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Case Report

Intravenous leiomyomatosis involved cor dextrum: A review of diagnosis and management with an illustrative case ☆

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ABSTRACT

Intravenous leiomyomatosis (IVL) is a benign disease that originates in the uterus and is characterized by aggressive intravenous growth that can extend to the inferior vena cava and even involve the intracardiac cavity. This extension of the IVL into the right heart is known as intracardiac leiomyomatosis (ICL). The clinical incidence of this disease is extremely low, and the characteristics of atypical aggressive growth lead to diagnostic dilemmas. Thus, studies on this disease have profound clinical significance. Here, we report a case of intracardiac leiomyomatosis and review the relevant literature. A 46-year-old female patient presented with exertive chest tightness and shortness of breath with an onset of approximately half a month. The patient underwent uterine myomectomy in 2018 and recovered well after surgery. On preoperative echocardiography, a hypoechoic mass was detected in the right atrium, which was diagnosed as a leiomyoma. Cardiac magnetic resonance imaging (MRI) revealed a T2-weighted mixed high-signal mass with partial cystic changes that extended from the inferior vena cava into the right atrioventricular cavity, occupying most of the atrial cavity and was misdiagnosed as an atrial mucinous tumor. The patient underwent cardiac tumor resection, tricuspid valvuloplasty, and lower-extremity vascular exploration under general anesthesia with extracorporeal circulation. The final pathological diagnosis was ICL. This is an illustrative analysis of various aspects of the disease, including pathology, etiology, clinical symptoms, imaging diagnosis, and treatment modalities.

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Introduction

Intraventricular leiomyomatosis (IVL) is a tumor with benign histopathological features that occurs in young and middle-aged women aged 35-50 years before menopause, usually with a clear history of uterine leiomyoma. The lesion grows aggressively and can protrude into the uterus or pelvic veins, extend into the inferior vena cava, and even involve the intracardiac cavity, which may cause severe circulatory disturbances and clinical symptoms, such as chest tightness, shortness of breath, and cardiac insufficiency. The first case of IVL was reported in 1896, while the first intracardiac leiomyomatosis (ICL) was reported in 1907 [1]. As of 2018, fewer than 300 cases have been reported in peer-reviewed literature [2]. Its rare incidence poses a diagnostic dilemma for clinicians unfamiliar with this disease. Herein, we review the imaging presentation of this case of ICL and the literature on the etiology, diagnosis, and management of this rare condition to improve the understanding and diagnosis of this condition.

Case report

A 46-year-old woman was admitted with "exertive chest tightness and shortness of breath and had an onset of approximately half a month." The patient underwent uterine myomectomy in 2018 (details not available) and recovered well after the operation. On April 3, 2023, the chest X-ray (CXR) suggested a few exudative lesions in both lower lung fields and a slightly enlarged cardiac shadow. Based on the CXR result and the patient's history of abdominal uterine fibroid surgery the initial physician recommended that the patient undergo abdominal and cardiac ultrasonography. On April 5, 2023, transabdominal gynecological ultrasonography revealed a right parametrial isoechoic mass with inhomogeneous echogenicity measuring approximately 31 × 28 mm, considered a possible broad ligament myoma. Cardiac ultrasonography showed a solids hypoechoic mass attached to the inferior vena cava near the entrance and extending into the right atrioventricle, measuring 71×32 mm. The mass oscillated back and forth with the cardiac cycle and did not cause tricuspid valve flow obstruction. After the injection of acoustic contrast, a negative filling defect area was observed in the right heart cavity, measuring approximately 84 × 34 mm, and a small amount of contrast agent was observed in the lesion. On April 19, 2023, cardiac MRI revealed that the right atrium was significantly enlarged, and an abnormal signal mass of approximately 36 × 58 × 57 mm was seen from the proximal inferior vena cava to the right atrium, with a slightly high signal on T1-weighted imaging and mixed high signal on T2-weighted imaging; the lesion was partially cystic in nature with a mild enhancement of the solids component after contrast injection. The lesion was irregular in morphology and had a "crutch head shape" in the sagittal position. The tumor was closely related to the tricuspid valve and shuttled within the right atrial chamber during the cardiac cycle, and was eventually misdiagnosed as an atrial mucinous tumor. Based on the preoperative diagnosis and evaluation, cardiac tumor resection, tricuspid valvuloplasty, and lower-limb vascular exploration were performed under general anesthesia and extracorporeal circulation on April 21, 2023. Intraoperative findings revealed that the heart was enlarged, particularly the right atrium. The Solids cystic mass in the right atrium measured approximately 6.0×4.0 cm, with the stalk located in the inner wall of the inferior vena cava (3 cm away from the entrance of the right atrium) and the mass growing across the tricuspid valve orifice into the right ventricle. The tricuspid valve leaflets were morphologically acceptable, but the annulus was significantly enlarged, resulting in incomplete valve closure. Pathological light microscopy revealed that the tumor was composed of spindle-shaped cells woven into a bundle-like arrangement, rich in cytoplasm, eosinotropic, and with mild cellular atypia (Figs. 1–3). The immunohistochemical results were as follows: SMA(+), CK(-), CD34(+), ERG(+), S-100(-), CD117(+), Dog-1(-), Vim(+), and Ki-67(+,about5%). The pathological diagnosis of LCL was confirmed. The patient was reviewed at 3 months after surgery, no abnormalities were reported. The patient recovered well after surgery, no signs of recurrence at 3 months later.

Discussion

Epidemiological characteristics

The incidence of IVL was low. The first case of IVL was reported in 1896, while the first case of ICL was reported in 1907. To date, < 300 cases of IVL have been reported. In recent years, with newer iterations of imaging techniques and improvements in diagnostic levels, the detection rate has gradually increased; however, the research is still mostly full of case reports and small-sample analyses. A related meta-analysis [3] noted that the onset of the disease was limited to women aged 20-81 years, with a mean age of 47.6 years. Approximately 94% of patients with IVL had uterine fibroids and a history of previous fibroid surgery, with lesions extending to the pelvic veins in approximately 80% of cases, to the inferior vena cava in approximately 30% of cases, and to the heart in 10% of cases.

Pathogenesis

The pathological mechanism of IVL is poorly understood, and Knauer's and Sitzenfry's theories are the 2 most widely accepted hypotheses. The Knauer hypothesis [4] suggests that the disease originates in the vascular wall of the uterus. The Sitzenfry hypothesis [5] suggests that IVL occurs as a result of the invasion of the venous system by a uterine leiomyoma. Our findings support the latter. It is believed that LVL pathogenesis is associated with estrogen levels. Kokawa et al. [6] reported a case of IVL with high levels of serum estrogen and estrogen receptors in the tumor tissue despite 3 years of menopause. Furthermore, Kir et al. [7] reported positive expression of estrogen and progesterone receptors in tumor cells constituting the LVL but not in adjacent endothelial and subendothelial cells constituting the vessel wall, further confirming that the IVL originates in the uterus and not in the ves-

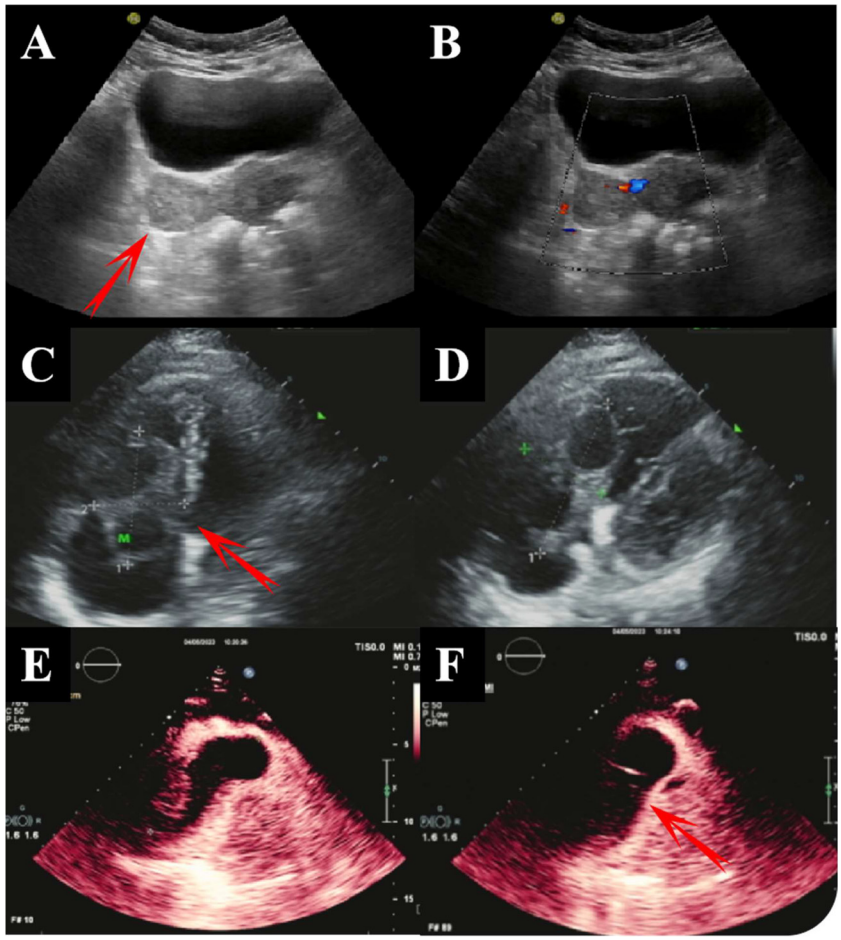

Fig. 1 – (A, B) Transabdominal gynecologic ultrasound revealed a right parametrial isoechoic mass. (C, D) Cardiac ultrasonography of the right atrioventricular showed a solids hypoechoic mass that measured 71 × 32 mm. (E, F) After injection of acoustic contrast, a negative filling defect area was seen in the right heart cavity, measuring about 84 × 34 mm, and a small amount of contrast agent was seen in the lesion. of contrast agent was seen in the lesion.

sel wall. Genetic studies have identified chromosomal aberrations of 12q15-qtr or 14q24-qter in IVL cells, and additional copies of 12q15-water and/or deletions of 14q24-water may be key regulators of intravascular invasion and proliferation. Approximately 40%-50% of uterine leiomyomas also have this chromosomal abnormality [8]. It has been found that IVL differs from ordinary smooth muscle tumors and has a unique pathogenesis associated with mutations in the Mediator Complex Subunit 12(MED12) gene, which is expressed at higher levels in smooth muscle [9].

Pathology

On histopathological examination, the presentation is similar to typical benign uterine leiomyomas. Homogeneous spindle-shaped smooth muscle cells are well differentiated, mitotic signs are rare, interstitial cells may be accompanied by edema or hyaloid degeneration, and the “heterogeneity” of tumor cells can be seen in a few cases. Notably, IVLs are distinguished from smooth muscle tumors by the tumor cells growing in the vasculature lined with endothelial cells and covered by flattened endothelial cells on the surface [10]. The tumor was positively immunolabelled with SMA, CD34, ER, vimentin, and desmin and negative for CD10 and cytokeratins.

Clinical symptoms

The clinical manifestations of IVL are nonspecific. Early IVL may have no obvious symptoms, but when the lesion extends into the pelvic venous system, the main symptoms include lower abdominal discomfort and menstrual disorders; when the lesion extends into the inferior vena cava, it may lead to venous hemodynamic disorders, causing lower limb edema and inferior vena cava syndrome. Furthermore, when the lesion extends into the heart, the most common clinical manifestations are palpitations, chest tightness, shortness of breath, and even fainting or sudden death in severe cases. During history taking, clinicians may overlook menstrual history, history of uterine pathology, or cardiogenic symptoms, leading to misdiagnosis and incomplete evaluation.

Preoperative assessment

Ultrasonography is the preferred auxiliary examination for real-time detection of the mass’s size, morphology, adjacency,

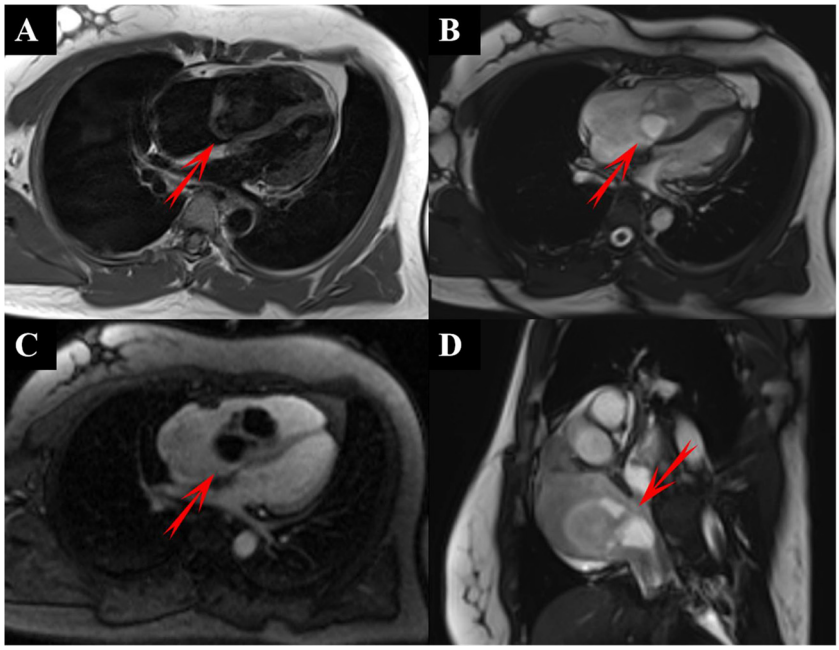

Fig. 2 – (A) T1-weighted axial magnetic resonance imaging (MRI) of the heart shows a slightly hyperintense lesion. (B) T2-weighted axial magnetic resonance imaging (MRI) of the heart shows a mixed hyperintense lesion. (C) T1-weighted enhanced scanning Axial magnetic resonance imaging (MRI) of the heart shows mild enhancement of the solids portion of the lesion. (D) T2-weighted sagittal magnetic resonance imaging (MRI) of the heart shows a lesion with a "crutch head sign."

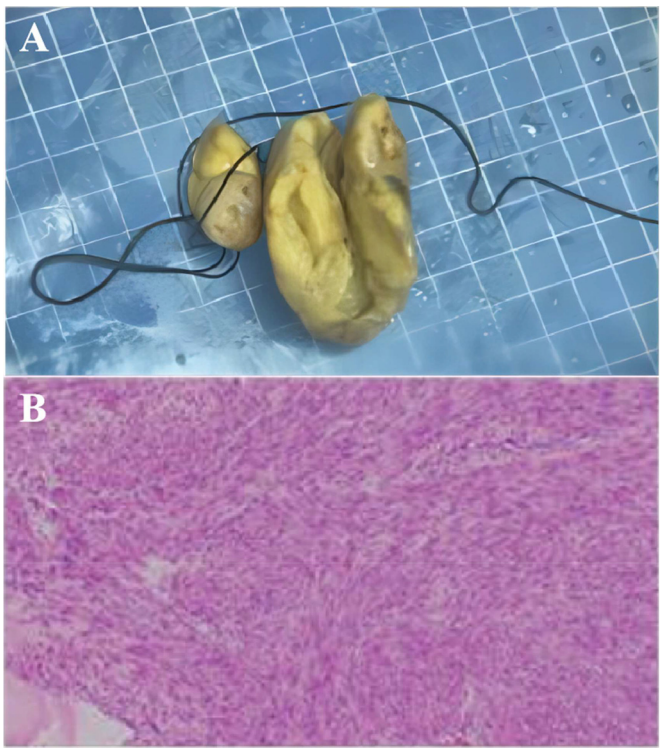

Fig. 3 – (A) Surgically removed leiomyomatosis that had been located in the inferior vena involved intracardiac cavity, and the gross pathology specimen dimensions were 5.7 x 4.6 x 3.2 cm. (B) Histopathological images (x10) show spindle-shaped cells woven into a bundle-like arrangement.

and tumor motion. The main feature of the disease is a striated inhomogeneous parenchymal echogenicity extending from the pelvic venous system and/or inferior vena cava into the right heart cavity with well-defined vascular and cardiac cavity borders. Doppler ultrasound can assess hemodynamic changes in the veins and heart and perfusion within the mass. With the advent of ultrasonic contrast, the sensitivity and specificity of ultrasound diagnosis have greatly improved, allowing for a more accurate reflection and observation of perfusion in normal and diseased tissues. In this case, ultrasonic contrast showed that the mass was not rich in blood.

Although computed tomography (CT) examination is not the preferred modality, it can provide a good reference for the particular growth pattern of the IVL and determine the extent of tumor lesion extension, growth pathway, and anatomical relationship with surrounding tissues. The typical CT presentation shows a parametrial, intrapelvic mass with lesions poorly demarcated from the uterus and broad ligament, enhancing similarly to uterine fibroids and involving the pelvic venous system, resulting in intravenous filling defects. When the lesion extends into the inferior vena cava and the cardiac cavity, it appears as a cord and lobulated mass shadow in the inferior vena cava and the heart cavity. Postprocessing techniques, such as multiplanar reconstruction (MPR) with multilayer spiral CT, can show the tumor in all directions and from multiple angles. For example, the CT reconstructed images depict the tumor extending from the inferior vena cava into the right ventricular system in a manifestation of the "crutch head sign". This imaging sign was considered an important informative imaging feature point to the diagnosis of LVL. Which has been described in previous case reports either [11]. We speculated that the "crutch head sign" might preferred related to morphological changes due to hemodynamics rather than the pathognomonic feature. However, no CT was performed in this case.

MRI is considered the most accurate and optimal preoperative examination as it provides a good assessment of the origin and extent of the lesion and the surrounding ratio and has a good soft tissue resolution, allowing an in-depth analysis of the tissue components of the mass. In this case, some cystic portions of the mass were observed on the MRI. The cine sequence of MRI can also dynamically display the motion of the lesion within the cardiac cycle, allowing a good assessment of the attachment point of the lesion, whether it involves the tricuspid valve, and the condition of cardiac blood circulation. Therefore, when LVL is highly suspected, ancillary examinations such as ultrasound, CT, and MRI, combined with the patient's medical history, can be very helpful in preoperative diagnosis and evaluation.

Differential diagnosis

It is important to differentiate IVL confined to the pelvis or perifocal area of the uterus from other uterine spindle cell tumors that may have vascular involvement, such as uterine smooth muscle sarcoma [12]. Uterine smooth muscle sarcoma is prone to liquefaction and necrosis and has a high signal on T1WI and irregular mixed high and low signals on T2WI, with marked enhancement and areas of no enhancement, and are poorly demarcated from the vessel wall. IVL tumors often have a clear boundary with the vessel wall. When IVL invades the veins and the right heart, it is also important to distinguish it from venous thrombosis, right atrial mucinous tumor, and metastatic malignant tumor [13]. CT or MRI enhancement scans can help to differentiate between tumors in the lumen of the IVL vein and venous thrombosis because IVL lesions invading the veins may be misdiagnosed as venous thrombosis. With contrast imaging, there is no enhancement of intraventricular thrombus, whereas tumors in IVL show heterogeneous enhancement. When IVL invades the right heart, it may be misdiagnosed as a right atrial mucinous tumor. A right atrial mucinous tumor is usually a pedunculated mass from the interatrial septum, is confined to 1 chamber of the heart, and rarely involves the inferior vena cava. However, IVL usually extends through the inferior vena cava into the right atrium. The diagnosis of a right atrial mucinous tumor by MRI in the present patient was due to a lack of experience with this condition. It is also necessary to identify metastatic malignant tumors that invade the inferior vena cava (eg, renal carcinomas), which may appear like IVL on imaging but have a shorter pathway of venous extension and a primary cancerous focus.

In conclusion, women with uterine fibroids or a history of surgery for uterine fibroids and concomitant findings of venous or intracardiac lesions, evaluated for mutual continuation of the 2 and with consistent signals and enhancement, should be considered for IVL or LCL.

Treatment

Surgical resection is the clinical treatment of choice, and there are high surgical risks and recurrence rates after surgery. Depending on the patient's preoperative evaluation, 1- or 2-stage surgery is usually selected [14]. One-stage surgery refers to the complete resection of tumors in the thorax and abdominopelvic region at 1 time, which has the advantage of reducing the occurrence of intraoperative embolism and lowering the cost of surgery; the disadvantage is that the surgery lasts long, is traumatic, has more bleeding, and has more postoperative complications. Two-stage surgery, which includes the suprarenal and infrarenal stages, starts with a combined thoracoabdominal incision to surgically remove the tumor from the inferior vena cava to the ventricle, followed by elective transabdominal resection of the uterus, adnexa, and diseased tissues. This procedure reduces surgical risk, facilitates postoperative recovery, and is suitable for patients with poor physical foundation during preoperative evaluation. One study summarized 77 cases of LVL reported from 1980 to 2008 in China and abroad and found a partial resection rate of 36%, a complete resection rate of 20% in stage I, and a complete resection rate of 36% in stage II. Ahmed et al. reported a recurrence rate of approximately 30% after LVL surgery [15]. Research has suggested the presence of estrogen and progesterone receptors in the IVL, which may be closely associated with mass growth and recurrence. Estrogen receptor antagonists and gonadotropin inhibitors are also used clinically to improve hormone regulation levels in patients; however, their effectiveness remains to be investigated [10].

Follow-up

The recommended follow-up intervals are 3, 6, and 12 months after operation, and then once a year thereafter. Venous ultrasound was recommended as the best imaging follow-up at clinical practice. A pelvic MRI can be used when it is difficult to clarify whether there is an emerging issue by US. There are currently no guidelines [11].

Conclusion

The analysis of this case and the summary of previous case reports will hopefully improve the diagnosis and treatment of IVL, a rare benign tumor with malignant behavior and unique pathogenesis. A thorough medical history taking and preoperative ancillary tests are essential for preoperative diagnosis. Surgical resection is the primary treatment modality, and adjuvant antiestrogen therapy may be important for controlling tumor recurrence and inhibiting tumor growth.

Ethics statement

The study involving human subjects was reviewed and approved by the Medical Research Ethics Committee of Hainan General Hospital in accordance with the Helsinki Declaration. In this retrospective study, this patient's written informed consent was obtained.

Patient consent

In this retrospective study, this patient's written informed consent was obtained.

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