International Surgery

A case of a rare internal intravenous leiomyomatosis was reviewed in the literature

--Manuscript Draft--

Manuscript Number:	INTSURG-D-24-00010R1
Full Title:	A case of a rare internal intravenous leiomyomatosis was reviewed in the literature
Article Type:	Case Report
Keywords:	intravenous leiomyomatosis, uterine fibroids, inferior vena cava, surgical resection
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Abstract:	Objective: Intravenous leiomyomatosis invasion of the inferior vena cava is a rare disease, and there are no guidelines for the diagnosis and treatment of this disease. This study reported the diagnosis and treatment process of a case of intravenous leiomyomatosis invading the inferior vena cava, which provides clinical reference experience for the diagnosis and treatment of IVL. Methods: A 59-year-old woman, because of "physical examination found inferior vena cava thrombosis one month" admitted to hospital, 4 years before left ovarian+right fallopian tube+myomectomy, after admission line chest and abdominal enhanced CT prompt: inferior vena cava vein (renal vein level) filling defect, the following lumen and branches without visible, considering thrombus or tumor thrombus formation, the cervix left visible 1 about 8cm diameter fat density mass, enhanced scanning period is not strengthening. A multidisciplinary team performed laparotomy+resection of intravena cava tumor+total hysterectomy+right oophorectomy+repair of inferior vena cava and left iliac vein. Postoperative pathology suggested: spindle cell tumor, leiomyomatosis. Results:IVL is a special type of benign tumor in the mesoderm lobe.Surgical resection is the main mode of treatment.Conclusion: Intravenous vascular leiomyoma onset is insidious, lack of clinical manifestations of specificity, and easy to misdiagnosis and miss diagnosis. Accurate preoperative evaluation, multidisciplinary team cooperation, and appropriate surgical plan are the important factors for obtaining the best treatment results. The possibility of leiomyoma in the vein should be considered in female patients with uterine fibroids combined with pelvic compression, venous return dysfunction and right heart insufficiency.

A case of a rare internal intravenous leiomyomatosis was reviewed in the literature

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First author: Ke Tian[1*](M.D.), Completed the case collection and complete the operation.
Co-first author: Jinxiu Jiang[2*]（M.D.）Completed the case collection and paper writing.
Yincheng Ran[1*](M.D.) Complete the operation.
Other author:Analyzed the data and collected data.
Corresponding author: Zhumin Cao[1#](MD,PhD) Completed the surgery and revised the paper.
Co-corresponding author:Kai Deng[2#](MD)Composing and proofreading.

Disclosure of conflict of interest

The authors declare that they have no competing interests.

Declaration

This research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

The ethics statement for animal and human studies is not applicable.

Informed consent has been obtained from the patient (or patient's family/guardian) for publication of the case report and accompanying images.

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Jan 1st, 2025

bmitting our manuscript entitled "A case of internal intravenous leiomyomatosis and was reviewed in the literature" to you.

In this research, To discuss the skills and clinical safety of ultrasound-guided implantation of a totally implantable venous-access port (TIVAP) via the axillary vein: We retrospectively studied the indicators of 40 patients with new techniques and 50 patients with traditional intra-well venous implantation through axillary vein, including operation time, complications, postoperative quality of life and so on. It can provide Ultrasound-guided implantation of a TIVAP is a safe and effective treatment with a low incidence of complications.

All authors have read and approve this version of the article, and due care has been taken to ensure the integrity of the work. No part of this paper has published or submitted elsewhere. No conflict of interest exits in the submission of this manuscript. We appreciate your consideration of our manuscript, and we look forward to receiving comments from the reviewers.

Sincerely,

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Abstract:

Objective: Intravenous leiomyomatosis invasion of the inferior vena cava is a rare disease, and there are no guidelines for the diagnosis and treatment of this disease. This study reported the diagnosis and treatment process of a case of intravenous leiomyomatosis invading the inferior vena cava, which provides clinical reference experience for the diagnosis and treatment of IVL. **Methods**: A 59-year-old woman, because of "physical examination found inferior vena cava thrombosis one month" admitted to hospital, 4 years before left ovarian+right fallopian tube+myomectomy, after admission line chest and abdominal enhanced CT prompt: inferior vena cava vein (renal vein level) filling defect, the following lumen and branches without visible, considering thrombus or tumor thrombus formation, the cervix left visible 1 about 8cm diameter fat density mass, enhanced scanning period is not strengthening. A multidisciplinary team performed laparotomy+resection of intravena cava tumor+total hysterectomy+right oophorectomy+repair of inferior vena cava and left iliac vein. Postoperative pathology suggested: spindle cell tumor, leiomyomatosis. **Results:**IVL is a special type of benign tumor in the mesoderm lobe.Surgical resection is the main mode of treatment.**Conclusion**: Intravenous vascular leiomyoma onset is insidious, lack of clinical manifestations of specificity, and easy to misdiagnosis and miss diagnosis. Accurate preoperative evaluation, multidisciplinary team cooperation, and appropriate surgical plan are the important factors for obtaining the best treatment results. The possibility of leiomyoma in the vein should be considered in female patients with uterine fibroids combined with pelvic compression, venous return dysfunction and right heart insufficiency.

Key words: intravenous leiomyomatosis, uterine fibroids, inferior vena cava, surgical resection

Introduction：

Intravenous leiomyomatosis intravascular leiomyomatosis (IVL) is a special type of benign tumor in the mesoderm lobe. IVL histopathology is benign, but it has a biological behavior similar to a malignant tumor[1-2]. The cause of the disease is not clear. After the benign smooth muscle tissue invades the uterine vein or ovarian vein, it continues to grow upward along the vein to the iliac vein, inferior vena cava and even involves the heart[3]. The clinical manifestations of IVL vary due to the different affected parts, without any clinical manifestations, the lesions involving large vessels and heart, can endanger the life of patients, and even sudden death[4]. The incidence of this disease is not yet known, but there are few clinical reports. At present, most reports of IVL focus on case reports, single-center experience, and there is still a lack of large sample, long-term and systematic studies.

At present, there is no unified diagnosis and treatment guide for this disease[5]. The diagnosis and treatment process of hysterogenic IVL is reported and relevant literature is reviewed to provide clinical reference experience for the diagnosis and treatment of IVL, and summarize the pathogenesis, clinical manifestations, diagnosis, treatment and prognosis.

Patients and methods:

The patient, a 59-year-old female, was admitted for "inferior vena cava thrombosis found in physical examination". After a healthy physical examination, the patient had no lower limb swelling, pain and walking disorder, normal menstruation, no abnormal vaginal exudation, exudation, no menstrual disorder, pelvic compression and other symptoms.18 years before the modified radical resection of right breast cancer, the postoperative pathology was unknown.4 years ago, left ovary + right fallopian tube + myomectomy, postoperative pathology indicated: uterine leiomyoma. Physical examination: T: 36.8℃, P: 80 times / minute, R: 20 times / minute, BP: 109 / 61mm Hg, no obvious tenderness, rebound pain and muscle tension in the whole abdomen, no edema in both lower limbs, and no varicose veins in the abdominal wall. Laboratory examination showed: human chorionic gonadotropin: 0.43 ng / mL, Carcinoembryonic antigen: 0.7 ng/mL, 125:11.13 U / mL, 199:17.58 U / mL, A-fetoprotein 2.69 ng / mL; Enhanced CT of chest and abdomen (Figure 1) indicates: filling defect of inferior vena cava (level of renal vein), The following lumen and its branches are not visible, Considering thrombus or cancer thrombus formation as possible, At the top of the uterus, a fatty density mass with a diameter of about 8cm, No enhancement was observed in all phases of enhanced scanning, The rest showed no obvious abnormalities.

After communication with the patient and his family members, a tumor resection was planned. After preoperative consultation and discussion, multidisciplinary experts from vascular surgery, anesthesiology, imaging, gynecology, blood transfusion and blood, considering that tumor invasion of the inferior vena cava and inferior vena cava reflux was blocked, but the nature of the tumor should be clear postoperative pathological biopsy. After adequate preoperative evaluation, it was decided to perform tumor resection + intraoperative freezing pathology examination, and the resection range was determined according to the results of freezing pathology. At the same time, ask a gynecologist to perform total hysterectomy at the same time, and perform right ovariectomy if necessary; prepare suspended red blood cells 10u and plasma 2000ml before surgery, and prepare for emergency blood use.

After the operation:

As seen in the operation (Figure 2): Full free of the inferior vena cava, right renal vein, right internal iliac vein, right iliac artery, respectively, from the inferior inferior vena cava. The inferior vena cava is obviously filled, a cord of tumor is palpable, the posterior inferior vena cava, extending down to the right internal iliac vein, the tumor texture is tough. The left tubal ovary deficiency, the right ovary atrophy, no surface space. The uterine body

showed a diameter of about 8cm convex to the pelvic cavity. After systemic heparinization, the inferior vena cava was opened in the plane of the right renal vein. During the operation, the vein left the lower cavity with forceps and the tumor was intact. During the operation, the gynecologist was consulted on the stage, with the uterus and right ovariectomy and sent for pathological examination. Intraoperative freezing indicated: spindle cell tumor was found in the inferior vena cava, and no tumor was found at the cervical margin.

Postoperative pathology:

General view: 1. The tumor in the inferior vena cava showed a tube-like tissue, 8.5c m long and 0.7-1.4cm in diameter; 2. A mass on the serous surface of the left anterior wall of the uterus, with the mass of about 7.5x5.2x3.3c m, multituberculate, gray, brown, solid and qualitative.

Pathological diagnosis (Figure 3): spindle cell tumors were found in the "inferior vena cava" and "uterus", and no tumor was found at the cervical margin of the specimen. Combined with the immunohistochemical results, it was consistent with leiomyomatosis.

discuss

The pathogenesis of IVL is still unknown, and some study reports suggest that the t (12,14) (q15, q24) mutation may be the main cause of the vascular invasion and growth of leiomyomas[6-7]. The study of Kokawa K et al. showed that IVL tumor cells had significantly higher expression, with the same characteristics of estrogen-dependent growth and recurrence as uterine fibroids, and most of IVL patients were treated with uterine leiomyoma or a previous history of uterine leiomyoma[8]Suggsuggests that the highly expressed progesterone receptor may be related to IVL; there are two main hypotheses about the origin of IVL[9]: (1) Knauer E et al showed that the IVL originates from smooth muscle cells in the vascular wall of the uterine vein[10]; (2) Sitzenfrey A It is believed that IVL originates from invasive uterine fibroid cells, and gradually grows into the lumen of the venous vein with the progression of the disease[11]. In this study, postoperative pathology showed positive female and progesterone receptor of "inferior vena cava" and "uterine" masses, which was consistent with the results of Kokawa K et al. However, further studies are still needed to confirm the origin of the tumor cells.

IVL has different clinical manifestations due to different sites of tumor involvement: (1) mild cases may have no obvious clinical manifestations; (2) Only the involvement of the uterus and adjacent uterine blood vessels are mainly gynecological symptoms: such as irregular vaginal bleeding, menstrual disorders, pelvic compression and other symptoms; (2) The involvement of the iliac vein, inferior vena cava, and the heart, such as lower limb weakness, edema, ascites, oliguria, In severe cases, chest tightness, palpitations, dyspnea and other symptoms can appear; In this patient, although the tumor invaded the inferior vena cava and the right internal iliac vein, But due to the establishment of the collateral cycle, The lateral branch circulation is still in the compensatory period, Therefore, the patient did not show significant clinical symptoms.

IVL preoperative diagnosis is difficult to, ultrasound examination has the advantages of noninvasive, quick, low cost, can accurately assess the size, scope and nature of the

tumor, is the first method to assist the diagnosis of IVL, in 2022 Ge found enhanced ultrasound diagnostic accuracy of IVI is higher than conventional ultrasound, by contrast ultrasound can be found specific signs of IVL[12]; CT enhanced scan, magnetic resonance imaging (magnetic resonance imaging, MRI) and digital subtraction angiography (digital subtraction angiography, DSA) can accurately show the location of IVL, intravascular space, tumor extension and collateral formation, and determine the relationship between tumor and venous system and heart[13], It is of great value to the diagnosis of diseases and the formulation of surgical plans. Pathological histological examination is the gold standard for confirmed diagnosis. Under IVL microscope, spindle cell tumors with vascular proliferation, nuclear division phase was rare, and the tumor body surface was coated with a layer of flat vascular endothelial cells[14]. IVL immunohistochemistry was positive for smooth muscle-derived antigens SMA, Desmin, etc[4]. Most of I VLER, PR, isohormones diffuse expression[13], The majority of IVL patients with uterine leiomyoma or a previous history of uterine leiomyoma also support the above opinion. In clinical work for perimenopausal, previous uterine fibroids history and the short term lower limb reflux blocked, pelvic compression in female patients should consider the possibility of this rare disease, targeted examination, in order to clear diagnosis as soon as possible, avoid missed diagnosis, misdiagnosis, individualized treatment.

Results:

Thorough resection of the tumor is the preferred treatment option for IVL[15-16], Although IVL is a benign tumor, it has a biological behavior similar to a malignant tumor. For frequent lesions or tumor metastasis to key sites, the operation is difficult, it is difficult to completely remove the lesion, tumor resection is not complete, is an important reason for postoperative recurrence and spread. The scope of vascular involvement should be fully evaluated and defined before surgery, and detailed treatment prescriptions should be formulated through multiple cooperation; during the operation, careful dissection and exposure of retroperitoneal organs and venous system should be explored to prevent intraoperative migration or residual; if uterine fibroids or tumor involving renal vein, we can seek the support of gynecology and urology departments. IVL is considered to be an estrogen-dependent tumor, so in principle, the scope of surgical resection should include the whole uterus, double appendage and extra-uterine lesions. After surgery, antiestrogen (Gn R Ha) is treated for ovarian function, which can reduce the recurrence and spread of IVL[17-18]. Close follow-up should be paid after surgery, and if recurrent lesions are found, early treatment should be required. In this case, the tumor did not closely adhere to the inferior vena cava during surgery. After separating the tumor from the inferior vena cava using tweezers, the inferior vena cava was stitched directly without revascularization. During the operation, the uterine body saw a mass of about 8cm in diameter, which was radical removed at the same time. The postoperative pathology suggested uterine leiomyoma. The pathology and immunohistochemical properties of the tumor in the inferior vena cava were the same as those of the uterine tumor, indicating the homology between the tumor in the inferior vena cava and the uterine tumor. After 3 months of

postoperative follow-up, the patient recovered well with no recurrent lesions.

DISCUSSION:

In conclusion, the clinical manifestations of IVL lack specificity, it is difficult to diagnose the diagnosis in clinical work, and postoperative pathological histological examination is the gold standard for diagnosis. For IVL patients involving the inferior vena cava and the right heart, the operation is difficult and the operation risk is high. Before surgery, detailed treatment plans should be fully evaluated and formulated. Multidisciplinary cooperation and complete resection of the mass is the key to a successful operation and the reduction of postoperative recurrence. Although IVL is a benign tumor, it still has the possibility of recurrence and progression. It needs long-term close follow-up after surgery. If the recurrent lesion is found, early treatment should be given.

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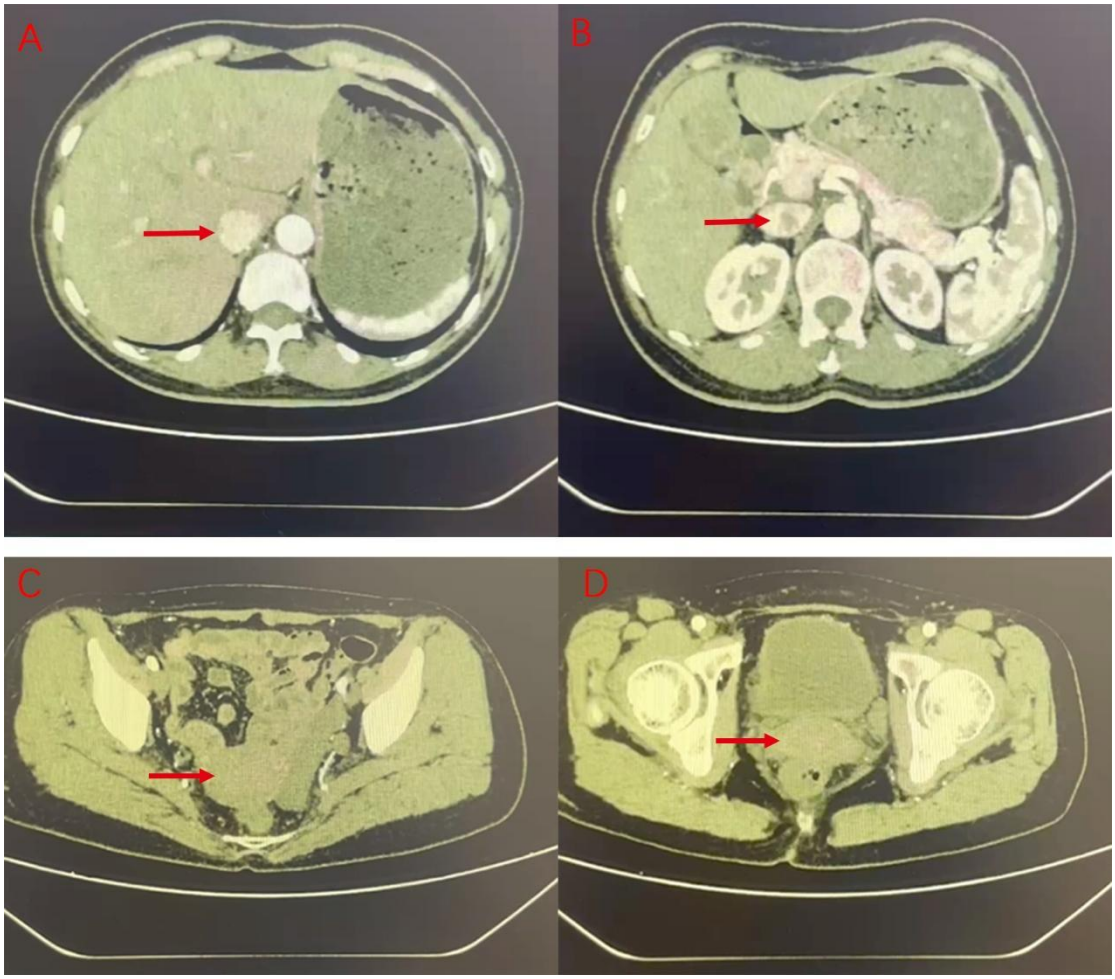

Figure 1

A, B: The retrohepatic inferior vena cava is filled, and some layer masses completely occupy the lumen; C: the pelvic mass with fatty density mass; D, the uterus with uneven enhancement

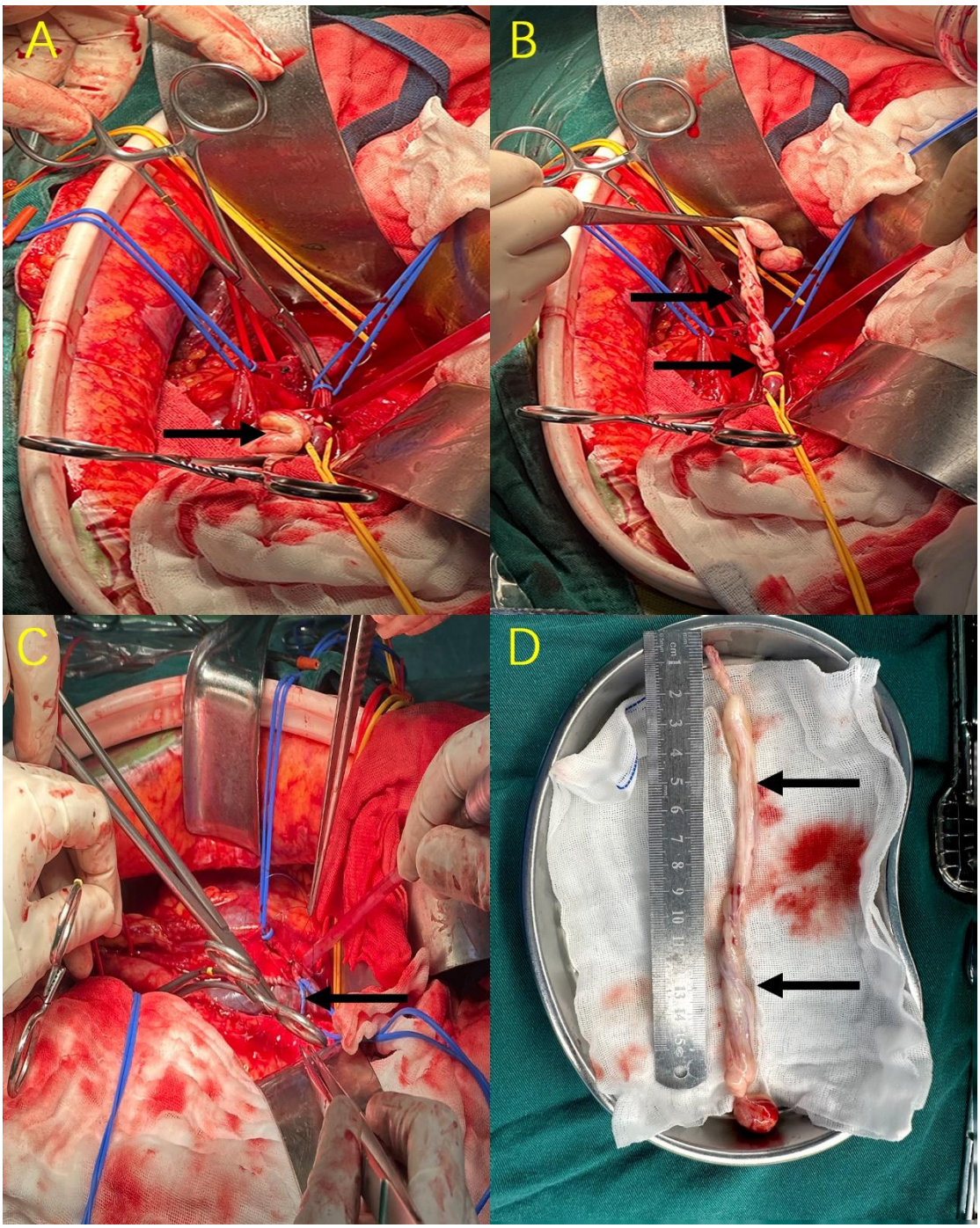

Figure 2

A, B, gray-white solid tube-like tumor was visible in the inferior vena cava; C, the tumor, and 4-0 P rolene; D, inferior vena cava tumor

Postoperative pathology:

General view: 1. The tumor in the inferior vena cava showed a tube-like

tissue, 8.5c m long and 0.7-1.4cm in diameter; 2. A mass on the serous surface of the left anterior wall of the uterus, with the mass of about 7.5x5.2x3.3c m, multituberculate, gray, brown, solid and qualitative.

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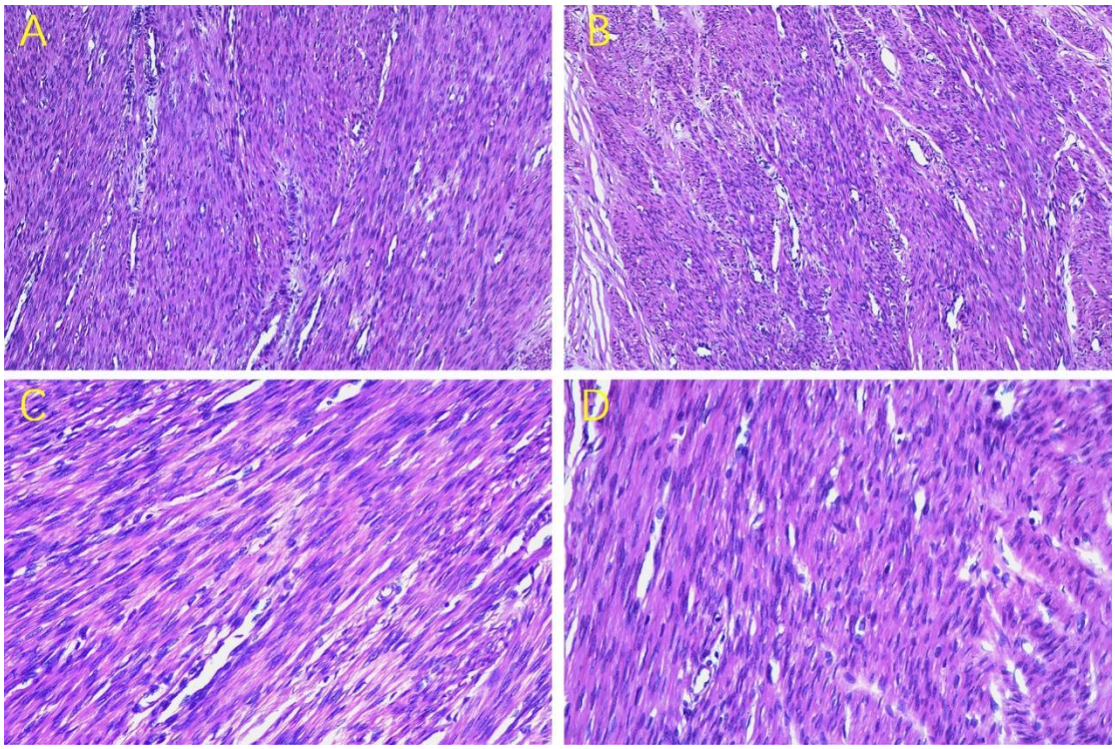

Figure 3

$\times 100 \times 200 \times 100 \times 200$ HE staining in () and C (); HE staining in inferior vena cava in B, () and D ()

Immunohistochemistry (Figure 3): SMA (+), Des min (+), Ca ldesmon (+), FH (+, not missing), EMA (-), WT 1 (+), ER (+), PR (+), CD-10 (-), S100 (-), CD34 (-), Ki-67 (+, less than 2%). Among them, SMA (+), Des min (+), and CD-10 (-) indicate

that tumors originated from smooth muscle cells but not endometrial stromal cells; ER (+), PR (+) indicate estrogen progesterone-dependent tumors; Ki-67 has low proliferation index, indicating low proliferative activity of tumors.