Abstract. Background: Intravenous leiomyomatosis (IVL) is defined as an intraluminal growth of benign smooth muscle cells in either venous or lymphatic vessels outside the confines or even in the absence of leiomyomas. Benign metastasizing uterine leiomyoma is defined as a histologically benign uterine smooth muscle tumor that acts in a somewhat malignant fashion and produces benign metastases. We report a case of a patient suffering from IVL of the uterus and pulmonary leiomyomatosis. Case Report: The patient presented with severe hypermenorrhoe and a rapidly growing uterine fibroid. She underwent laparotomy with total abdominal hysterectomy. The nodules were classified as endovascular leiomyomatosis. Postoperatively, the patient developed a pulmonary embolism and additionally diffuse, multiple nodules of the lungs were detected in the lung scan. An open lung biopsy led to the diagnosis of pulmonary leiomyomatosis. The patient was put on a regimen of gonadotropin-releasing hormone for a total of 6 months and a lung scan after 6 months revealed stable disease. Conclusion: Though intravenous leiomyomatosis imitates a malignant neoplasm concerning the pattern of growth and extension, and benign metastasizing leiomyoma produces benign metastases, they must be differentiated histologically from malignant tumors to prevent overtreatment.

Intravenous leiomyomatosis (IVL) is a rare uterine tumor defined as an intraluminal growth of benign smooth muscle cells in either venous or lymphatic vessels outside the confines or even in the absence of leiomyomas (1). Although histologically benign, life can be threatened due to tumor extension along the vessels, with mechanical obstruction of the inferior vena cava and/or right cardiac cavities (3). The cornerstone of treatment consists of complete excision of the tumor, usually by total abdominal hysterectomy, as well as an excision of any extratorine tumor when technically feasible. Because most of these tumors are estrogen receptor-positive and recurrence of the disease is reported in patients in whom the ovaries have been preserved, bilateral oophorectomy is also recommended (2). If a complete excision of the tumor is not possible, vascular interruption cranial to the tumor has been suggested to prevent tumor growth along the inferior vena cava (4). In cases of incomplete resection, systemic therapy with tamoxifen or medroxyprogesterone should be applied (5).

Benign metastasizing uterine leiomyoma is also a rare condition in which a histologically benign uterine smooth muscle tumor acts in a somewhat malignant fashion and produces benign metastases, usually to the lungs or lymph nodes (6). In most cases, IVL is not demonstrable. The metastasizing myomas are capable of growth at distant sites, whereas the intravenous tumors spread only by direct extension within blood vessels. Both experimental and clinical evidence suggests that these tumors are stimulated by estrogen. Therefore, removing the source of estrogen, by castration or withdrawal of exogenous estrogen, or treatment with progestins, tamoxifen, or a gonadotropin agonist has an ameliorating effect (7). Surgical treatment of benign metastasizing uterine leiomyoma should consist of total abdominal hysterectomy and bilateral salpingo-oophorectomy, as well as resection of pulmonary metastases if possible.

We report a case of a patient suffering from endovascular leiomyomatosis of the uterus with metastases to the lung (pulmonary leiomyomatosis).

Case Report

The patient, a 30 year-old woman, gravida 1 para 1, presented with therapy-resistant hypermenorrhoe at our outpatient department. Her medical history was significant for adipositas permagna. The past surgical history of the patient included only tubectomy due to ectopic pregnancy. Physical examination and ultrasonography were performed and revealed an irregularly shaped enlarged uterus with a submucosal uterine fibroid of 7 x 6 cm. The submucosal nodule resembled typical leiomyoma. Postoperative follow up was uneventful and the patient was discharged after one week.
One year later the patient presented again with severe hypermenorrhea and a rapidly growing uterine fibroid, 7x6 cm in diameter, close to the cavum uteri. The patient therefore underwent re-laparotomy with total abdominal hysterectomy. Laparatomy revealed an uterus myomatous and multiple severe adhesions.

**Histopathology.** Tissue was prepared with routine histological procedures. The samples were embedded in paraffin, sectioned at 5 μm and stained with hematoxylin and eosin.

The nodules were classified as endovascular leiomyomatosis. The cellular composition was similar to leiomyoma, consisting of uniform, spindle-shaped smooth muscle cells in a whorled arrangement. Mitotic activity was 1 mitosis per 20 high-power fields, and pleomorphism was absent. Immunohistochemically, the intravascular parts of the tumor showed a positive staining reaction for 1A4, HHF35, vimentin and desmin. The tumor also reacted for antibodies against estrogen and progesterone receptors. Ki-67 was <5%. Biopsies of the peritoneum and the omentum majus as well as the appendix and the left follopian tube were inconspicuous.

Postoperatively, the patient developed pulmonary embolism and additionally diffuse, multiple (up to 10) nodules of the lungs were detected. An open lung biopsy revealed tumor that was composed of smooth muscle cells consistent with the diagnosis pulmonary leiomyomatosis.

The patient was first treated with anticoagulant therapy with heparin 2x80 mg s.c. and later warfarin was administered for 6 months to prevent recurrent thromboembolism. The patient was put on a regimen of the gonadotropin-releasing (GnRH) analog, leuproide (Enantone), which was applied at a dose of 7.5 mg s.c. every 4 weeks. Therapy was continued for a total of 6 months and a lung scan was then repeated. No progression of the pulmonary nodules was detected. The patient is now followed up at 3-month intervals by means of vagino-rectal palpation and half-yearly computed tomography.

**Discussion**

In our patient, the tumor did not demonstrate fingerlike projections into the pelvic veins. Additionally, the age of our patient was not typical for this disease as the median age of patients with IVL of the uterus is reported to be about 45 years (2). Our patient presented with symptoms of severe uterine bleeding and uterine enlargement. This is in line with the most common symptoms reported for IVL (1, 8). The histopathology and immunohistochemistry of our case revealed an endovascular leiomyomatosis of the uterus, as well as a pulmonary leiomyomatosis. As tumor spread in this disease is only by the direct extension within blood vessels as described, one theory could be that the smooth muscle cells were spread to the lungs via pulmonary embolism.

The second possible hypothesis is that our patient suffered from a benign metastasizing leiomyoma instead of IVL. Another argument for this hypothesis seems to be that benign metastasizing leiomyomas are typically found in the lungs and affect women with a history of uterine leiomyomata. Speculation on its pathogenesis include a benign uterine leiomyoma colonizing the lung, a metastatic low-grade uterine leiomyosarcoma, and primary pulmonary leiomyomatosis. On the other hand, it is not entirely clear whether the term “benign metastasizing leiomyomas” is a misnomer and whether these lesions are low-grade malignant tumors that have a lower proliferation index (7).

In our patient, the pulmonary tumors had benign histology and immunohistochemical profiles identical to that of uterine leiomyoma.

The treatment of choice for IVL as well as for benign metastasizing leiomyomas is a complete resection with hysterectomy and bilateral oophorectomy because of the estrogen-dependence of the tumor (1, 2). As our patient was quite young, the ovaries were preserved but a regimen of GnRH analogue was applied monthly for a total of 6 months.

In conclusion, knowledge about these rare uterine tumor entities is important for adequate treatment and exact differential diagnosis. Though IVL as well as benign metastasizing leiomyomas imitate a malignant neoplasm concerning the pattern of growth and extension, they must be differentiated histologically from malignant tumors to prevent overtreatment. Because of the rarity of both diseases, a long-term follow-up of the patients is recommended.

**References**


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