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# Intravenous leiomyomatosis. Case report

**Diana Žilovič[1,2,3], Dovilė Čerkauskaitė [4], Kotryna Kvitkovskaja[4], Rūta Čiurlienė[3].**

*[1] Institute of Biosciences, Life Sciences Center, Vilnius University, Saulėtekio Avenue 7, LT-10222 Vilnius, Lithuania;*
*[2] Laboratory of Clinical Oncology, National Cancer Institute, Santariškių 1, LT-08406 Vilnius Lithuania;*
*[3] Oncogynecology Department, National Cancer Institute, Santariškių 1, LT-08406 Vilnius Lithuania;*
*[4] Lithuanian University of Health Sciences, Faculty of Medicine, Vilnius Lithuania;*

**Abstract**

Uterine leiomyoma is a very frequent pathology, which affects up to 30% of female population over the age of 35. Although leiomyomas are benign tumors there are some unusual locations and growth patterns of how they can develop and progress. Intravenous leiomyomatosis is one of the extra uterine types of leiomyoma, which is described as intralumenal growth of smooth muscle into either venous or lymphatic vessels outside the limits of myoma. Intravenous leiomyomatosis is a rare benign tumor, but despite its benign histological features, invasion of large vessels and cardiac extension can occur and be fatal (1-3). We present a case of 46-year-old woman who was histologically diagnosed with uterine leiomyoma after vaginal hysterectomy. The aim of the study is to investigate all possible treatments of the intravenous leiomyomatosis and determine the further follow-up.
**Keywords:** intravenous leiomyomatosis, uterine leimyoma.

## Introduction

Uterine leiomyomas is a very frequent pathology, which affects 20% to 30% of female population over the age of 35. Leiomyomas are benign tumors and mainly located in the uterus, but there are some unusual locations and growth patterns of how they can develop and progress (1-3). Group of extra uterine types of leiomyoma consists of: benign metastasizing leiomyoma, disseminated peritoneal leiomyomatosis, parasite leiomyoma (located in the broad ligament/retroperitoneal space) and intravenous leiomyomatosis. Intravenous leiomyomatosis (IVL) is described as a smooth muscle cell tumor that grows within the venous channels without invading them. The etiology of IVL revolves around two major hypotheses: first one suggesting that tumor arises from the uterine vein walls, while the second proposes that the uterine leiomyoma is a primary tumor with intravascular projections into an adjacent venous channel (4-7). IVL was first described by Birch-Hirschfeld in 1896 in an then in 1907 Dursk et al. described the first case of IVL with intra-cardiac extension (8). Although it is a very rare condition with less than 300 case reports in English literature, it can be easily overlooked due to the risk of sudden death caused by total outflow tract obstruction (8, 9).

## Case presentation

A 46-year-old woman presented with heavy and irregular bleeding from the uterus lasting for around 12 months. She was previously treated with hormonal intrauterine device (IUD) although no effect was achieved. On further evaluation, pelvic ultrasound was performed and showed myoma on the posterior wall of the uterus, about 4 cm. ( Described as type 3 according to the International Federation of Gynecology and Obstetrics classification )(10). Transvaginal hysterectomy without salpingo-oophorectomy was performed. Upon revision, smooth, 6 week-sized-uterus was found and 4,0 cm 3$^{rd}$ type myoma on posterior wall was seen, adnexal masses were intact. Patient was referred to National Cancer Institute of Vilnius for further evaluation and treatment, as histological findings showed leiomyoma, most likely sarcoma. Thoracic, abdominal and pelvic computed tomography (CT) was performed and showed no signs of metastases. Histological specimens were re-examined and conclusion of histology and immunohistochemical staining was IVL. Mitotic activity was low (3/10 high-power fields). Immunohistochemical staining showed that 100% of the cells had positive (+++) desmin (DES) cytoplasmic reaction, 80% of the cells had positive (+++) smooth muscle actin (SMA) reaction, >95% of the cells expressed positive (++/+++) estrogen receptors, 100% of the cells expressed positive (+++) progesterone receptors. CD10 receptors were negative (-), MYOD1/MYOG receptors were negative (-), there was positive (+++) D240 endothelial cytoplasmic reaction, positive (+++) CD34 endothelial cytoplasmic reaction, KI67 proliferative activity <3%. As the tumor is hormone-dependent, medical multidisciplinary team agreed on necessity of bilateral salpingo-oophorectomy, however - patient refused any further surgical treatment. Hormonal therapy with gonadotropin-releasing hormone agonists (GnRH agonists) and follow up after 3 months was recommended.

## Discussion

The clinical presentation IVL usually depends on the extension and size of the tumor. Usually, it affects premenopausal women, they may experience pelvic, abdominal or cardiac symptoms (9-10). Various non-specific symptoms including dyspnea, edema of lower extremities, palpitation, fatigue and ascites can appear (9-11). Chest tightness and palpitation were considered to be results of impaired heart pumping function caused by tumor obstacles in the heart chambers. Lower extremities swelling was related to tumor-induced blood reflux occlusion in the inferior vena cava. Other rare manifestations of IVL with inferior vena cava extension (IVCE) or intracardiac extension (ICE) include stroke, pulmonary embolism, heart failure, and Budd-Chiari syndrome (12,13). Serious complications, like syncopal episodes, cardiogenic shock or even sudden cardiac death, have also been reported. In some cases IVL can be asymptomatic and usually first symptoms can be associated with uterine myomas, which include abnormal uterine bleeding and lower abdominal tenderness (9-11).

## When to suspect?

Early diagnosis of IVL is very difficult, as patients may have only symptoms of fibroids or even be asymptomatic, despite extensive intravenous

extension. The presence of tumor extension within the venous system would be difficult to define intraoperatively, unless the patient has undergone some pre-operative imaging. Patients who have large fibroid with unusual features or extensions into the pelvic side walls should be under close supervision. The condition should also be suspected if there are other cardiac or venous compression symptoms. In our case, diagnosis was not suspected preoperatively and confirmed only on histological examination of the uterus. IVL can be suspected during surgery, when fibroids seem to extend beyond the uterus into the broad ligaments or show extensions into vascular systems.

To reduce the chance of missed diagnosis of IVL, women between 40 and 60 years old, with a history of hysterectomy due to fibroids with symptoms of chest tightness, hernia, and lower extremity edema have to be examined (4, 5). Examinations for such patients include CT or MRI, echocardiography, and if necessary, CT pulmonary angiography, PET/CT, or PET/MRI (14,15). Echocardiography can be used to identify atrial occupancy and mobility (floating or adhesion), assess the size of the cardiac chambers and function of the tricuspid valve and overall heart, and provide a diagnosis (14). Echocardiography usually reveals a right atrial mass with caval involvement, and an intravascular and intra-atrial mass not attached to the endothelial surface of endocardium, but instead freely mobile within the IVC and right-sided cardiac chambers. These masses are typically long and serpentine, and they can resemble "walking-stick heads" or "snakeheads"(11).

**Staging.**

IVL is categorized into 4 stages reflecting tumor progression before the surgery:

- Stage I: tumor penetrates the uterine venous wall, but is confined to the pelvic cavity.
- Stage II- tumors extends into the abdominal cavity, but does not reach renal vein.
- Stage III- tumor reaches renal vein and IVC, and extends into right atrium but does not reach pulmonary arteries.
- Stage IV- tumor reaches pulmonary arteries and/or lung metastases are observed (5).

**Treatment**

Radical surgical approach remains „the gold standard" and includes complete tumor excision, total hysterectomy and bilateral salpingo-oophorectomy with total resection of the IVL extensions, when it is technically feasible (16-18). Radical parametrectomy and intravenous tumor resection may be necessary (3). To prevent tumor migration ligation of the ovarian arteries and veins at high position is recommended. For patient in whom the tumor cannot be removed completely, ligation of the proximal vascular end of the tumor is recommended to prevent tumor thrombus entering the inferior vena cava (14). To achieve a successful operation for complex IVL cases, a multidisciplinary team meeting with gynecologist, oncologist, anesthesiologist, general surgeon, vascular surgeon and cardiothoracic surgeon is mandatory for optimal surgical planning. Steps taken should depend on a patient's symptoms, previous operative history, as well as the tumor's extension (6). If the patient is ineligible for one stage surgery because of poor clinical condition, due to cardiac and pulmonary comorbidities, a two-stage operation may be favorable (6).

Given the fact that estrogen and progesterone receptors are present in myoma and its intravenous extension, bilateral salpingo-oophorectomy is essential and exogenous estrogens must be avoided to prevent subsequent growth of microscopic or unresected foci of IVL (3). Tamoxifen, gonadotropin-releasing hormone agonists, medroxyprogesterone and other drugs are used postoperatively due to their antiestrogenic effects to control possible residual tumors or preoperatively, to inhibit tumor growth and reduce tumor volume (14,16). Hormone therapy may also be used for poor surgical candidates. Individuals who refuse surgery or for non-castration cases (3,11).

Ma et al. showed outcomes of patients treated surgically for IVL. Recurrence was reported in only 4 of 76 cases of IVL, all of whom opted for total surgery. Removal of both ovaries is necessary for inhibiting tumor growth and avoiding recurrence (3,17). Literature review showed that complete tumor excision with total hysterectomy and bilateral salpingo-oophorectomy had lower recurrence rates (7,6%) compared to patients treated with preservation of adnexes (25%) and patients treated with simple myomectomy (75%) (3,5,6).

**Monitoring and follow up**

The true recurrence of completely resected leiomyomatosis is unknown, but regrowth of the tumor has been documented in up to 30% of patients, from 7 months to 15 years after primary surgery (3). Therefore due to late, but serious clinical manifestation, long term monitoring after hysterectomy is recommended (16). Predisposing factor of recurrence may be young

age, size of the initial tumor and multiparity. Post-surgery, patients need to be followed up every 6 months. At each follow up appointment, chest and abdominal CT scan or MRI with MRI venography, pelvic ultrasound and echocardiography is necessary (5).

**Conclusions:** IVL is rare, benign disease with a spectrum of clinical presentations, which imitates malignant tumors regarding its patterns of growth and extension. Also, IVL has a tendency for recurrence, especially when complete resection of the tumor is not performed. Radical surgery is main treatment, which can be combined with neoadjuvant hormonal therapy to counter estrogenic stimulatory effects. Long-term follow-up of patients is recommended.

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