Case Report

Uterine intravascular leiomyomatosis involves the heart: a case report and literature review

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Background: Intravascular leiomyomatosis (IVL) of the uterus is extremely rare in clinical practice, often involving the pelvic and abdominal veins. Involvement of the heart and pulmonary arteries is rarer but can lead to severe clinical outcomes. It is difficult to diagnose the disease before operation, and most of them are found accidentally during the operation or postoperative pathology of uterine fibroids. This article will report a special case of IVL involving the heart, and comprehensively analyze and discuss the relevant domestic and foreign literature. Through real clinical cases, we hope to understand the core characteristics of this disease to guide clinical diagnosis and treatment.

Case Description: Here, we present the case of a 47-year-old woman with intrauterine venous leiomyomatosis whose tumor had spread to the right atrium. The patient lacked any distinct clinical symptoms. During uterine fibroid surgery, the tumor bolt was unintentionally discovered. The combined utility of multiple disciplines resulted in total removal of the tumor thrombus in the patient's venous system and right atrium during the same procedure. Following surgery, the patient achieved a significant recovery. After a follow-up of 2 years, there was no sign of neoplasm recurrence.

Conclusions: IVL mainly occurs in premenopausal women. The early clinical manifestations are non-specific, and preoperative diagnosis is difficult. In order to improve the preoperative diagnosis rate, preoperative examination should be strengthened for patients with large uterine fibroids, long duration, chest tightness, shortness of breath, syncope and other medical history. During the operation, the pelvic and abdominal vessels should be comprehensively explored, and all intravascular lesions should be removed at one time, especially for those involving the heart, which often requires multidisciplinary collaboration. Complete resection of the lesion is the key factor affecting the recurrence. Endocrine therapy is an option for postoperative treatment, and it is used selectively according to the specific condition of the patient to reduce the risk of recurrence.

Keywords: Uterine leiomyoma; intravascular leiomyomatosis (IVL); involve the heart; surgery; case report

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Introduction

Intravascular leiomyomatosis (IVL) is defined as a particular type of smooth muscle tumor, in which smooth muscle tissue in blood vessels, especially veins, proliferates and protrudes into the lumen to form a tumor and grows along the wall of the veins (1-3). Birch-Hirschfeld made the initial report on IVL in 1896 (4). Most instances are recorded in females, there women are often accompanied by uterine

leiomyomas. According to the histological categorization of female genital tumors, the World Health Organization (WHO; 2014) declared that IVL should be categorized as a benign disease (5,6). However, it has malignant characteristics, including extending growth and a tendency to relapse. The tumor develops from cells of uterine smooth muscle tumors, grows, invades the venous system, and then proceeds to spread along the venous system to the pelvis, internal iliac, common iliac vein, inferior vena cava, right atrium, and even the right pulmonary artery, resulting in the corresponding clinical signs and, in extreme cases, heart valve obstruction and pulmonary embolism (7). Therefore, it is also known as intravascular smooth muscle disease of the uterus in the medical community. The mechanism of IVL is complex. It is still unknown how IVL develops and how its invasion and proliferation are regulated at the molecular level.

This paper presents a case of IVL involving the heart, which is even rarer in clinical practice. The patient only showed clinical symptoms of uterine fibroids before surgery, and the heart tumor thrombus was misdiagnosed as a thrombus. The IVL was found accidentally during surgery, and a complete resection of the tumor was performed after a multidisciplinary operation. Uterine IVL involves the heart, which can cause severe clinical outcomes and even sudden death. Preoperative diagnosis, adequate evaluation and multidisciplinary treatment are the keys. It is hoped that through this case report, the core characteristics of the disease are understood to guide clinical diagnosis and treatment. We present this case in accordance with the CARE reporting checklist (available at https://tcr.amegroups.com/article/view/10.21037/tcr-23-1462/rc).

Highlight box

Key findings

- Our case is the first report of intravascular leiomyomatosis (IVL) invasion of the heart, but the patient did not have any clinical symptoms. This patient has a large fibroid and a short history of uterine fibroids.

What is known and what is new?

- IVL is a rare clinical anomaly, most IVL can invade pelvic vessels. Which can be diagnosed by imaging examination and clinical symptoms.
- In this patient, no intravascular tumor thrombus was found on imaging examination, but the tumor thrombus was found to have invaded the heart during operation. Surprisingly, the patient did not have any clinical symptoms.

What is the implication, and what should change now?

- For patients with large uterine fibroids, the presence of IVL should be considered. The patient's history and clinical symptoms should not be relied upon entirely.

Case presentation

The patient was a 47-year-old woman with regular menstruation and no symptoms such as menstrual disorder. The patient was an ethnic minority farmer in Yunnan, with poor living and medical conditions, and did not receive routine physical examination. The patient was admitted to the hospital due to a self-felt pelvic and abdominal mass in recent 2 months. Ultrasound examination in the local hospital showed a huge pelvic and abdominal mass. An atrial thrombus was found and warfarin anticoagulation therapy was initiated. Due to limited local medical conditions, the patient was admitted to Yunnan Cancer Hospital (The Third Affiliated Hospital of Kunming Medical University).

An irregular pelvic mass and lobular alteration was visible on the computed tomography (CT) scan upon admission, with a maximum diameter of approximately 37 cm. The lesion was supplied by the uterine artery branch, surrounded and pressed upon on the uterus, and the uterine body density was uneven, accompanied by fibroids. The inferior vena cava was poorly filled. The gynecological examination revealed that the cervix was compressed and could not be exposed, but was smooth to palpation. A similar normal uterus-like mass was palpable in the right superior portion of the symphysis pubis. There was a solid mass approximately 40 cm in diameter with a smooth surface, reaching to under the xiphoid process. Thus, we surmised that the abdominopelvic cavity space-occupying mass was likely a gigantic uterine myoma. Intraoperatively, it was discovered that the tumor originated in the left uterine wall or adnexa. It extruded the right uterus and bladder, with a cystic solid feature. The appearance of the right ovary and fallopian tube was normal. Then, we performed a total uterus with left adnexa and tumor resection. After the tumor excision, further palpation detected a solid cord-like mass at the left stump of the pelvic funnel ligament. Meanwhile, the abdominal and pelvic veins were checked thoroughly, revealing that the right pelvic funnel ligament drained into the inferior vena cava. Then, a cord-like mass was palpated in the inferior vena cava, extending upward into the heart. The mass was moveable and visible through the vein wall. By this time, we suspected that the patient had an endovascular smooth muscle tumor,

so we called in a vascular surgeon to aid with the procedure. When the left pelvic funnel ligament stump was released, we discovered that the tumor thrombus could be easily and completely retracted. Finally, a re-examination of the vena cava, bilateral common iliac veins, external iliac vein, and internal iliac vein revealed no evidence of a residual tumor embolus. The tumor plug was removed for rapid pathological examination, the results of which indicated a spindle cell tumor. After consulting with the patient's family, it was decided that the right adnexa should be removed due to the possibility of it being an endovascular smooth muscle tumor. Following surgery, the patient made a full recovery. A repeat cardiac ultrasound 1 week after surgery revealed the disappearance of the neoplasm thrombus in the atrium. No tumor recurrence was seen on imaging 2 years after surgery. Ultimately, postoperative pathology revealed the following: uterine neoplasms, and endovascular neoplasm. It was therefore considered an atypical smooth muscle tumor. All procedures performed in this study were in accordance with the ethical standards of the institutional and/or national research committee(s) and with the Helsinki Declaration (as revised in 2013). Written informed consent was obtained from the patient for the publication of this case report and accompanying images. A copy of the written consent is available for review by the editorial office of this journal.

Discussion

IVL predominantly occurs in premenopausal women and is a benign tumor with unique biological behavior. Most patients have a history or symptoms of uterine leiomyoma. This 47-year-old patient has no history of menstrual disorders because uterine fibroids, which are predominantly subserosal, do not interfere with menstruation. In addition, the patient lived in an ethnic minority area with a poor economic standard of living, and did not undergo routine physical examination. The tumor was not found until it was very large, resulting in a huge tumor occupying the entire pelvic cavity. On imaging review, the focus on the tumor and the neglect of intravascular lesions led us to disregard the possibility of IVL before surgery. However, the intravascular lesion was found during surgery and it was confirmed that it had extended to the heart.

There is considerable debate over the molecular mechanisms of invasive growth and the etiology of IVL. Although some scholars think that the tumor originates from smooth muscle tumor cells in the vein wall, most believe that the tumor is caused by uterine smooth muscle tumor cells migrating along the vessel wall and into the vessel's lumen (8). Reviewing this case, we found an intravascular tumor originating from the uterus during surgery and gradually spreading toward the venous return. At the time of neoplasm removal, there was no tight adhesion between the tumor and the vessel wall. Finally, the tumor was able to be removed intact from the vessel by pulling, so we prefer the second hypothesis; the clinical presentation of this female patient is more compatible with the second hypothesis. Oddly, men rarely develop IVL. Moreover, the finding (9,10) that IVL is consistent with typical uterine smooth muscle tumors in terms of immune expression and this patient's immunohistochemistry data confirm the homology of IVL with uterine smooth muscle tumors (*Figure 1A-1D*). Additionally, it has been discovered that IVL exhibits a chromosomal translocation that is distinct compared to typical uterine smooth muscle tumor cells, leading researchers to speculate that the occurrence of IVL may be linked to this chromosome 12q14-15 (6,11). The expression of hyaluronic acid is also much higher in IVL than in typical uterine smooth muscle tumors, which may be one of the mechanisms of IVL invasion into blood vessels as hyaluronic acid has viscoelastic properties, according to Yaguchi (12).

The clinical diagnosis of intravascular smooth muscle disease in the uterus is challenging, and the early clinical manifestations are predominantly signs of uterine fibroids. Non-specific symptoms appear as the uterine tumor grows, including menstrual changes, pressure symptoms, and increased abdominal girth. Additionally, early imaging is non-specific, which makes it easy to overlook intravascular lesions or mistake them for thrombus when the neoplasm is large. Cardiac ultrasound can identify the lesions when the tumor has progressed to the heart, but they are also easily mistaken for a thrombus. Pre-operative imaging in this patient revealed a huge space-occupying lesion in the pelvic and abdominal cavities, which was thought to be a tumor of uterine origin, but an intravascular lesion was not detected. The local hospital's cardiac ultrasonography misidentified the atrial tumor thrombus as a thrombus, and anticoagulation therapy was administered. However, after the procedure, the imaging doctor was invited to analyze the films again, which led to the discovery of an intravenous tumor thrombus (*Figure 2*). Due to its rarity, IVL is often misdiagnosed, and tumors involving the heart are much less common. Further, if the tumor spreads to the heart, it could impede the tricuspid valve and the venous

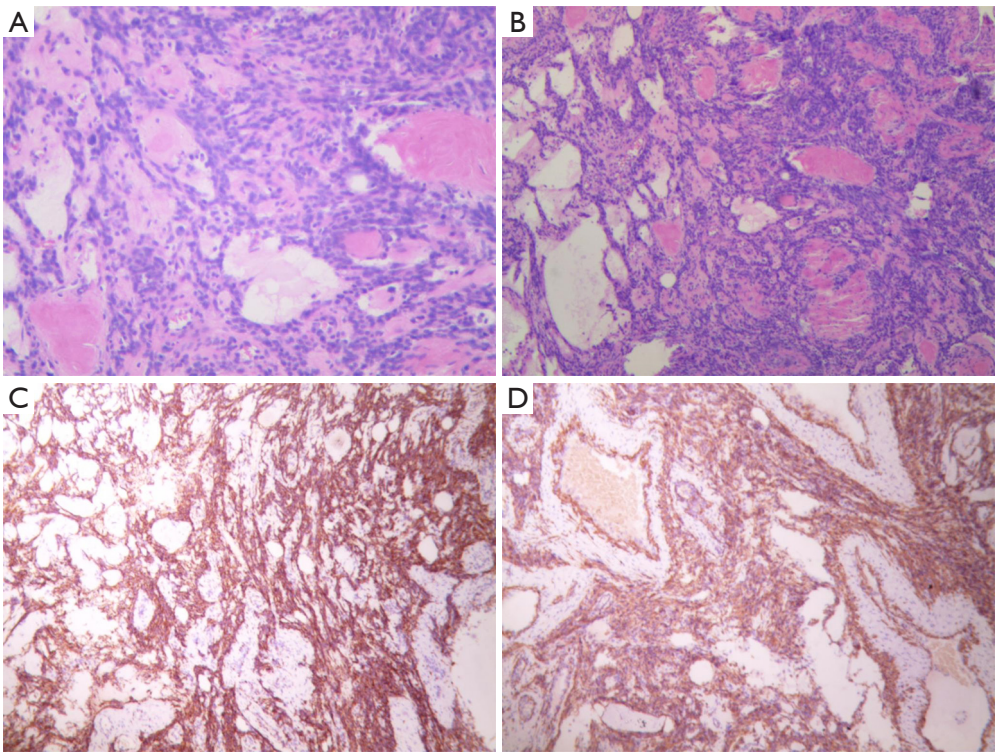

Figure 1 Pathological results of intravascular tumor. (A,B) HE staining shows that the tumor is nodular, partially involving blood vessels, and the tumor's nuclear division is visible, HE ×40. (C,D) Desmin and SMA were diffusedly expressed in tumor cells, IHC ×40. HE, haematoxylin and eosin; SMA, smooth muscle antibody; IHC, immunohistochemistry.

return, resulting in congestive heart failure. Characteristic clinical symptoms include dyspnea, syncope, pulmonary embolism, and even sudden shock death. There have been some reports of cases in which IVL extended to the right heart, mainly with dyspnea and syncope as the initial symptoms (13,14). Moreover, there have been several reports of right heart obstruction resulting in death (15,16). Therefore, in clinical work, pre-operative cardiac and vascular ultrasound should be strengthened in patients with giant tumors, long-standing uterine fibroids, and those with a history of syncope, shortness of breath, and chest tightness. In patients with high imaging suspicion of intravascular lesions, adjuvant scans for inferior vena cava CT intravascular imaging, magnetic resonance imaging (MRI), and angiography should be undertaken to enhance the diagnostic rate. In this case, the patient's preoperative tumor involved the right atrium, but her hemodynamics had not yet been impacted. Thus, the absence of distinctive clinical symptoms made the clinical diagnosis challenging.

The most straightforward and effective method of treatment for IVL is surgical resection. Theoretically, to fully understand the vessels involved in the tumor and develop a detailed surgical plan, a thorough preoperative assessment should be carried out for patients with IVL. This evaluation should include the pelvic and abdominal vena cava, the inferior vena cava, the right atrium, and the pulmonary artery. It often involves combined surgery of several departments and mainly requires the involvement of cardiovascular surgeons. Usually, complete resection can be performed in several sessions if it cannot be achieved all at once. Furthermore, cases that do not encroach on the pulmonary arteries or the heart can be removed in a single procedure. Total hysterectomy plus vein dissection and embolization is the primary surgical operation. However, the majority of IVL cases are difficult to diagnose before surgery and are frequently discovered during surgery. Due to the large tumor in this instance, the preoperative assessment did not detect the presence of a combined intravenous smooth muscle tumor. However, a neoplasms embolus was unintentionally found in the vena cava following surgical excision of the uterus and tumor. It was strongly suspected that the patient had endovascular smooth

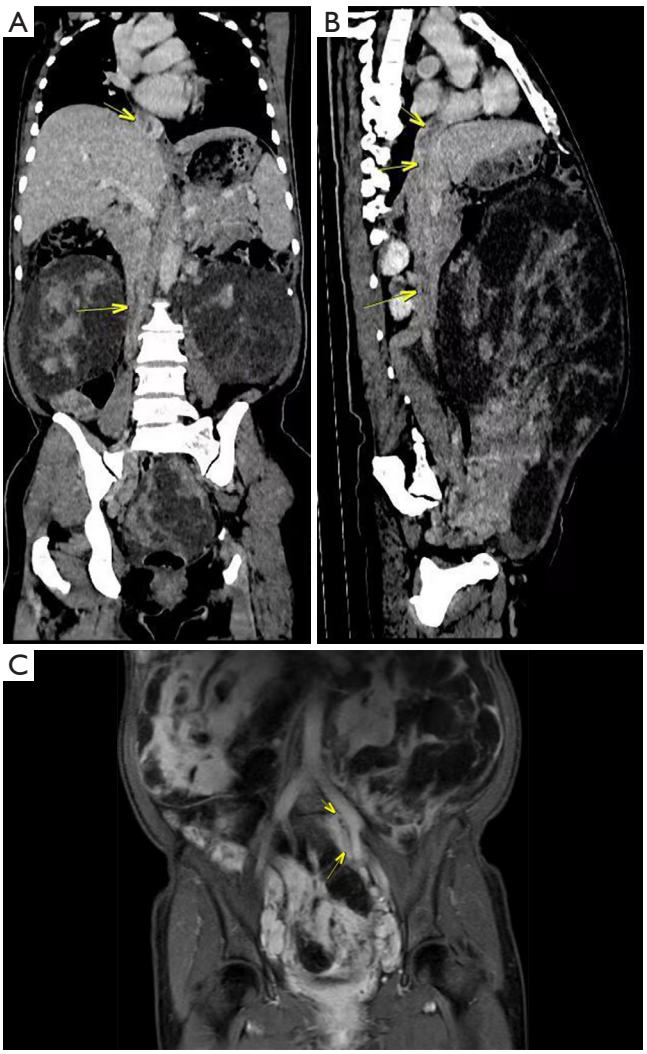

Figure 2 Image of thorax, abdomen, and pelvic CT scan. (A) Coronal CT imaging shows tumor thrombus (arrow) in Inferior vena cava; (B) sagittal CT imaging shows tumor thrombus (arrow) in Inferior vena cava; (C) coronal CT imaging showing tumor thrombus (arrow) in the left common iliac vein. CT, computed tomography.

muscle tumor disease, mainly stemming from the left ovarian vein into the inferior vena cava and then extending upward and downward along the vena cava, respectively. While performing surgery, the vascular surgeon was consulted on the stage, analyzed the imaging report again, and considered an intravenous neoplasms thrombus (*Figure 2*). After deciding on the surgical approach, we incised the venous wall at a suitable location in the inferior vena cava, and a solid grayish-white colored mass was seen to spill out. The tumor at the proximal end was difficult to extract after the distal end's total removal, and it was only fully removed when the left pelvic funnel ligament's stump was released. It was once more shown that the tumor thrombus from the left ovarian vein eventually converged into the vena cava (*Figure 3*).

The etiological mechanism of IVL is still unclear, and what factors may influence the biological behavior of malignant diseases in IVL also remains unknown. Several studies have considered that it is estrogen-related (6,17,18). For this patient, after intraoperative detection of the intravascular lesion, we removed the bilateral ovaries to prevent tumor recurrence. Moreover, some investigations (18,19) have discovered that estrogen receptor (ER) and progesterone receptor (PR) were positively expressed in some patients' tumor tissue. According to Nishizawa (20), and Wu (21), the neoplasms volume in IVL could be significantly reduced by applying gonadotropin hormone-releasing hormone (GnRH) before surgery. Additionally, it has been mentioned that GnRH can be used to lower the risk of recurrence in IVL with postoperative residual lesions (22). Thus, postoperative GnRH maintenance therapy could be an option for young, ovarian-preserving patients. However, endocrine therapy's indications, the length of the treatment's maintenance phase, and its actual effectiveness are still controversial. Although the tumor in the present case expressed positive ER and PR, both ovaries had been removed intraoperatively, and there was no residual tumor in the postoperative evaluation. Hence, endocrine therapy was not given.

Whether the recurrence of current IVL is closely related to the presence of postoperative residual disease is questionable. In other case reports and case studies, individuals with surgical residual lesions—particularly those affecting the inferior vena cava, heart, pulmonary artery, and other vessels—make up the bulk of recurrence instances. Although surgical residual lesions lead to a greatly reduced surgical resection rate, tumor recurrence is significantly increased (23). In this case, the tumor involved the inferior vena cave and atrium, but the tumor plugs were completely removed intraoperatively without residue. Since the patient underwent bilateral oophorectomy intraoperatively, no GnRH treatment was recommended postoperatively. As of the publication date, the patient was 2 years postoperative with no signs of recurrence. Given the current evidence-based medical evidence, we recommend GnRH treatment for premenopausal patients with residual postoperative lesions and preserved ovaries. We also recommend follow-

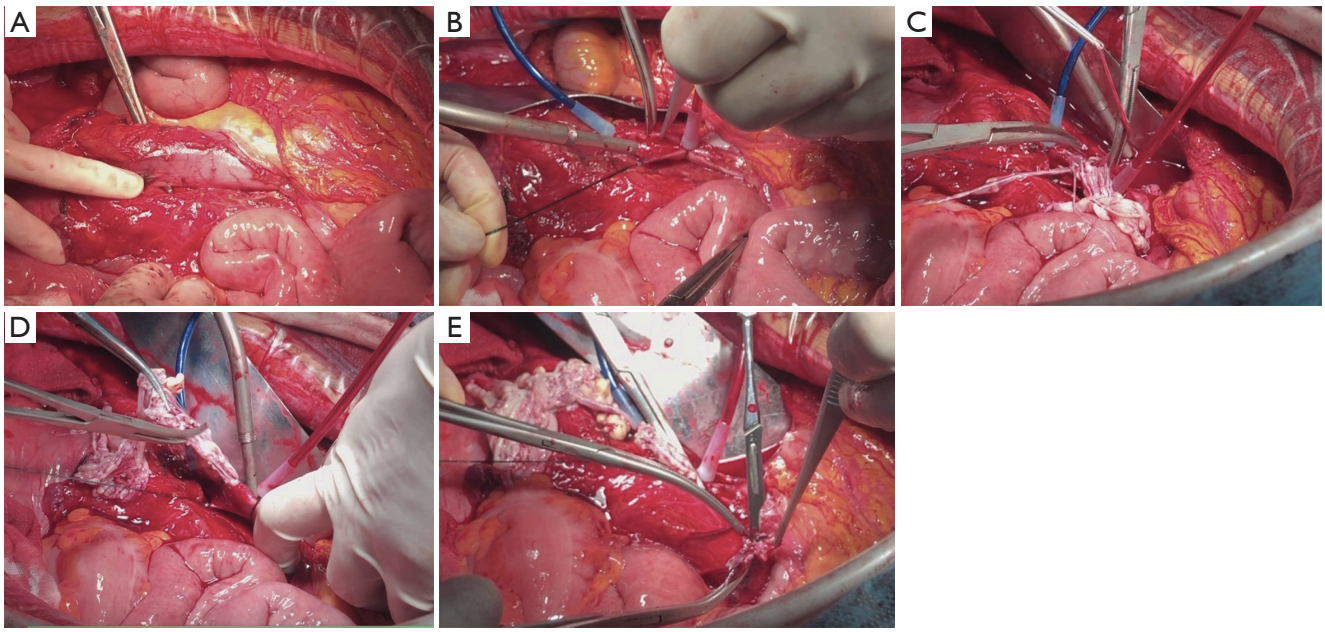

Figure 3 Tumor embolus was removed during operation. (A) The thrombus in the inferior vena cava; (B) block off the blood flow and cut through the wall of the vena cava; (C) remove the distal telangioma embolus; (D) it is complex to remove the proximal telangioma thrombus; (E) after the left pelvic funnel ligament was released, the proximal telangioma plug was removed completely.

up for patients with both ovaries removed and no residual neoplasms. Based on the advantages of this study, combined with this case study, we systematically reviewed the possible mechanisms of the occurrence and development of this type of disease, and explored surgical and drug treatment methods for women at different stages. It is emphasized that patients with a history of uterine fibroids should more readily undergo preoperative vascular ultrasound and cardiac ultrasound examination. For patients with high suspicion of intravascular lesions in imaging, auxiliary examinations such as inferior vena cava CT intravascular imaging, MRI, and angiography should be selected to improve the diagnostic rate. There were also some limitations to our research. The post-surgical follow-up time was relatively short, and further follow-up investigation is needed to determine whether recurrence and other complications will occur, in order to provide more reference opinions for early detection, diagnosis, and treatment of this type of disease in the future.

Conclusions

We have reported a case of IVL with intracardial extension and, in combination with published studies, explored the choice of diagnostic and therapeutic modalities for this disease. When a cardiac mass is detected in a woman with a history of uterine leiomyoma, the source of the mass should be further determined, and timely diagnosis and standardized treatment should be made for patients with the suspected disease to improve the prognosis.

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Footnote

Reporting Checklist: The authors have completed the CARE reporting checklist. Available at https://tcr.amegroups.com/article/view/10.21037/tcr-23-1462/rc

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Conflicts of Interest: All authors have completed the ICMJE

uniform disclosure form (available at https://tcr.amegroups.com/article/view/10.21037/tcr-23-1462/coif). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. All procedures performed in this study were in accordance with the ethical standards of the institutional and/or national research committee(s) and with the Helsinki Declaration (as revised in 2013). Written informed consent was obtained from the patient for the publication of this case report and accompanying images. A copy of the written consent is available for review by the editorial office of this journal.

References

1. Li H, Xu J, Lin Q, et al. Surgical treatment strategies for extra-pelvic intravenous leiomyomatosis. Orphanet J Rare Dis 2020;15:153.
2. Shi P, Xiao H, Li H, et al. Management and prognosis comparison between incidental and nonincidental intravenous leiomyomatosis: a retrospective single-center real-life experience. Ann Transl Med 2022;10:503.
3. Gwacham NI, Manyam M, Fitzsimmons CK, et al. Multidisciplinary approach to pelvic leiomyomatosis with intracaval and intracardiac extension: A case report and review of the literature. Gynecol Oncol Rep 2022;40:100946.
4. Birch-Hirschfeld FV. Lehrbuch der Pathologischen Anatomie. 5th edition. Leipzig: FCW Vogel; 1896.
5. Shen D, Chen D. Interpretation of changes in the WHO classification of tumours of the female reproductive organs, 4th Edition. Chin J Obstet Gynecol 2014;49:717-20.
6. Ordulu Z, Nucci MR, Dal Cin P, et al. Intravenous leiomyomatosis: an unusual intermediate between benign and malignant uterine smooth muscle tumors. Mod Pathol 2016;29:500-10.
7. Castagneto Gissey L, Mariano G, Musleh L, et al. Massive pelvic recurrence of uterine leiomyomatosis with intracaval-intracardiac extension: video case report and literature review. BMC Surg 2017;17:118.
8. Sitzenfrey A. On venous myoma of the uterus with intravascular. Ztschr f Geburth u Gynak 1911;68:1.
9. Dal Cin P, Quade BJ, Neskey DM, et al. Intravenous leiomyomatosis is characterized by a der(14)t(12;14)(q15;q24). Genes Chromosomes Cancer 2003;36:205-6.
10. Hayashi T, Yaegashi N, Konishi I. Molecular pathological approach of uterine intravenous leiomyomatosis. Ann Transl Med 2022;10:724.
11. Buza N, Xu F, Wu W, et al. Recurrent chromosomal aberrations in intravenous leiomyomatosis of the uterus: high-resolution array comparative genomic hybridization study. Hum Pathol 2014;45:1885-92.
12. Yaguchi C, Oi H, Kobayashi H, et al. A case of intravenous leiomyomatosis with high levels of hyaluronan. J Obstet Gynaecol Res 2010;36:454-8.
13. Thapa S, Ghimire B, Thapa P, et al. A Case of Syncope Due to Intracardiac Leiomyomatosis. Cureus 2022;14:e22666.
14. Wei JL, Ji X, Zhang P, et al. Complete intravenous leiomyomatosis: a case report and literature review. Ann Palliat Med 2021;10:12039-45.
15. Marcus SG, Krauss T, Freedberg RS, et al. Pulmonary embolectomy for intravenous uterine leiomyomatosis. Am Heart J 1994;127:1642-5.
16. Roman DA, Mirchandani H. Intravenous leiomyoma with intracardiac extension causing sudden death. Arch Pathol Lab Med 1987;111:1176-8.
17. Mizoguchi C, Matsumoto H, Nasu K, et al. Intravenous leiomyomatosis treated with radical hysterectomy and adjuvant aromatase inhibitor therapy. J Obstet Gynaecol Res 2016;42:1405-8.
18. Kokawa K, Yamoto M, Yata C, et al. Postmenopausal intravenous leiomyomatosis with high levels of estradiol and estrogen receptor. Obstet Gynecol 2002;100:1124-6.
19. Li B, Wu L, Ma S. Intravenous leiomyomatosis of the uterus: A report of 3 cases and review of the literatures. Chin J Clin Oncol 2005;32:1058-60.
20. Nishizawa J, Matsumoto M, Sugita T, et al. Intravenous leiomyomatosis extending into the right ventricle associated with pulmonary metastasis and extensive arteriovenous fistula. J Am Coll Surg 2004;198:842-3.

21. Wu K, Wei LH. Clinical analysis of intravenous leiomyomatosis: Report of 9 cases. Chin J Cancer Prev Treat 2009;16:704-6.
22. Hameleers JA, Zeebregts CJ, Hamerlijnck RP, et al. Combined surgical and medical approach to intravenous leiomyomatosis with cardiac extension. Acta Chir Belg 1999;99:92-4.
23. Chen J, Bu H, Zhang Z, et al. Clinical features and prognostic factors analysis of intravenous leiomyomatosis. Front Surg 2023;9:1020004.

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