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A long-term follow-up case of intravenous leiomyomatosis treated with anticoagulant therapy following conservative surgery

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Abstract

An intravenous leiomyomatosis is a benign smooth muscle tumor that develops in a vein. Approximately 200 cases have been reported in the literature thus far; however, no case has been reported to date of an intravenous leiomyomatosis treated conservatively with anticoagulant therapy that has received long-term follow-up. We here present a case report of patient a 44-year-old G2P2. Hysterectomy and adnexectomy were performed and the uterine vein and internal iliac vein were removed, but the superior-located masses were conserved. Currently, in the 6th post-operative year, no changes have been detected in the location, size, and property of the remaining masses. In addition, thromboses in the deep vein and along the inferior vena cava were confirmed pre-operatively and anticoagulant therapy has been administered continuously post-operatively. Thus, a thorough pre-operative search for thrombi is required in patients with intravenous leiomyomatosis. Anticoagulant therapy may be necessary for patients with tumor conserved in the IVC following conservative surgery.

Key words: intravenous leiomyomatosis, endometrial cancer, uterine myoma, deep vein thrombosis, anticoagulant therapy

Introduction

An intravenous leiomyomatosis was first described by Birch-Hirschfeld as a benign leiomyoma growing within venous channels.[1] Intravenous leiomyomatosis was defined by Norris et al. in 1975 as "the growth and extension into venous channels of a histologically benign smooth muscle tumor, arising either from a uterine vein or from the walls of a uterine vein.[2]" Approximately 200 cases of intravenous leiomyomatoses have been reported thus far in the literature.

We report a case of intravenous leiomyomatosis which had extended to the inferior vena cava (IVC), with deep vein thrombosis and thrombosis along the inferior vena cava. We undertook a conservative approach by conserving the mass existing in the IVC followed up for 6 years post-operatively with serial contrast-enhanced CT examinations that have confirmed no growth of the remaining tumor or thrombosis. No case has been reported to date of an intravenous leiomyomatosis treated conservatively with anticoagulant therapy that has received long-term follow-up.

Case

Patient: 44-year-old G2P2
Family history: Unremarkable
Anamnesis: Surgically-treated appendicitis at 15 years of age
Cesarean deliveries at 30 and 32 years of age

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Menstrual history: Regular 28-day cycle

History of the present illness

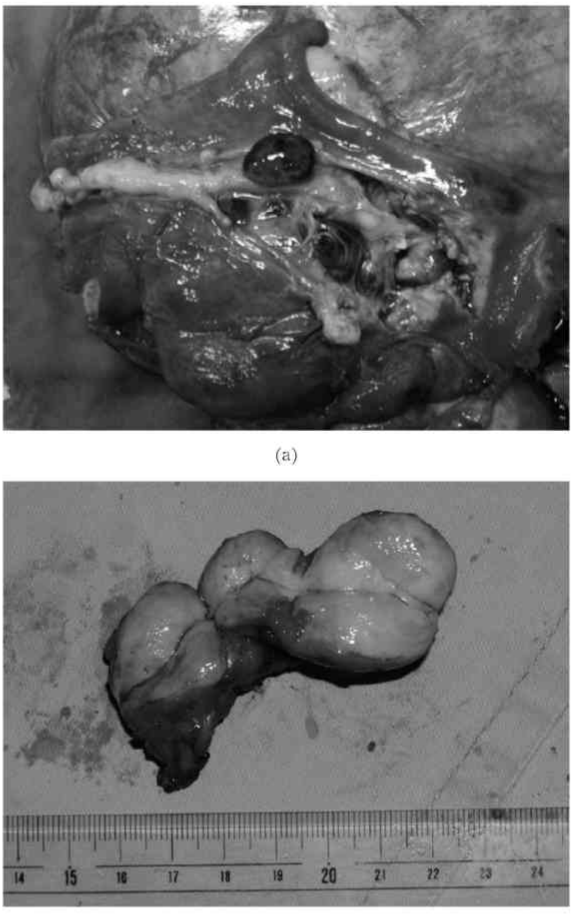
The patient consulted a local doctor due to abdominal bloating, and the examination revealed a huge uterine myoma. CT revealed a uterine leiomyoma and intravenous leiomyomatosis extending from the internal iliac vein to the IVC, and up to the level of the upper edge of the liver. The diagnostic evaluation revealed an enlarged, mobile uterus about 16 weeks in size. The cervical cytology was class II, and the endometrial cytology was indeterminate due to the previous cesarean section. Hyperplasia of the endometrium was not noted on ultrasound. An elevated pre-operative D-dimer fibrin level at 3.29 mg/dl (normal value, <0.50 mg/dl) was suggestive of a deep vein thrombosis (DVT) and ultrasonography of the leg vein revealed a DVT in the left thigh. Contrast-enhanced CT also revealed a thrombus along the mass in the IVC. Beginning 2 weeks prior to surgery, anticoagulant therapy was initiated with heparin. The dose of heparin was increased carefully, after monitoring the activated whole blood clotting time (ACT) and the activated partial thromboplastin time (APTT). Acceptable control with an ACT of 200 sec and an APTT of 52.8 sec (control, 30.5 sec) was achieved before surgery. On the day of surgery, heparin was replaced with lower molecular weight heparin (Fragmin®) and the surgery was performed.

Surgical findings

Ureteral catheters were inserted to confirm the course of the ureters. At laparotomy, the uterus had enlarged to 20 weeks in size. The presence of a luminal mass extending from the right uterine vein to the internal iliac vein and the IVC was confirmed by palpation. A total abdominal hysterectomy and bilateral adnexectomy were performed. The uterine vein and the internal iliac vein were removed, but the myoma at the proximal position in the IVC was conserved (Fig. 1). The operative time was 240 minutes with blood loss of 2,538 ml. Uterine weight was 4,300 g.

Post-operative course

The lower molecular weight heparin was replaced with heparin on post-operative day 1. The patient's general condition improved and ambulation was begun on post-operative day 6. No pulmonary emboli occurred. Beginning on post-operative day 12, warfarin replaced heparin therapy. The warfarin dose was adjusted according to the PT level, and good control of PT was achieved (INR=2.0). There were no other major changes in the post-operative course, and the patient was discharged on post-operative day 33. The blood estradiol level fell to 10 pg/ml post-operatively from a pre-operative level of 72 pg/ml. Contrast-enhanced CT performed before discharge showed that the mass remaining within the IVC was unchanged as compared with the pre-operative image with respect to location, size, and properties. Post-operative histopathology revealed a leiomyoma invading the myometrium and tumor veins. The pathologic examination also revealed a G1 endometroid adenocarcinoma that had not been previously identified. The tumor had invaded the myometrium to a depth of 4/27 in the serosa and partial lymphatic involvement was confirmed, which was consistent with the diagnosis of stage IB endometrial cancer.



(a)

(b)

Fig. 1 Removed uterine site between the uterine vein and internal iliac vein Isolated intravenous leiomyomatosis.

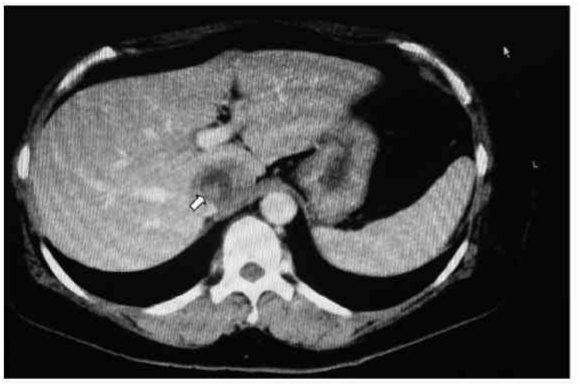


Fig. 2 Contrast-enhanced CT images acquired during the warfarin-free period.
Recurrent thrombus along the mass in the IVC is shown.

Six cycles of chemotherapy (paclitaxel and carboplatin therapy) followed the diagnosis to treat the endometrial cancer. Post-operative oral administration of warfarin continues due to prevention of pulmonary embolism. The patient has been monitored every 3-6 months to date to detect possible signs of endometrial cancer and intravenous leiomyomatosis, using serial contrast-enhanced CT scans. In the 6 years since surgery, no changes have been observed in the location and size of the residual tumor in the IVC. In postoperative year 2, warfarin administration was suspended when the patient was involved in a motor vehicle accident. Contrast-enhanced CT images acquired during the warfarin-free period showed a recurrent thrombus along the mass in the IVC that had existed before surgery (Fig. 2). When warfarin administration was resumed, the thrombus resolved.

Discussion

An intravenous leiomyomatosis is a benign, smooth muscle tumor that develops in the vein. Intravenous leiomyomatoses occur more commonly in women in their 40s and 50s, and usually cause symptoms similar to those of uterine leiomyomas, including polyhypermenorrhea, dysmenorrhea, and irregular vaginal bleeding of uterine origin3. In approximately 30% of cases, the myoma reaches the IVC and the right atrium, at which point symptoms of cardiac arrest may appear, including abrupt dyspnea and absence seizures.[3] Some myomas extending into the right atrium are lethal, and in such cases, removal of the tumor by thoracotomy is required.[4] Recent reports include a case of intravenous leiomyomatosis, 50 cm in length, which reached the pulmonary artery and was successfully extirpated, and another case accompanying deep hypothermia and circulatory arrest which was also successfully extirpated.[5,6] Complete resection of the myoma is desirable, even for those not yet reaching the heart. Indeed, Lo et al. reported 13 post-operative recurrences of 43 cases in which tumor removal had been incomplete.[7]

However, it is difficult to completely remove the myoma within the IVC, and a fatal case of excessive bleeding during surgery has been reported.[8] Other studies have reported that even if the tumor remains in the vein, the recurrence rate is low and the post-operative prognosis is good.[2,3,9,10] Norris et al. reported 2 post-operative recurrences in 14 cases in a follow-up period of 2-20 years, while Clemet et al. reported lethality in 6 cases of 22 in which the tumor had reached the right atrium among 76 total cases.[2,3] Malvany et al. reported that none of 22 cases was lethal following surgery. On the other hand, based on the fact that uterine myomas are estrogen-dependent, it is considered necessary to reduce the estrogen level by performing a bilateral adnexectomy.[9,11] This is supported by the report of Evans et al. that the ovary was conserved in 3 of 4 recurrent cases.[11] Drug therapy with a Gn-RH agonist and tamoxifen has also been described.[12]

In our case, surgical treatment was completed, conserving an intravenous mass which was difficult to remove. Bilateral adnexectomy was performed, lowering the post-operative blood estrogen level. In the 6th postoperative year, no changes have been observed in the location, size, and properties of the remaining mass.

For thrombi confirmed pre-operatively in the thigh and along the intravenous leiomyomatosis, heparin anticoagulant therapy was initiated to maintain the APTT (sec/cont ratio) at 1.5-2.5 during surgery.[13,14] Post-operative warfarin therapy continues to date, and is adjusted to maintain a PT (INR) of 1.5-2.0.[15] There is one previous report of a thrombus in the vein within the intravenous leiomyomatosis, however, this earlier report included no information regarding anticoagulant therapy.[16] As long as a mass exists in the IVC, there is a likelihood of thrombus formation along the mass that may result in pulmonary embolism. The relevant information obtained in this case was reformation of the thrombus during the suspension of anticoagulant

therapy due to a motor vehicle accident. Thus, a thorough pre-operative search for thrombi is required in patients with intravenous leiomyomatosis. Anticoagulant therapy may be necessary for patients with tumor conserved in the IVC following conservative surgery.

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