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Case report

Multidisciplinary management of extensive intravenous leiomyomatosis: A coordinated effort of a single institution

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1. Introduction

Intravenous leiomyomatosis (IVL) is a rare tumor that is found in reproductive age women, often with a history of leiomyomas. We report a case of extensive IVL diagnosed initially as a presumed primary cardiac tumor and the multidisciplinary surgical approach to management.

2. Case presentation

A previously healthy 64-year-old G2P1011 woman initially presented to an outside facility with chest pain, dyspnea on exertion and a "flopping" sensation in her heart. Echocardiogram revealed an intracardiac mass suspected to be an atrial myxoma. She underwent a sternotomy with cardiac exploration, with the intent of removing the intracardiac mass. However, no cardiac masses were appreciated during intraoperative cardiac arrest. Subsequent evaluation with a transesophageal echocardiogram (TEE) suggested an inferior vena cava (IVC) thrombus. A computed tomography (CT) of the chest, abdomen and pelvis demonstrated an extensive venous filling defect that extended from the superior vena cava (SVC) to the right internal and external iliac veins, as well as an enlarged uterus with an obscured serosal contour. A pelvic MRI revealed a multilobulated uterus, measuring 11.4 × 11.2 × 7.4 cm, with left pelvic soft tissue nodules separate from the uterus and presumed pelvic lymphadenopathy.

The patient was transferred to the gynecologic oncology surgery service at our institution on postoperative day 4 status post sternotomy for management of her extensive IVC thrombus and uterine masses. Medical history was remarkable for menopause at age 50 with episodes of postmenopausal bleeding and histologically benign endometrium on sampling with both dilation and curettage and endometrial biopsy throughout the previous 10 years. Pertinent medical comorbidities included hypertension, hyperlipidemia, class II obesity with BMI of 39 kg/m^2 and hypothyroidism.

Due to the extensive presumed thrombosis in her SVC, IVC and right internal and external iliac veins, the primary differential diagnosis included malignancy of renal, ovarian or uterine origin with accompanying thrombosis versus extensive IVL. The patient was anticoagulated with intravenous heparin. She underwent a pelvic magnetic resonance venogram (MRV) that revealed a large mass arising from the uterus measuring 10.5 × 10.0 × 7.2 cm with extensions into the adnexa and parametria and the ovaries were not able to be identified separately from the mass (Fig. 1a). Findings suggested tumor thrombus in the IVC, extending from the uterus through the right internal and common iliac veins to the intrahepatic IVC at the level of the hepatic veins consistent with the presumed diagnosis of IVL (Fig. 1b–d).

A multidisciplinary surgical team was assembled to surgically remove the extensive IVL. This included gynecologic oncology surgery, vascular surgery, hepatobiliary surgery, and urology. Initial exploration revealed an enlarged uterus with no evidence of extrauterine peritoneal disease and all surgical teams agreed that the disease process could be surgically resected.

The IVC was dissected through its course with suprarenal IVC exposure (Fig. 2a). Right and left common iliac veins were dissected out and the liver was mobilized to expose the suprahepatic IVC. A cavotomy was performed in the infrarenal IVC and a portion of the thrombus was extracted through the cavotomy without difficulty (Fig. 2b). A venotomy on the right common iliac vein was made longitudinally. The mass was then brought down through the venotomy to move it out of the IVC where it was not adhered. A type II radical hysterectomy and bilateral salpingo-oophorectomy was then performed (Fig. 2c). Tumor was noted to be extending through bilateral uterine veins into the internal iliac veins, even though the MRV had not demonstrated extension of the tumor thrombus into the left internal iliac venous system. Given these findings, the internal iliac veins were excised to the level of common iliac vessel bifurcations bilaterally. The remainder of the caval thrombus was then extracted in two pieces via

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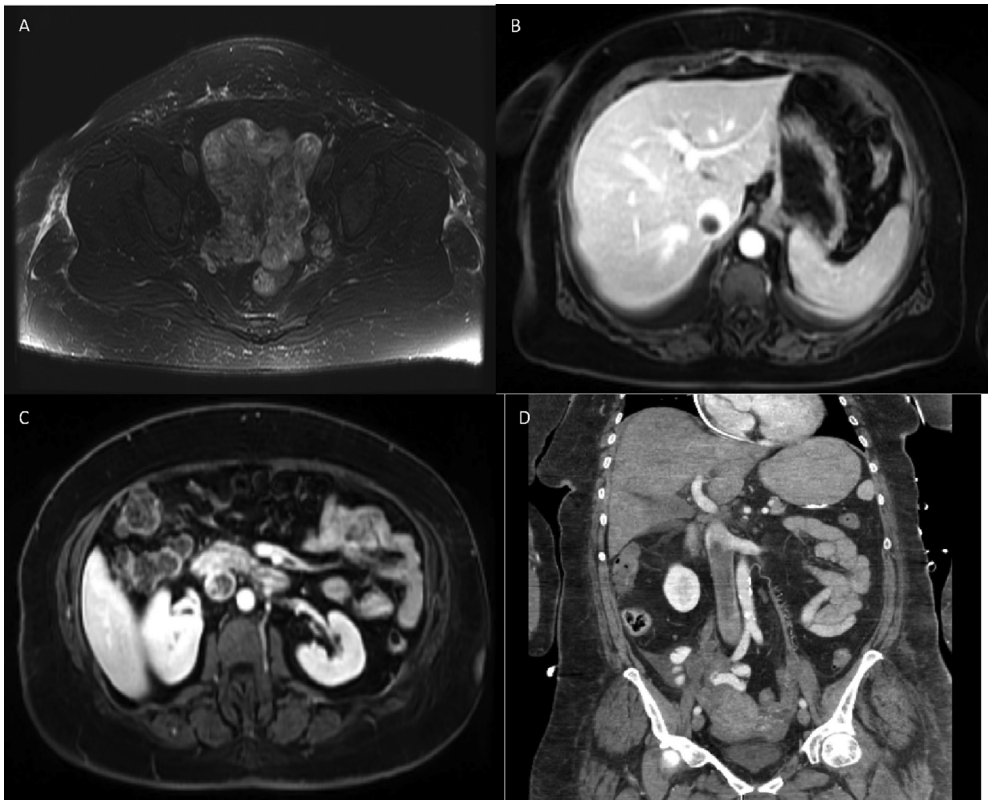

Fig 1. (a) Preoperative MRV demonstrating a lobulated heterogeneous pelvic mass arising from the anterosuperior aspect of the uterus involving both adnexa and parametrium, measuring approximately 10.5 × 10.0 × 7.2 cm (a). The IVC thrombus extends superiorly from the intrahepatic IVC (b), extending inferiorly with majority of the IVC thrombosed at the level of the renal veins (c), and continuing inferiorly into the right common iliac and internal iliac veins (d).

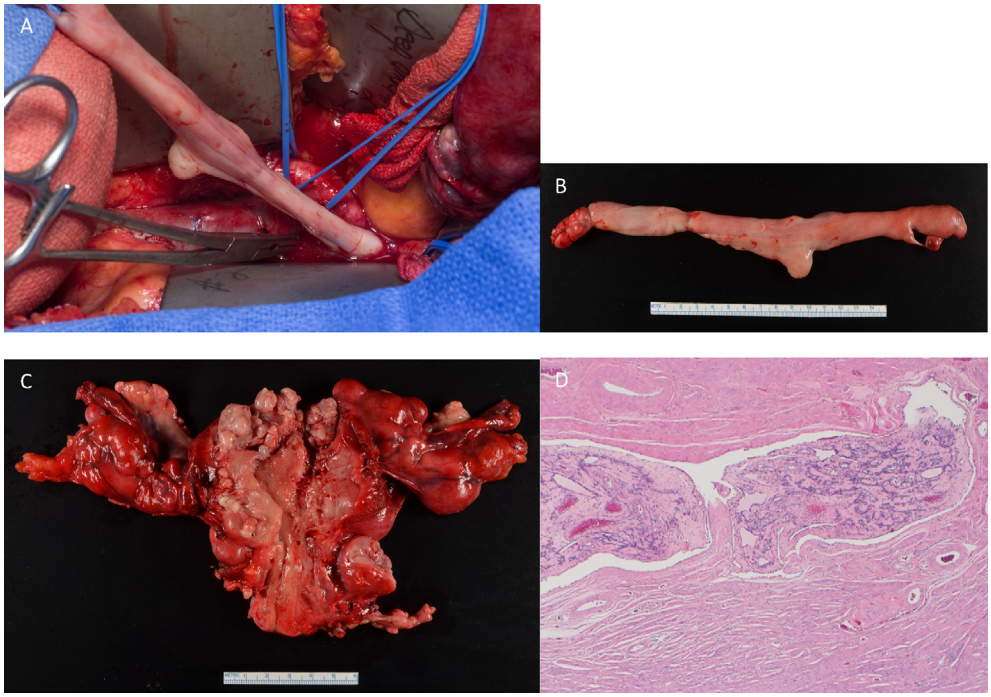

Fig. 2. Surgical dissection of the inferior vena cava (IVC) (a) and gross pathology specimen including the IVC thrombosis (b), uterus, bilateral fallopian tubes, bilateral ovaries, and bilateral parametrium (c). Photomicrograph demonstration of morphologically bland smooth muscle within vascular spaces (d).

cavotomy. Frozen section pathology evaluation of the caval thrombus demonstrated morphologically bland smooth muscle within vascular spaces by microscopic examination consistent with leiomyomatosis. (Fig. 2d). A stage IA, grade 1 endometroid endometrial cancer was also identified in the hysterectomy specimen on frozen pathology; therefore, she also underwent bilateral pelvic lymphadenectomy. All lymph nodes were negative for tumor.

In total, the patient had a 7L blood loss and received 13 units of packed RBCs, 4 units of FFP, 2 units of platelets, 10 pack of cryoprecipitate and a total of 6L of crystalloid. She was discharged on postoperative day 6. She had a follow up MRI two months after surgery that did not show any residual tumor thrombus. The patient was followed with serial MRA of the abdomen and pelvis and demonstrated no evidence of residual disease (Fig. 3a and b). She has now remained disease

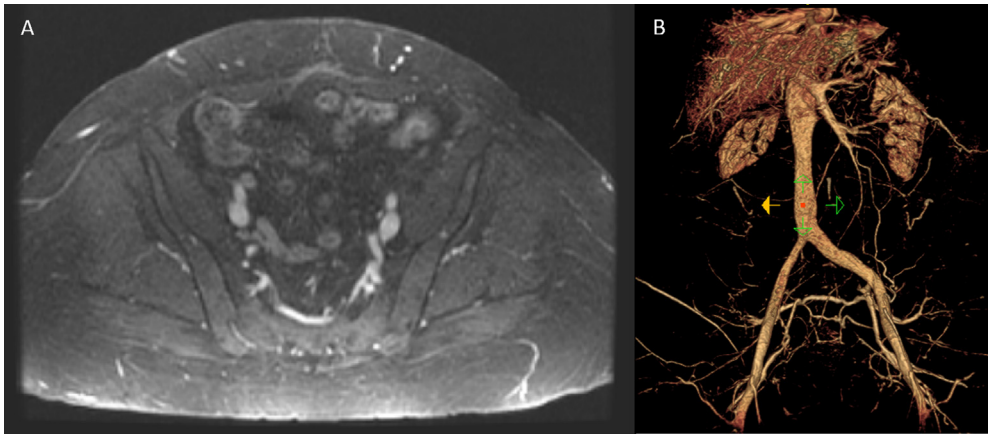

Fig. 3. MRI at the level of the pelvis at 20 months after surgery demonstrating no residual disease (a) and 3D reconstruction of venous collecting system from MRV (b).

free for over 4 years.

3. Discussion

Over the past century fewer than 200 cases have been reported on IVL. The first initial cases reported in the early 1900 s were all diagnoses of IVL discovered at the time of autopsies. All reports illustrate the potentially aggressive course of IVL (Mulvany et al., 1994; Fornaris et al., 2015); however, the mortality rate of IVL has never been clearly documented.

IVL is characterized by intravascular growth of morphologically bland smooth muscle into either venous or lymphatic vessels outside the limits of a typical leiomyoma. It is hypothesized that IVL either arises directly from the venous wall of uterine or pelvic veins or that there is vermiform extensions of uterine fibroids into veins (Kommoss et al., 2019; Clement et al., 1988). IVL predominantly occurs in women who are postmenopausal in the 5th or 6th decade of life, and symptoms are most often nonspecific including abdominal pain, vaginal bleeding, bilateral pedal edema, dyspnea with exertion, chest pain, and even cardiac arrhythmias. The tumor can cause life-threatening symptoms, especially if it involves the inferior vena cava (IVC), superior vena cava (SVC) and/or right atrium. IVL involving the heart can cause pulmonary emboli and cardiac failure (Stolf et al., 1999). As evidenced by our patient, if extensive enough, IVL can be misinterpreted as a primary cardiac tumor such as an atrial myxoma thus, leading to the initial workup including cardiac testing. Atrial myxomas, however, tend to be highly mobile pedunculated masses arising from the atrial septum and are limited to one chamber of the heart with little infiltration into the IVC.

In our patient's case, cardiac TEE provided critical information about the source of the mass seen on pre-sternotomy echocardiogram. CT and MRV subsequently traced the origin of the extensive intravascular lesion to the uterus. The MRV played a crucial role not only in narrowing the diagnosis but in assessing extension of the thrombus and guiding surgical planning. Given the degree of extension into the IVC, a multidisciplinary surgical team was critical for successful surgical extirpation.

Whether IVL can be completely resected depends on the extent and involvement of the associated vessels and the surgical approach. Forced detachment of the tumor can lead to pulmonary embolization, damage to vasculature, and life-threatening hemorrhage. Alternately, an incomplete resection increases the risk of recurrence of residual disease (Doyle et al., 2015). The recurrence risk of IVL is 16–22%; however, this is based on limited data, heterogenous surgical approaches, and unclear proportion of cases with residual disease at the end of surgical extirpation (Ma et al., 2016; Worley et al., 2009). As such, perioperative planning for removal of IVL should include expertise from vascular surgery, gynecologic surgery, radiology, pathology, anesthesia, and other surgical subspecialities, such as hepatobiliary surgery, urology and cardiac surgery. In addition, the surgical procedure sequence should be mapped out to minimize anticipated potential complications.

Unique to this specific case of IVL was the resection of the internal iliac vasculature to the level of the common iliac vessels. In our patient, we found IVL extending bilaterally through the uterine veins and into the internal iliac veins. With extraction of all IVL extending into the IVC and common iliac veins and a hysterectomy, there still remained a possibility that the IVL originated from the uterine or internal iliac venous system (Lam et al., 2004). As such, the resection of the internal iliac vasculature may have aided in decreasing the risk of IVL recurrence in our patient. This has not previously been described in literature but warrants further study. Thus far it is unclear whether ligation or resection of bilateral internal iliac veins offers a significant reduction in recurrence risk; however, our patient has remained disease-free for over four years.

Of note, 10–50% of IVL tumors express both estrogen and progesterone receptors, and are postulated to be hormone dependent (Kir et al., 2004). As such, there may be a role of GnRH agonists as an adjuvant therapy to control and eradicate remnant disease. This would be specifically favorable for patients who refused or were unfit medically for surgery, required fertility preservation, or had an incomplete tumor resection. GnRH agonists work by creating a state of systemic hypoestrogenism, thereby, reducing growth stimuli of the tumor (Kir et al., 2004). Outcomes have been noted to be short-term as recurrence is present with cessation of these medications. However, there may be a role for short term use of GnRH agonist therapy to reduce the burden of disease prior to operative management and potentially increase the likelihood of complete resection. Further study of preoperative GnRH agonist therapy is warranted.

Author contributions

1. Aneesa Thannickal, MD: Drafted the manuscript, manuscript editing and approval of final manuscript
2. Anousheh Shafa, MD: Manuscript writing, image and figure collections, manuscript editing and approval of final manuscript
3. Joy Maharaj, MD: Manuscript editing and approval of final manuscript
4. J. Kenneth Schoolmeester MD: Manuscript writing, manuscript editing and approval of final manuscript.
5. Julie Heimbach, MD: manuscript editing and approval of final manuscript
6. Randall DeMartino, MD: Provided input with regards to surgical

management, manuscript editing and approval of final manuscript
7. Jamie N. Bakkum-Gamez, MD: Manuscript writing, manuscript editing and approval of final manuscript, corresponding author

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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