning with MPR reconstruction. The imaging showed intracardiac or intravenous filling defects of cord-like soft tissue density, with clear margin from cardiovascular walls. The IVL of the first patient was located in right atrium and extended into the inferior vena cava, hepatic vein (**Figure 1A**), and renal vein. The tumor of the second patient was also located in right atrium and extended into the inferior vena cava, left iliac vein (**Figure 2A**, **2C**). The third patient had IVL imaging located in the right ventricle and right atrium (snake-head in shape) and extended into pulmonary artery, the inferior vena cava, and right iliac vein (**Figure 3A**, **3B**). In arterial phase, all lesions in 3 patients showed mild heterogeneous enhancement and strips-like vascular shadow with high density (**Figure 1A**). In the venous phase, the lesion exhibited a significant heterogeneous enhancement with an annular gap between the inferior vena cava wall and the lesion (**Figure 1B**). The findings demonstrated that Spiral CT scanning with MPR play a significant role in the diagnosis and timely surgery of IVL.

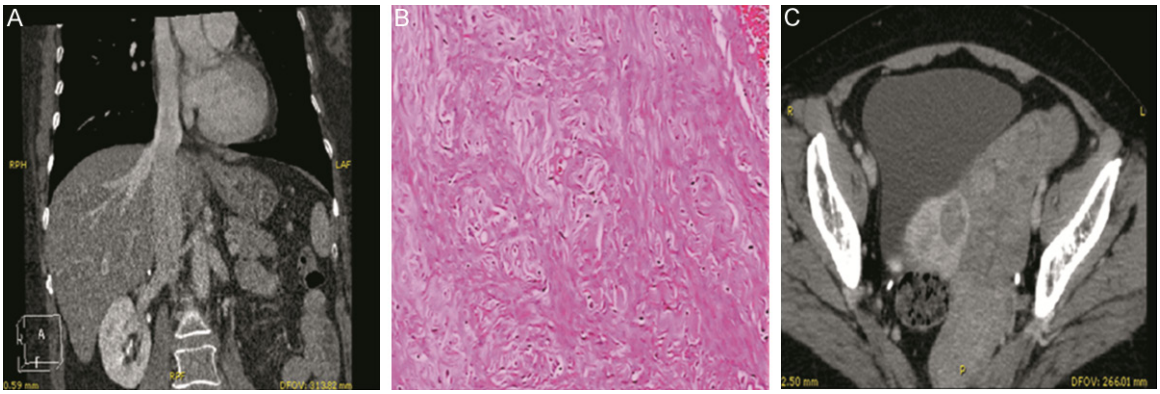

Figure 2. Patient 2 (female, 56 years old). A. CT with MPR displaying mass with mild continuous enhancement in right atria and the inferior vena cava. B. Tumor cells exhibiting as fusiform leiomyoma with hyaline changes in the tumors (original magnification ×100, HE staining). C. CT scanning demonstrating the strips-like soft tissue density mass with heterogeneous enhancement in left uterus.

Pathological analysis

The fresh specimens of tumor tissues were obtained from 3 patients. Surgical exploration revealed that the tumor were grey or yellowish-grey, sausage-shaped, firm, with smooth surface (**Figure 3C**). The length of two tumors was about 20 cm and 15 cm, while the length of third tumor was not measured due to the inadequacy of surgical exploration. The maximum diameter of 3 tumors was 5.0 cm, 3.0 cm and 2.5 cm, respectively. The tumor cells were spindle in shape and well differentiated. There were large amounts of small vessels with hyaline changes in the tumors. There were endothelial cells at the edge of the tumor (**Figures 1C**, **2B**, **3C** and **3D**). Immunohistochemistry revealed that tumor cells were SMA (+), actin (+), CD34 (-), ER (++), PR (++), S-100 (-) and CD68 (-), respectively (**Figure 1C**). The positive rate of Ki-67 was less than 1%. Based on these clinical and radiographic examinations, a diagnosis of IVL was confirmed.

Discussion

Previous studies demonstrated that all cases of IVL were female especially premenopausal parous women and usually occurred at age ranged from 35 to 63 years [2, 8]. However, 2 cases (23 and 81 years old, respectively) of IVL involving right ventricular cavity were reported by Li [9] and Okada [10]. Besides, the most patients have a history of uterine fibroids with or without surgery. Similarly, the age of patients in this study was 31, 42 and 56 years old respectively, and 2 of them had a history of uterine fibroids surgery. IVL involving heart is difficult to diagnose due to its non-specific clinical manifestations. For example, one case of IVL misdiagnosed as hypertension was reported by Fornaris [11]. Similarly, in our study, the IVL had been misdiagnosed as a right atrial myxoma in 2 cases and inferior vena cava thrombosis in the third case. The major clinical symptoms of IVL with intracardiac extension may present as cardiac insufficiency (chest tightness, chest pain, shortness of breath, tachycardia, syncope etc.) or even cardiac arrest and sudden death in serious cases [12, 13]. In this paper, one patient was performed emergency operation due to cardiac arrest. Some mild cases do not have obvious symptoms, as well as one patient in this study presenting lower limb weakness.

The tumor, with rope-like shape, is generally free or in different degree attached to venous lumen or heart chambers and wave along with the heartbeat. Gross pathology shows that the tumor was grey or yellowish-grey, rope-like or tubular, and firm, with smooth surface [7, 14]. Histopathology shows endothelium-covered proliferations of benign smooth muscle, the tumor cells exhibit as spiral arrangement, hyaline degeneration in different extent, and abundant small vessels in the mass [14]. IVL is a special type of leiomyoma, its growth is closely related to the level of estrogen (E2) [15]. This conclusion was also confirmed by the immunohistochemical positivity of ER and PR in one case in this study.

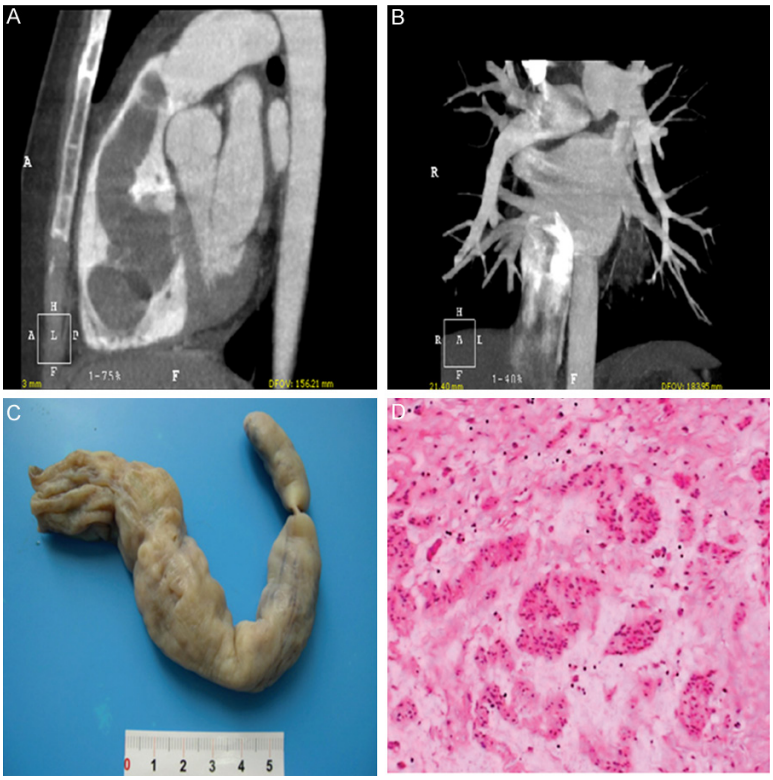

Figure 3. Patient 3 (female, 31 years old). A. The soft tissue density mass located in the right ventricle and right atrium extended into pulmonary artery, the inferior vena cava, and right iliac vein. B. The snake-head shape signal of IVL in heart chambers. C. Gross pathology displaying the masses were rope-shaped, grey or yellowish-grey, and firm, with smooth surface. D. The tumor cells appear as fusiform, circular section, fascicles, uneven density, rare mitotic count, and well-differentiated cells. Some areas were hyaline and myxoid degenertion, with vessels distribution (original magnification ×100, HE staining).

CT scanning plays an important role in the diagnosis of IVL. Plain CT shows an enlarged right atrium and expanded veins, while the contrast enhanced CT with MPR reconstruction reveals the characteristics of the tumors in shape, size, density, margin and the relative location with the surrounding vascular walls. This information will provide valuable supports for the diagnosis and surgical therapy. In our study, contrast enhanced CT scanning revealed a ropes-like or snake-headed filling defect of soft tissue density in venous lumen or heart chamber respectively, with clear margin from cardiovascular walls. The lesion usually exhibited mild or moderate heterogeneous enhancement and was of relatively lower density compared to the enhanced blood. In some lesions, there were vascular shadows which were banded in shape. These findings were consistent with the reports from Lu [16] and Wang [17]. Furthermore, Zheng et al. [18] reported 4 cases of IVL with the small vessels traveling through inter-vascular tumor; 2 of them showed a heterogeneous margin-enhancement and a weak central enhancement; while 1 of them were obvious enhanced. In addition, the soft tissue mass with heterogeneous enhancement was visible in the left or right pelvic cavity. In fact, the soft tissue mass was tortuous, dilated venous vessels. In our study, 2 cases being performed abdominal enhanced CT scanning were found soft tissue mass in the left and right of pelvic cavity, respectively; 1 case without abdominal CT examination was confirmed vascular leiomyoma in the left ovarian vein and uterine fibroids by gynecological surgery. Finally, MPR reconstruction can display continuous mass which looks like radish root or rope in the heart and inferior vena cava, and multi-directly display the relationship between the cardiovascular wall and the mass, as well the features of mass in the pelvic cavity.

IVL grows slowly, but is easy to relapse, and the most important treatment is radical surgery. Study from Carr [8] demonstrated that early diagnosis and timely surgical treatment significantly improved the survival rate and prognosis of patients with IVL. Anti-estrogen therapy could, in a certain extent, inhibit tumor growth and recurrence [19]. The relapse of tumor is closely related to outcome of tumor resection, tumor size and the age of patient [20, 22]. In our study, all patients had cardiac and vena cava tumor resection (the first stage surgery) followed by gynecological operation (the second stage surgery) with an interval of 4-6 weeks. In one case, the patient has been followed up for 20 months and no recurrence was observed.

Conclusion

In summary, IVL with right heart extension has the characteristics of clinical and imaging features. It is of great value to get familiar with these characteristics for early diagnosis and treatment. The exact diagnosis can be obtained in most patients who have unique symptoms and history of uterine fibroids, with typical CT findings [23].

Disclosure of conflict of interest

None.

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