Journey From the Pelvis to the Heart: Are Leiomyomas Truly "Benign"?

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INTRODUCTION

Intravenous leiomyomatosis (IVL) is a rare condition and can be mistaken for malignancy or venous thrombus-in-transit. Intravenous leiomyomatosis should be considered when evaluating female patients with a history of leiomyoma and an intracardiac mass. Multimodality imaging helps guide diagnosis and surgical approach. Intracardiac involvement can lead to extensive surgery with further cardiac complications.

CASE PRESENTATION

A 54-year-old woman with a history of uterine fibroids presented to the outpatient gynecologist for evaluation of abnormal uterine bleeding. The patient experienced menopause at age 52 and required hormone replacement therapy consisting of progesterone micronized 200 mg/day and subdermal estrogen pellets to manage hot flashes. Transvaginal ultrasound revealed complex bilateral adnexal masses and an enlarged heterogeneous uterus. Computed tomography (CT) of the abdomen and pelvis showed a poorly defined endometrium and indiscernible uterine borders concerning for malignancy (Figure 1A and B). The CT also reported nonocclusive venous thrombus extending from the suprarenal inferior vena cava (IVC) to the right atrium (RA) and a right interlobar pulmonary embolism with associated calcifications suggestive of an old embolism (Figure 1C). The infrarenal IVC could not be evaluated due to poor quality.

Based on the CT findings, the patient was sent to the emergency department, and intravenous heparin was empirically started until further workup was completed. Vascular surgery recommended no urgent procedure as the patient was clinically stable. Endometrial and CT-guided pelvic biopsies revealed benign spindle cell pathology consistent with leiomyoma. After 1 week of uncomplicated hospitalization the patient was discharged on apixaban to complete further workup and interventions as an outpatient.

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Outpatient magnetic resonance imaging (MRI) of the pelvis revealed an enlarged uterus with leiomyomas (Figure 2A and B) and a nonocclusive venous thrombus-like lesion extending from the right common iliac vein, through the IVC, and to the RA (Figure 2C). Despite benign pathology, the oncology team remained highly suspicious of malignancy, and pelvic biopsy was repeated, which again showed benign leiomyoma. Given extensive leiomyomas and a concern for possible malignant conversion, the patient was offered elective total abdominal hysterectomy/bilateral salpingo-oophorectomy (TAH/BSO). After counseling, surgery was deferred and surveillance CT was done a month later, which showed stable masses, suggesting a chronic etiology.

The patient was referred to cardiology for investigation of the intra-atrial mass. A transthoracic echocardiogram (TTE) showed an ejection fraction of 50% to 55% (Video 1) and tricuspid regurgitation. It also revealed an elongated pedunculated soft tissue mass oscillating between the RA and the right ventricle (RV; Figure 3, Video 2) extending from within the IVC (Video 3).

Visualization of the mass and its oscillatory movement through the tricuspid valve (TV) raised concerns for a high risk of embolization. The patient was readmitted to the hospital, where apixaban was switched to heparin infusion given the high concern for thrombosis and embolism.[1] Multidisciplinary team discussions between the cardiology, cardiothoracic surgery, gynecology, and oncology teams led to a decision to pursue thoracotomy and RA mass resection prior to TAH/BSO.

An intraoperative transesophageal echocardiogram revealed an intra-atrial 4.8 × 2.9 cm mass with questionable adhesion to the distal posterior IVC and severe tricuspid regurgitation (Videos 4 and 5). Median sternotomy with right atriotomy revealed torn TV chords and flail septal leaflet likely due to chronic traumatic injury from repetitive contact with each cardiac cycle (Figure 4). The TV and the chords were surgically repaired. A 19 cm long mass extending into the IVC was extracted (Figure 5). Surgery was complicated by development of a third-degree atrioventricular block with a stable junctional escape rhythm of 50 beats per minute (Figure 6). Temporary epicardial pacing wires were placed; atrioventricular activity did not recover by postop day 4, necessitating placement of a dual-chamber pacemaker. The patient was discharged on postop day 5 in stable condition on aspirin and apixaban. Pathology obtained from the intracardiac mass showed benign spindle-shaped cells in a collagenous and vascularized stroma consistent with leiomyomas (Figure 7).

Given a diagnosis of IVL with extensive involvement, the oncology team treated the patient with intramuscular leuprolide for 3 months to reduce residual estrogen and eventually completed TAH/BSO via exploratory laparotomy without complications. Cardiac surgical follow-up confirmed a well-healing sternotomy scar. Pacemaker evaluation showed normal function. For management of menopausal hot flashes, they were placed on venlafaxine and advised to avoid hormonal therapy.

VIDEO HIGHLIGHTS

Video 1: Two-dimensional TTE, apical 4-chamber view, demonstrates low normal left ventricular systolic function, normal size and function of the RV, and a large pedunculated mass oscillating between the RA and the RV through the TV.

Video 2: Two-dimensional TTE, right ventricular inflow tract view, demonstrates normal RV and RA size, normal RV systolic function, and a large pedunculated mass oscillating between the RA and the RV through the TV.

Video 3: Two-dimensional TTE, subcostal view, demonstrates the extension of the IVL from the IVC into the RA.

Video 4: Intraoperative transesophageal echocardiogram, midesophageal RV-focused 4-chamber systolic view (0°) with color-flow Doppler, demonstrates severe tricuspid regurgitation (vena contracta width, 0.7 cm).

Video 5: Three-dimensional transesophageal echocardiogram, midesophageal volume-rendered reconstruction view (0°) with RV focus, demonstrates a large, pedunculated mobile mass oscillating between the RA and the RV through the TV. The RV and RA size and function are normal.

View the video content online at www.cvcasejournal.com.

DISCUSSION

Intravenous leiomyomatosis with cardiac extension is a rare presentation of benign uterine neoplasia. It is characterized by proliferation of uterine smooth muscle cells through the venous circulation, which can involve the IVC, right heart chambers, and, more rarely, the pulmonary arteries. Intravenous leiomyomatosis has been suggested to originate from either a uterine leiomyoma with vascular invasion or the venous smooth muscle wall itself.[2] When extending through the right heart chambers, the tumor is referred to as intracardiac leiomyomatosis (ICLM) and can have more severe and rarer complications such as TV injury. The clinical presentation depends on the severity of cardiac involvement.[2] The most severe complication is right-sided cardiac outflow tract obstruction, which can lead to cardiac arrest and death. Therefore, complete resection of the intracardiac mass is recommended.[3] Due to high risk of thrombosis, anticoagulation is recommended during the perioperative period and 6 months after resection.[1]

Our patient was similar to most women who are affected by IVL, middle-aged women mostly between the ages of 40 and 50 and multiparous.[2] Based on case reports, IVL is also more common in women with a previous hysterectomy or myomectomy or coexisting uterine leiomyoma.[2] Furthermore, the presence of female gonadal hormones appears to be related to positive IVL tumoral growth, as leiomyomas are responsive to estrogen and progesterone.[4] Our patient was on hormone replacement therapy for menopausal symptoms, which may have contributed to progression of disease.

The preferred initial imaging modality for ICLM is TTE as it can provide high-resolution and real-time images of intracardiac lesions. It also provides both structural and functional information such as right ventricular function and valvular involvement. Computed tomography and MRI are then used for their multiplanar and large fields of view that can show the extent of the extracardiac lesion.[5] Cardiovascular magnetic resonance has become the reference standard imaging modality for evaluation of intracardiac masses as it allows optimal tissue differentiation and characterization of a mass. Cardiovascular magnetic resonance enables the differentiation of intracardiac thrombus from a tumor due to avascular composition.[6] Early gadolinium enhancement imaging is the ideal technique; thrombus manifests as the absence of gadolinium uptake and appears almost black. Cardiovascular magnetic resonance was not performed in this patient since after the echo findings a decision was made to pursue excision of the mass for definite diagnosis.[6] Cardiovascular magnetic resonance may have been helpful after CT and MRI findings and should be considered as an early diagnostic tool in the multimodality assessment of cardiac masses. The supplementary information provided by these imaging modalities can help with identifying the extension of the lesion to its associated uterine leiomyomas and guiding operative management.

The treatment of IVL has 2 goals: to remove the tumor and to prevent its recurrence, which can occur through unclear mechanisms.[7] Given that leiomyomas are stimulated by estrogen and progesterone, TAH/BSO is essential to limit recurrence. Additionally, exogenous estrogens must be avoided to prevent subsequent growth of microscopic or unresected foci of intravenous leiomyoma. Gonadotropin-releasing hormone agonists and antiestrogen therapy have also been used to reduce the tumor mass and prevent regrowth. Their effectiveness is unknown, but it is believed that such therapies are ineffective against fast-growing tumors.[4] More research is needed to fully understand IVL and ICLM, their associated risk factors, and effectiveness of different treatment approaches. Surveillance is crucial for IVL due to

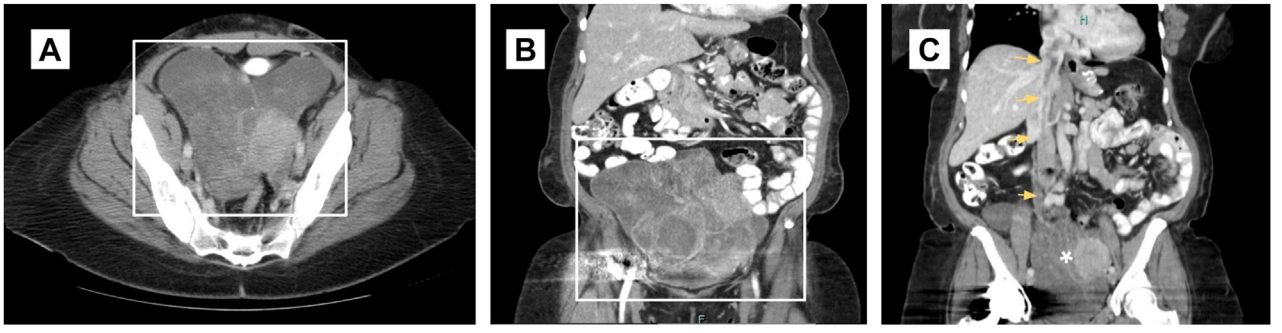

Figure 1 Computed tomography of the abdomen and pelvis, **(A)** axial and **(B)** coronal view, demonstrates a large globular uterus with irregular borders, consistent with fibromas (*white box*); the enlarged globular uterus with leiomyomas (*asterisk*) and IVL (*arrows*) extending from the uterus to the RA via the IVC is demonstrated in panel C. *H*, Heart.

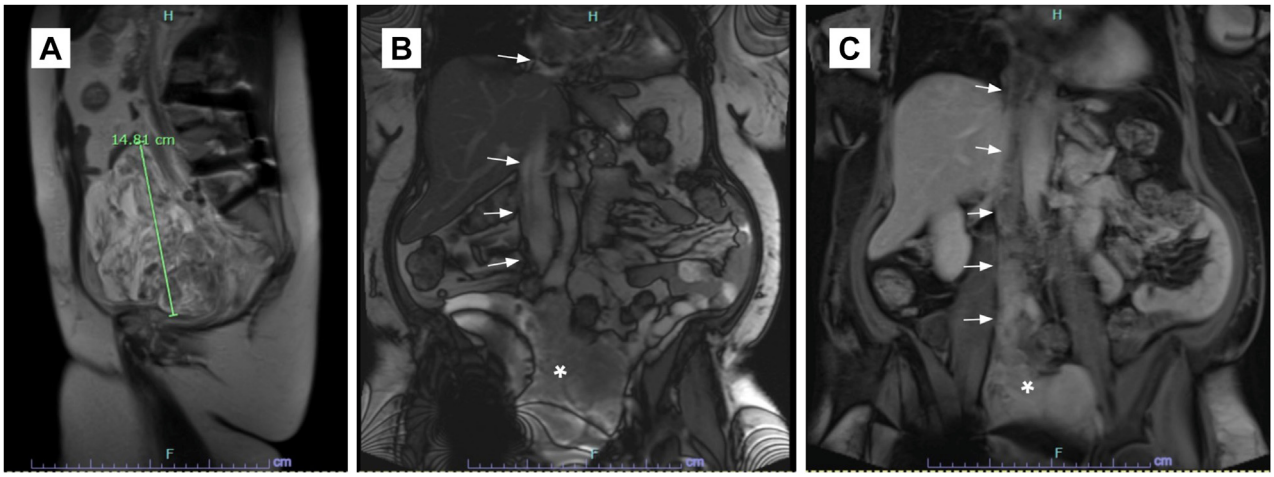

Figure 2 **(A)** T1-weighted MRI, sagittal view, demonstrates the enlarged globular uterus with irregular borders (uterine height, 14.81 cm); **(B)** T1-weighted MRI, coronal view, demonstrates the uterine leiomyoma (*asterisk*) and IVL (*arrows*) extending from the uterus to the RA via the IVC; **(C)** T2-weighted MRI, coronal view, demonstrates the elongated mass extending from IVC to the heart (*arrows*).

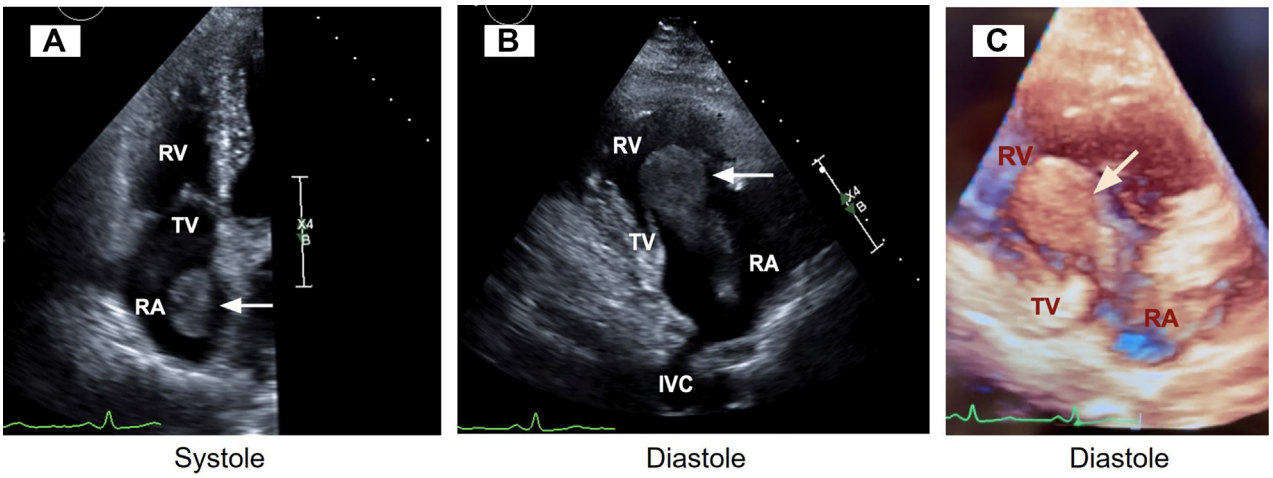

Figure 3 **(A)** Two-dimensional (2D) TTE, apical 4-chamber systolic view with right heart focus, demonstrates a normal size RV with a mobile globular mass (*arrow*) in the RA; **(B)** 2D TTE, right ventricular inflow tract diastolic view, demonstrates a pedunculated mass (*arrow*) between the RA and the RV; **(C)** three-dimensional TTE, reconstruction of the right ventricular inflow tract, diastolic view, demonstrates a pedunculated mass within the RV (*arrow*).

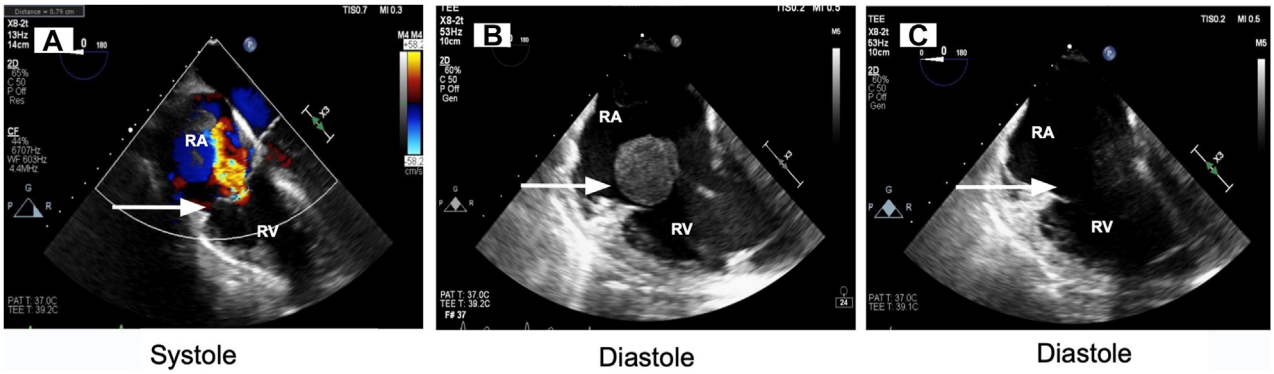

Figure 4 **(A)** Intraoperative TEE, midesophageal RV-focused 4-chamber systolic view (0°) with color-flow Doppler, demonstrates severe tricuspid regurgitation (*arrow*; vena contracta width, 0.7 cm). **(B)** Intraoperative two-dimensional (2D) TEE, midesophageal long-axis systolic view (0°), demonstrates the mass (*arrow*) within the RA and abutting the septal leaflet. **(C)** Postoperative 2D TEE, midesophageal long-axis diastolic view (0°), demonstrates removal of the mass and TV repair (*arrow*).

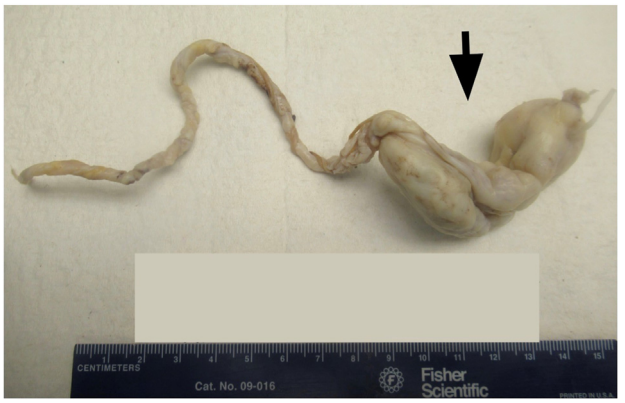

Figure 5 Gross specimen obtained after resection. A sperm-like fibronodular mass consisting of a bulb-like end measuring 7 × 3 × 3 cm which is the intracardiac portion (*arrow*). Elongated 19 cm attachment had extension into the IVC to the suprarenal vein. Outer surface is smooth and homogenous without hemorrhage or necrosis.

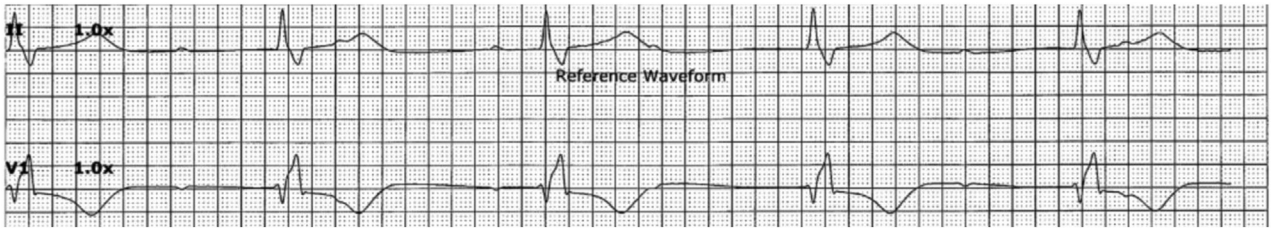

Figure 6 Intraoperative telemetry recording demonstrates third-degree atrioventricular block.

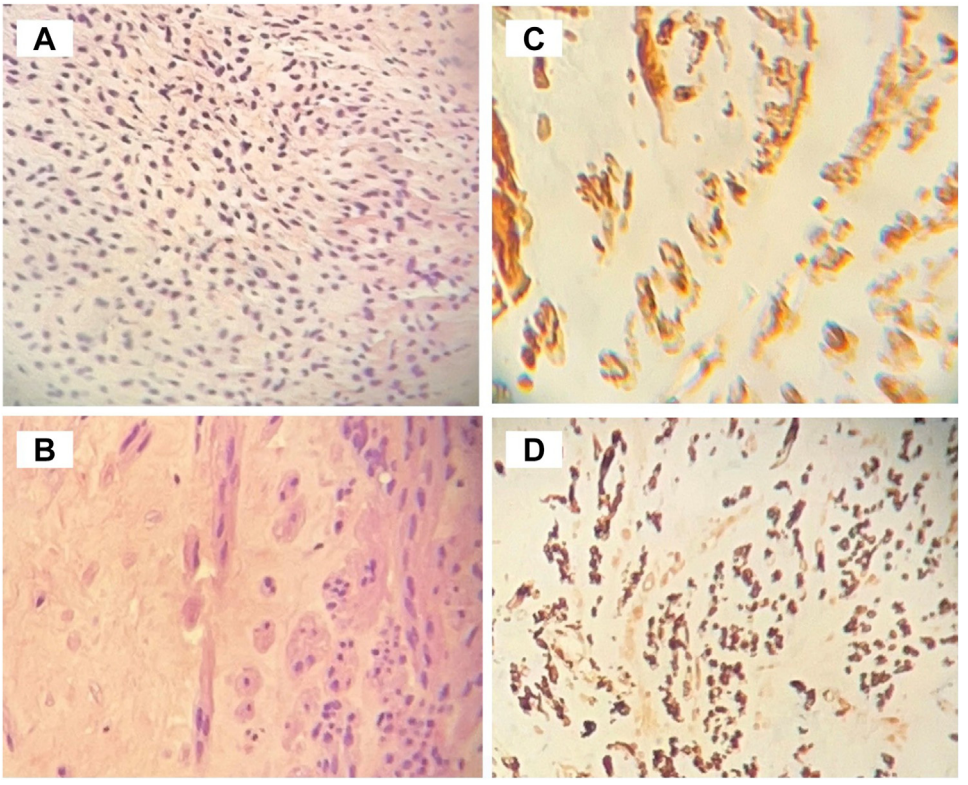

Figure 7 Histology images. **(A)** Tissue extracted from the TV cords mass showing bundles of spindle-shaped cells in collagenous stroma consistent with leiomyoma. There is no nuclear pleomorphism or mitosis. Note the classic "cigar-shaped" nuclei of spindle cells. **(B)** Tissue extracted from the RA and IVC tissue mass showing benign spindle cell neoplasm most consistent with leiomyoma. Tumor shows extensive ischemic necrosis and therefore is not as cellular as in panel A. **(C)** Immunohistochemical stain for smooth muscle actin (SMA), which is positive. **(D)** Immunohistochemical stain for Desmin, which is positive. Presence of SMA and Desmin confirms that this smooth muscle tumor is consistent with benign leiomyoma.

its risk of recurrence. The literature suggests that in case of radical resection there is almost no recurrence risk, and partial resection has a 5-year recurrence rate of 33.3%.[2] However, with the probability of incomplete resection and possible different rates of growth, more guidelines specifying postsurgical surveillance are required.

CONCLUSION

Due to rarity, IVL and ICLM are usually misdiagnosed or diagnosed late, which can lead to inadequate treatments and further cardiac complications. An increased awareness of IVL and ICLM and the use of comprehensive imaging modalities can help in improving diagnosis and management for patients affected by this rare condition. Diagnosis must be confirmed by postoperative pathological examination.

ETHICS STATEMENT

The authors declare that the work described has been carried out in accordance with The Code of Ethics of the World Medical Association (Declaration of Helsinki) for experiments involving humans.

CONSENT STATEMENT

The authors declare that since this was a non-interventional, retrospective, observational study utilizing de-identified data, informed con-sent was not required from the patient under an IRB exemption status.

FUNDING STATEMENT

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DISCLOSURE STATEMENT

The authors report no conflict of interest to disclose. Artificial intelligence has not been used in the generation of any material of this manuscript.

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SUPPLEMENTARY DATA

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