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Intravenous Leiomyomatosis that was Difficult to Distinguish in Treatment-Resistant Thrombosis Complicated with a Large Leiomyoma: A Case Report

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Abstract

Background: Intravascular leiomyomatosis (IVL) is a rare benign tumor that grows within the veins, similar to cancer, without invading them.

Case presentation: We report the case of a 55-year-old woman who had a large leiomyoma (20 cm × 16 cm × 9 cm) and was scheduled for surgery. Contrast-enhanced computed tomography was performed preoperatively and it revealed clots in the Inferior Vena Cava (IVC). This led to a diagnosis of deep venous thrombosis. Anticoagulation therapy was initiated, but the thrombus did not decrease in size. She was diagnosed with an organized thrombosis, and under general anesthesia which closed monitoring patients, total abdominal hysterectomy and bilateral salpingo-oophorectomy were performed. During the surgery, leiomyoma moved up to the blood vessel. We diagnosed IVL based on a histopathological examination.

Conclusion: The possibility of IVL should be amply considered when suspecting treatment-resistant thrombosis associated with a large leiomyoma.

Keywords: Intravenous leiomyomatosis; Deep venous thrombosis; Inferior vena cava

Abbreviations:

IVL: Intravascular Leiomyomatosis; IVC: Inferior Vena Cava; CECT: Contrast-Enhanced Computer Tomography; DVT: Deep Venous Thrombosis

Background

FLeiomyomas are extremely common benign tumors in the field of gynecology. Among variations of leiomyoma, intravascular leiomyomata extend into the veins without invading the organs. Histologically, Intravascular Leiomyomatosis (IVL) resembles typical benign leiomyoma at both the gross and microscopic levels, but with different growth patterns [1], which extend outside the uterus. Sometimes, IVL extends to the inferior vena cava (IVC) and right atrium, and cardiovascular events such as syncope occur [2,3].

IVL was reported first by Bisch Hirschfeld in 1896 [4]. Subsequently, it was defined by Norris et al. as follows: "IVL is uterine leiomyoma or histologically benign leiomyomas originating from the wall of the vein that grow and spread in the veins." [5].

IVL is difficult to distinguish from deep venous thrombosis (DVT), and treatment is often delayed. Here, we report a case of IVL that resulted in difficulty in deciding the timing of surgery for a large leiomyoma with DVT that did not respond to anticoagulant therapy.

Case

A 55-year-old nulliparous woman with abdominal bloating had a large leiomyoma size of 20 cm × 16 cm × 9 cm (Figure 1) and was scheduled for surgery. During preoperative examination, D-dimer levels were within the reference range, but there were clots in the IVC, as observed using contrast-enhanced computed tomography (CECT; Figure 2) which lead to a diagnosis of DVT. For the thrombus, anticoagulation therapy (edoxaban 30 mg) was implemented for 6 months, but the thrombus size did not decrease, suggesting an organized thrombosis. We performed total abdominal hysterectomy and bilateral salpingo-oophorectomy under strict anesthesia management. During the surgery, it was observed that the leiomyoma extended into the parametrium and paravesical space and entered the veins in a cord shape (Figure 3). We were able to extract the tumor-like cord easily from the vein, and histopathological examination revealed a smooth muscle tumor similar to leiomyoma (Figure 4). When CECT performed 2 months after surgery revealed that the tumor in IVC disappeared (Figure 5), we finally diagnosed the patient with IVL. Three months postoperatively, anticoagulant therapy was implemented. No recurrence of the tumor in the IVC was observed, even 4 years postoperatively.

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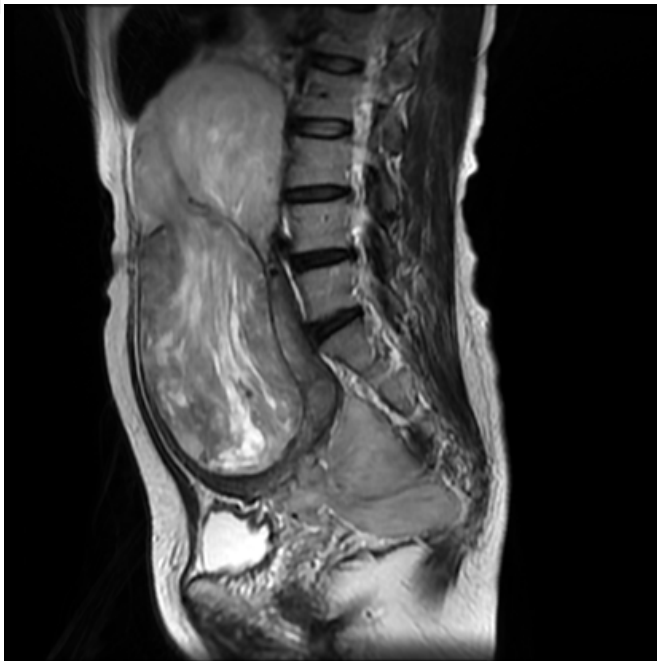

Figure 1: Preoperative T2-weighted MRI in the sagittal plane. A large leiomyoma of approximately 20 cm extending 10 cm above the umbilicus.

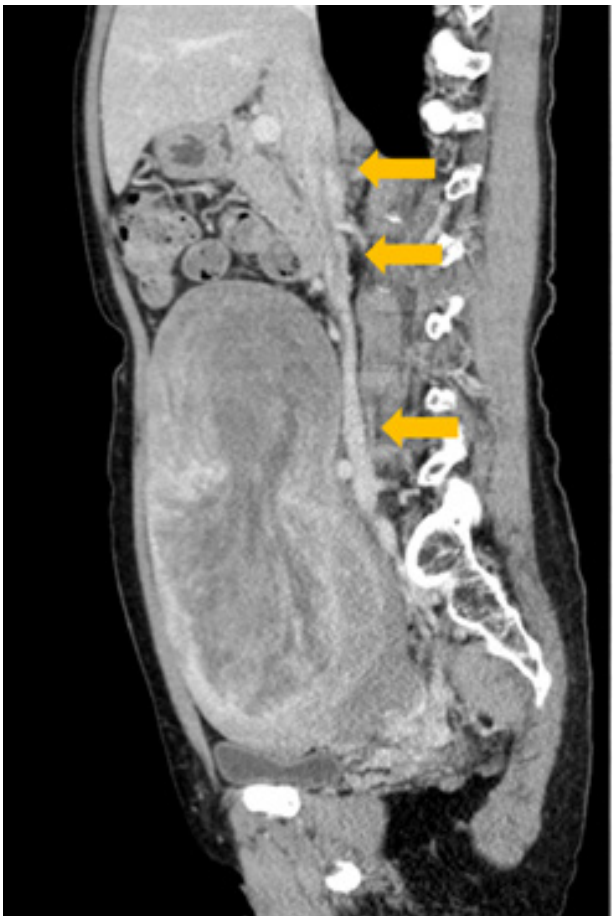

Figure 2: Preoperative CECT in the sagittal plane. Low-absorption regions in the IVC suspected to be a deep vein thrombosis (yellow arrow).

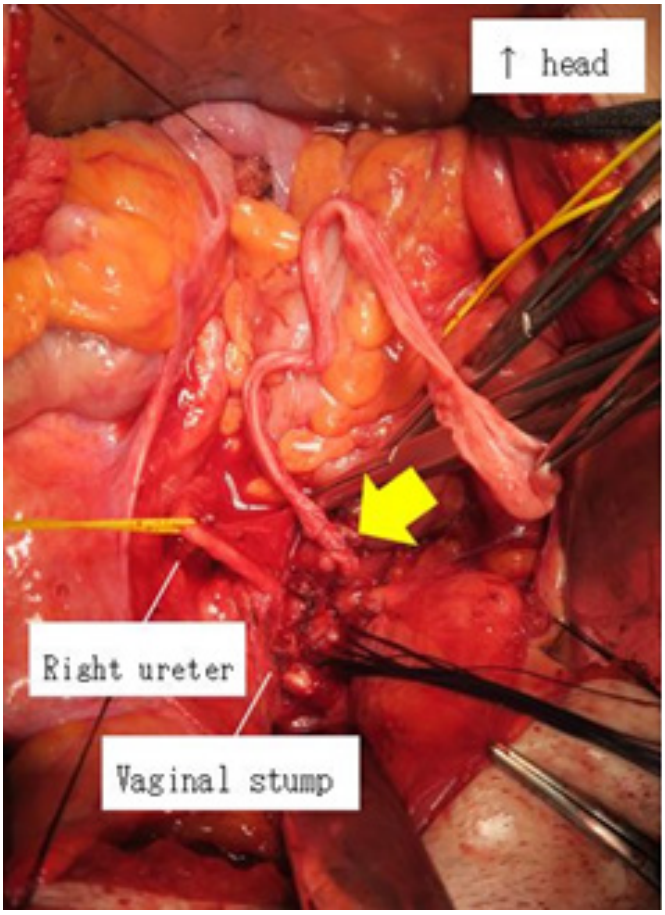

Figure 3: Surgical findings. The leiomyoma had become cord-like and extended into the vein from the paravesical space (yellow arrow).

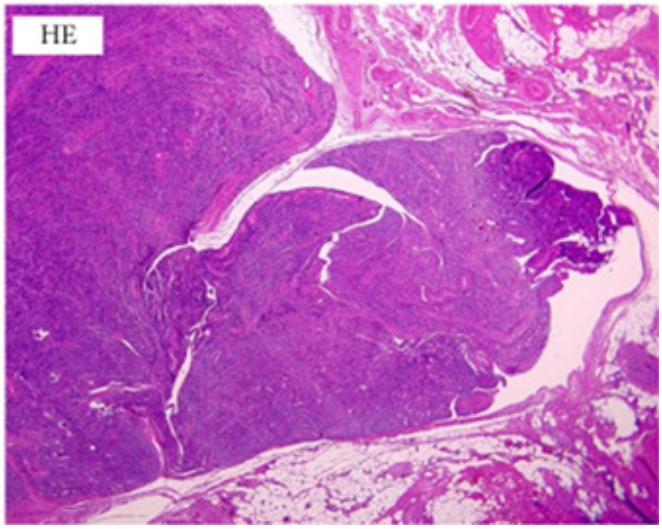

Figure 4: Histopathological examination of the tumor-like cord. The tumor was a smooth muscle tumor similar to leiomyoma. Nuclear atypia was weak, mitotic division was slight, and consisted of proliferation of short spindle-shaped cells.

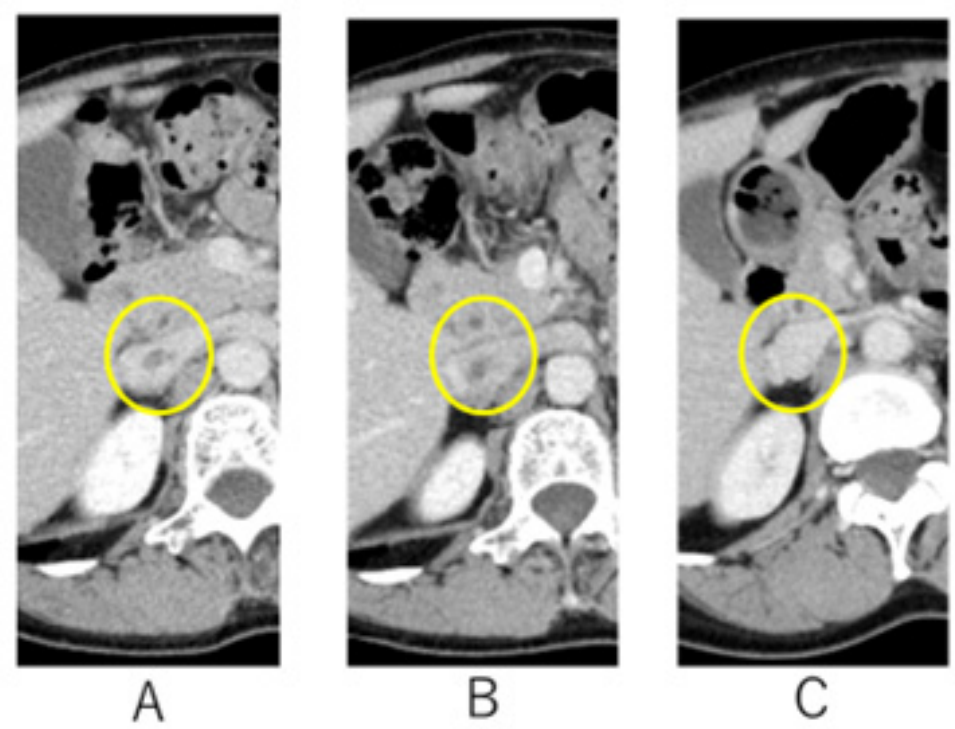

Figure 5: Change over time, as detected on CECT (A) Initial diagnosis (B) Six months after anticoagulant therapy (C) Two months postoperatively. The thrombus, which did not disappear even after 6 months of anticoagulation therapy from the initial diagnosis, disappeared on CECT 2 months postoperatively.

Discussion

Histologically, IVL resembles a typical benign leiomyoma at both the gross and microscopic levels, but with different growth patterns [1]. IVL is characterized by benign smooth muscle tumor growing in the blood vessel without invading organs, occasionally from the pelvis to the right atrium or right ventricle via the IVC. IVL rarely causes symptoms and is often detected accidentally, but when it extends into the right atrium it may cause complications such as syncope and pulmonary embolism, resulting in death [6,7]. CECT and MRI are useful for diagnosis [8,9]; if detected accidentally, IVL may get misdiagnosed as DVT. Treatment-resistant thrombosis with leiomyoma, as in our case, should be diagnosed along with considering the possibility of IVL.

There is no established treatment for IVL. Standard treatments include surgical treatment and anti-estrogen therapy. Surgical treatment involves removal of the uterus, ovary, and fallopian tube in two steps followed by a cardiovascular operation aimed at complete removal or performing both surgeries combined in one step. According to recent reports, the aforementioned surgeries are performed in one step [10], and in any case of IVL, cooperation and collaboration with cardiovascular surgery is necessary. In this surgery, heparinization is necessary because the extent of surgery includes endovascular lesions. Considering the risk of bleeding, it is common to perform surgery on gynecological organs after the surgery for endovascular lesions [11,12]. Complete removal of the tumor is preferred because it has a low rate of recurrence [13]. If these tumors are not completely removed, there is a 33% chance of recurrence within 3 years, as reported by Bin Li [14]. IVL is a hormone-dependent tumor [15]; thus, salpingo-oophorectomy or aromatase inhibitors and anti-estrogen therapy are preferred to prevent recurrence [1]. However, hormonal therapy does not guarantee a reliable effect, as there are some cases in which recurrence occurs even if hormonal therapy is performed [16].

Ordulu analyzed the expression of HMGA2, MDM2, and CDK4 proteins in the IVL by immunohistochemistry [17]. Seven of 12 (58%) IVL cases expressed HMGA2, and none expressed MDM2 or CDK4. HMGA2 is a protein involved in cell differentiation and proliferation. The frequency of HMGA2 protein expression in IVL was 58%, which was higher than that reported in uterine leiomyoma (32%) [18]. Accordingly, it is considered that the expression of HMGA2 protein may be involved in IVL progression. In our case, since there was no expression of HMGA2 (data not shown), we could remove the tumor completely. No recurrence was observed 4 years after surgery. IVL is a rare benign disease, but it may be life-threatening. Therefore, it is necessary to invent new therapeutic methods and identify prognostic factors. There is an urgent need for gene analysis in multiple cases in collaboration with other hospitals.

Conclusion

IVL is a disease with few symptoms, and if subjective symptoms occur, the risk of cardiovascular events is high and life-threatening. Furthermore, IVL may get misdiagnosed as thrombosis, since preoperative diagnosis is difficult. When suspecting treatment-resistant thrombosis associated with large leiomyoma, as in this case, it is important to consider the possibility of IVL, which helps to create an appropriate surgical plan. Since IVL is a rare case, it is necessary to collect cases at other facilities and clarify the treatment method and pathophysiology.

Ethics Approval and Consent to Participate

This investigation was conducted in accordance with the ethical standards and according to the Declaration of Helsinki and national and international guidelines, and has been approved by the institutional review board of Shimane University Hospital (IRB No. 201912120-1).

Consent for Publication

The participant provided written informed consent to participate in the study.

Availability of data and materials

Not applicable.

Competing interests

The authors declare that they have no competing interests.

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Author's contributions

YY and KN drafted the manuscript. RF, HY, TI, MI, HS, SS contribute to data collection. KN participated in the design of the study. SK conceived the study, participated in its design and coordination, and helped in drafting the manuscript. All authors have read and approved the final manuscript.

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