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Case report

Successful one-stage resection of intracardiac intravenous leiomyomatosis: A case report

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ABSTRACT

This case report is about a 47-year-old patient, who was diagnosed with intracardiac intravenous leiomyomatosis and received treatment at our institution. Intravenous leiomyomatosis is a rare, histologically benign, uterine neoplasm, which is characterized by non-invasive intravascular proliferation of smooth muscle cells. Intravenous leiomyomatosis arises from the myometrium and, in its most extensive form, can reach the heart via the pelvic veins and the inferior vena cava, causing hemodynamic complications. Treatment of choice is the complete resection of the tumor, even though there is no consensus on the optimal surgical approach. In this case, complete resection of the tumor was accomplished in a one-stage procedure. The patient recovered well and CT scan did not show any signs of recurrence after five months.

1. Introduction

With less than 300 published cases intravenous leiomyomatosis is a rare medical condition, which is characterized by non-invasive intravascular growth of smooth muscle cells from their origin through the uterine vascular channels. It almost always originates from uterine leiomyomatosis (Lan et al., 2022). In its most extensive form, intravenous leiomyomatosis may reach the right heart chamber via the inferior vena cava, which is then described as intracardiac leiomyomatosis. Even though the pathogenesis is not fully understood yet, it is theorized that intravenous leiomyomatosis either arises from muscular tissue of the venular walls or from the pre-existing myoma tissue (Lan et al., 2022). Intravenous leiomyomatosis mostly occurs in pre-menopausal women. Patients tend to be asymptomatic until the tumor has extended to the heart. Cardiac involvement is described in 47.1% (right ventricle) to 87.4% (right atrium) of all cases (Stilidi et al., 2020; Matsuo et al., 2012; Bewersdorf and Loch, 2018). If symptomatic, most patients present with dyspnea (51.7%), chest pain (24.1%), or dizziness (21.8%), whereas abdominal symptoms are less frequent (19.5%) (Matsuo et al., 2012). Even though intravenous leiomyomatosis is a benign disease, it is associated with severe life-threating physical conditions such as cardiac arrest, organ failure, treatment-related complications, or recurrence. The treatment of choice should be complete surgical resection of the tumor to relieve the circulatory system from the intravascular mass and further prevent recurrence (Liang et al., 2021; Luo et al., 2019).

Due to its rarity, evidence is still lacking on the clinical and pathological behavior of intravenous leiomyomatosis. The objective of this case report is to describe the diagnostic and therapeutic approach of an advanced case of intravenous leiomyomatosis reaching the right atrium and review the published literature to support better understanding of this disease (Figs. 1–3).

2. Case presentation

A 47-old-patient was referred to our institution from a local community hospital for suspicion of a massive thrombus extending from the right Iliac vein to the inferior vena cava. The finding was incidentally diagnosed during preoperative routine examination for a scheduled hysterectomy. Indication for surgery was a recent increase in size of multiple uterine fibroids. The patient was cardiorespiratory stable and

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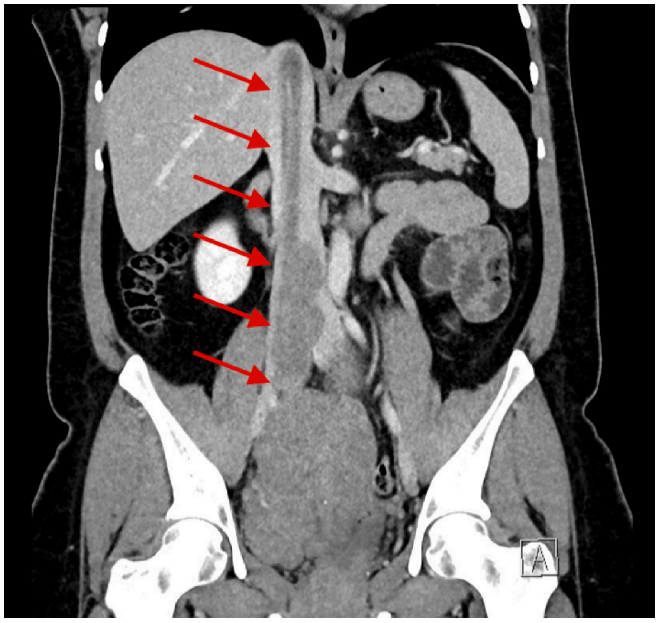

Fig. 1. Radiographic findings. Coronal reformation CT in venous phase after i.v. administration of iodine based contrast agent shows a large thrombus expanding from the right common iliac vessel into the inferior vena cava and right atrium (not depicted). The thrombus shows intravascular contrast enhancement consistent with a tumor thrombus in this patient with known intravenous leiomyomatosis. Axial T2-weighted (a), T1-weighted after i.v. administration of Gadolinium based contrast agent (b), diffusion weighted b800 image (c) and ADC-map (d) shows expansion of the inferior vena cava with inhomogeneous intravascular material with contrast enhancement and diffusion restriction in line with intravascular leiomyomatosis.

reported neither respiratory, cardiac nor gynecologic symptoms at any time. No medical condition or blood clotting disorder underlying such a massive thrombotic event could be identified. The patient was referred to the Division of General Gynecology and Gynecologic Oncology to rule out a paraneoplastic etiology of the suspected diagnosis, i.e. potential uterine sarcoma. Apart from a BMI of 30.8 kg/m^2, moderate arterial hypertension and a massively enlarged uterus with a craniocaudal diameter of 17 cm (cm), medical history and clinical examination provided normal findings. The patient reported two previous vaginal births. Her surgical history included an appendectomy as a child, a cholecystectomy twenty years ago and a curettage after missed abortion. The patient had no family history of oncologic diseases. Transthoracic echocardiography showed a 23 × 22 mm (mm) free-floating structure in the right atrium in direct contact to a solid structure from the inferior vena cava. During diastole, the thrombus completely obstructed the inflow tract of the right ventricle. CT scans of thorax and abdomen and MRI of the pelvis confirmed multiple uterine fibroids with a maximum diameter of 11 cm and dilated pelvic vessels without any signs of malignancy such as central necrosis, hypervascularization, ascites or pathologically enlarged lymph nodes. The structure previously suspected as a thrombus was presumed to be an intravenous leiomyomatosis of the uterus arising from the right internal iliac vein to the inferior vena cava, the right atrium and reaching the tricuspid valve. The following radiographic findings, such as presence of enhancement, appearance of vessel expansion and diffusion restriction, corroborated the diagnosis of intravenous leiomyomatosis unlike a bland thrombus. Due to the extensive findings surgical treatment was planned to avoid hemodynamic complications. Therapy with enoxaparin sodium 8000 IE twice a day, a low-molecular-weight heparin, was established during the course of diagnostic workup.

3. Surgical approach

Due to the complexity of this case, surgical approach was planned in close collaboration with gynecologic oncologists, thoracic and cardiovascular surgeons, anesthesiologists, and intensive care specialists. Since the patient was in good general condition the surgical team agreed to aim for the one-stage procedure consisting of tumor resection in the pelvic cavity along with total hysterectomy by laparotomy and resection of the intravascular tumor by median sternotomy.

As planned, the first surgical step was a total hysterectomy and bilateral salpingo-oophorectomy. The uterus was found to be enlarged (20 × 20 cm) by multiple uterine fibroids. Numerous fibroids were further occupying the pelvic cavity infiltrating the right parametrium and paracolpium. Remarkable was a fibroid infiltration of the right uterine vessels, suggesting the beginning of the intravascular leiomyomatosis. Step by step the uterus was mobilized under visualization of the ureters. Hysterectomy with bilateral salpingo-oophorectomy was performed. Hysterectomy was followed by excision of uterine fibroids found in the parametrium and paracolpium.

Prior to the second surgical part, heparin was administrated, and cannulas were placed in the ascending aorta, superior vena cava, and left femoral vein for extracorporeal circulation. The inferior vena cava was then visualized right above the iliocaval bifurcation, followed by a longitudinal venotomy and a right atriotomy. The intravascular tumor was removed by dividing it in two parts at the preparation site of the superior vena cava to avoid embolism. Since the tumor was oscillating without invasion of vascular walls or adjacent anatomic structures, the major part of the intravascular tumor was removed in toto through the right atrium. The smaller distal parts of the tumor were removed from the incision of the inferior vena cava, followed by venotomy and atriotomy closure. During removal of tumor parts from the right internal iliac vein, the inferior vena cava ruptured at the site of primary incision. Consequently, the patient was reconnected to extracorporeal circulation. Diffuse bleeding could be finally controlled with application of a pericardial patch that was sutured on the vena cava injury site.

Total duration of surgery was 660 min. Intraoperatively the patient received 26 units of packed red blood cells, 6 units of platelet concentrate and 16 units of fresh frozen plasma.

4. Histology

The clinical diagnosis of intravenous leiomyomatosis was confirmed by final histopathology. Samples were embedded in FFPE and 3 μm sections were cut by experienced technicians. Sections were then stained with hematoxylin–eosin according to standard procedures. Histologically, the parts of the tumor resected from different areas showed comparable histologic features: The lesions showed nodular architecture with varying degree of cellularity. The nodules contained intersecting fascicles of spindle cells and hyaline strands. The cells featured cigar shaped nuclei with tapered ends and eosinophilic cytoplasm with blurred cell borders, and focal epithelioid cell morphology. No atypia or mitoses were present. There were foci of regressive changes.

5. Clinical course

After surgery the patient was hemodynamically stable and was transferred to the intensive care unit, where she spent the following 28 days. Post operative course was initially complicated by mild acute respiratory distress syndrome (ARDS). Due to increasing infection parameters and fever episodes antibiotic therapy was established and CT scan was performed. Findings were as follows: first, a mass (8.7 × 13.8 × 15.9 cm) in the lower abdomen, on imaging suspicious for infected hematoma, which was successfully CT-guided drained. Second, bilateral thrombosis of the iliac vein and the femoral vein and pulmonary embolism in the left lower and middle lobe occurred. Therapeutic anticoagulation was primarily established with low-molecular-weight

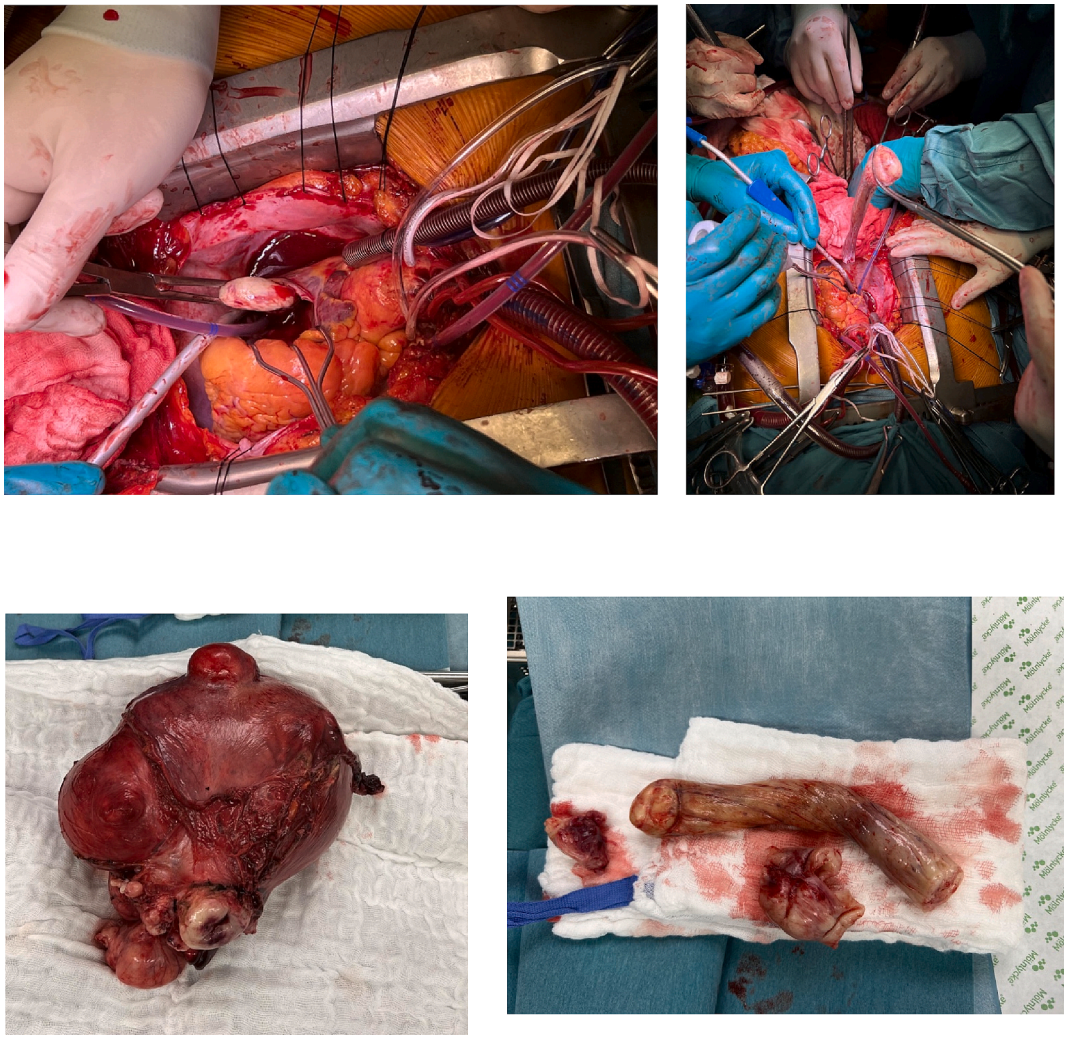

Fig. 2. Extraction of the intravascular tumor through the right atrium. Uterus and intravascular Tumor.

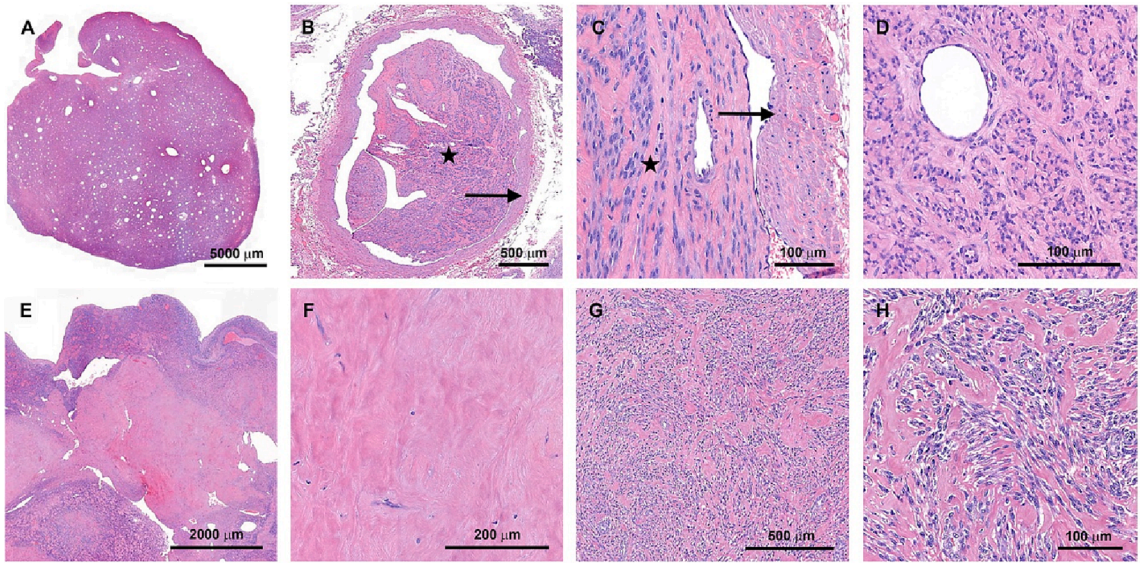

Fig. 3. Facettes of intravenous leiomyomatosis: A) Thrombus from vena cava inferior, HE; B) Intravascular tumor, HE; C) close up of intravascular tumor, HE (star: tumor; arrow: vessel wall); D) signs of neovascularization in Thrombus from vena cava inferior, HE; E) focal areas of hyalinization, HE; F) close up of hyalinized area, HE; G) and H) intersecting fascicles and monotonous spindle cells with cigar shaped nuclei, HE.

heparin. Because of heparin induced thrombocytopenia, therapy was changed to directly acting oral anticoagulants. Continuous hemodialysis was performed for two days until kidney function was stabilized. On the 28th day after surgery the patient was transferred to the regular ward. The further inpatient course was generally unremarkable. The patient continuously recovered physically and mentally and was discharged in good general condition after 13 days.

First follow up was five months later in our outpatient's clinic. The patient denied any physical constraints, such as pain or cardiorespiratory symptoms. CT scan did not reveal any suspicious findings.

6. Discussion

This is a case report of an extremely rare, potentially life-threating, medical condition. The patient presented herself with an extended form of intravenous leiomyomatosis ultimately reaching the right ventricle. Surgery was planned in a multidisciplinary team and could be completed in a one-stage procedure. Postoperatively the patient recovered well and there were no signs of recurrence after five months.

6.1. Clinical presentation

Intravenous leiomyomatosis is seldom diagnosed in an early stage since patients tend to be asymptomatic until cardiac involvement. This coincides with our case as diagnosis of intravenous leiomyomatosis was an incidental finding. Depending on the localization and size of the tumor, symptoms may vary and include dyspnea, syncope, edema of the lower extremities and palpitations (Li et al., 2013).

6.2. Differential diagnosis

Right atrial myxoma is the most common misdiagnosis as almost one third of all patients with intravenous leiomyomatosis are preoperatively believed to have right atrial myxoma. Other differential diagnosis include thrombus-in-transit, renal cell carcinoma, Wilms' tumor, intracardiac leiomyosarcomatosis, benign metastasizing leiomyoma and other metastatic cardiac tumors (Li et al., 2013).

6.3. Treatment and prognosis

Tumor resection is the strongest prognostic factor for recurrence. Liang et al. found complete resection to be associated with a recurrence rate of 4.29%, compared to a significantly higher recurrence rate of 37.84% in patients with incomplete resection (Liang et al., 2021). One-stage surgery is generally recommended, due to a shorter duration of surgery, less intraoperative blood loss and a shorter length of hospital stay. Two-stage surgery with removement of the cardiac mass first is acceptable in patients with poor general condition who would not be able to tolerate extensive surgery, or in cases where complete resection is expected to be technically complex (Zhang et al., 2017). A second pillar of treatment may be hormone-based, given the fact that intravenous leiomyomatosis seems to express high levels of estrogen and progesterone receptors. Pre- or postoperative administration of GnRHa appears to shrink tumor masses and further prevents growth of residual disease in case of incomplete resection. Therefore, GnRHa is a therapeutic option for patients with non-resectable intravenous leiomyomatosis. Additionally, it is recommended that surgical treatment should consist of hysterectomy and bilateral salpingo-oophorectomy (BSO). The lowest recurrence rate (3.13%) was in patients with complete resection of the tumor and BSO, compared to a progression rate of 45.45% in patients with incomplete tumor resection and BSO and a progression rate of 75% in patients with incomplete resection without BSO. In case complete tumor resection was performed without BSO, recurrence rate was 15.38% (Liang et al., 2021).

6.4. Follow up

Due to the rarity of intravascular leiomyomatosis, there is no evidence on optimal follow-up regimes. Stilidi et al. suggests follow up every 3–6 months for the first two years after surgery and once a year after the second year. CT scan of the chest, abdomen, and pelvis is recommended at least once a year (Stilidi et al., 2020).

6.5. Limitation

This is the first case of intravenous leiomyomatosis at our institution within decades, therefore our experience with this disease was limited and treatment decisions were made upon available evidence.

7. Conclusion

Intravenous leiomyomatosis is a rare pathology, which, even though histological benign, shows malignant clinical behavior and may be lethal due to cardiac arrest, organ failure, intra- or postoperative complications, or recurrence. Evidence on diagnosis, treatment and follow up is still limited, which is why we hereby present our case management of a patient with intravenous leiomyomatosis.

8. Patient consent

The patient signed a written declaration of consent to give permission to publish this case report.

Alexander Reinthaller has received consulting fees from Astra Zeneca, EISAI, Roche Austria, PharmaMar, GSK, MSD, Roche Diagnostics, Sandoz and Novartis.

All the other authors declare that they have no conflicts of interest.

9. Author contribution section

Postl M. collected data and wrote the manuscript.

Bartl T. wrote the manuscript.

Poetsch N. contributed data.

Reinthaller A. was involved in patient's care and reviewed the manuscript.

Andreas M. was involved in patient's care and reviewed the manuscript.

Neumayer C. was involved in patient's care and reviewed the manuscript.

Nanobachvili J. was involved in patient's care and reviewed the manuscript.

Nackenhorst M. contributed data.

Polterauer S. was involved in patient's care, reviewed the manuscript and supervised the project.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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