CASE REPORT

Intravascular leiomyoma with heart extension

Marcia Maria Morales,[I,II] Alexandre Anacleto,[I,II] João Carlos Leal,[II] Sérgio Carvalho,[II] Jerônimo Del'Arco[II]

[I]Instituto de Cirurgia Vascular e Endovascular (INVASE), São José do Rio Preto/SP, Brasil. [II]Hospital Beneficência Portuguesa de São José do Rio Preto/SP, Brasil.

Email: marciammorales@gmail.com
Tel.: 55 17 91130208

INTRODUCTION

An intravascular (or intravenous) leiomyoma is a histologically benign tumor characterized by the proliferation of smooth muscle cells arising from the intrauterine venules and/or the myometrium (1-4); however, exceptional cases that arise from cutaneous vessels and pelvic or retroperitoneal veins have been found (5,6). This tumor affects only women, particularly middle-aged women (median age, 44 years) with a history of hysterectomy (4). Usually, an intravascular leiomyoma enters through the lumen of the iliac veins and grows into the inferior vena cava, sometimes reaching the right heart chambers (1-4,7-10). In this situation, one- or two-stage surgery has been used to prevent fatal complications (e.g., total tricuspid obstruction) (3,4,9-13).

Here, we report the case of a 34-year-old totally asymptomatic woman with a history of uterine myoma and with evidence of a pelvic intracaval mass extending to the right atrium. The patient was treated with a one-stage surgical protocol that combined cardiac and vascular procedures in a thoracoabdominal approach under cardiopulmonary bypass at 32℃. The histological analysis of the excised specimen was consistent with an intravascular leiomyoma. The more recent findings on the pathogenesis, incidence, clinical presentation, diagnosis, and treatment of intravascular leiomyo are discussed in this communication.

CASE REPORT

The patient was a 34-year-old nulliparous woman who was admitted to our cardiovascular center in July 2009. According to her medical history, she underwent a myomectomy in 2002. Seven years later, in 2008, the patient presented with a recurrence of the myoma. A hysterectomy was attempted but was unsuccessful due to adhesions from the previous surgery. During the course of the procedure, the surgeon had (inadvertently) ligated the ureter, and the patient had developed a vesicoureteral fistula.

Upon admission, the patient was completely without cardio-respiratory symptoms. Her vital signs were as follows: heart rate of 77 beats/minute; blood pressure of 140/80 mmHg; respiratory rate of 15 breaths/minute; and temperature of 36.2℃. The physical examination revealed a hard and painless abdominal mass extending from the hypogastric region to the right flank. There were no signs of venous hypertension in the lower extremities, such as lipodermatosclerosis, edema, or hyperpigmentation. The routine laboratory examinations of the blood and the urine were normal.

A thoracoabdominal computed tomography scan (Figure 1A) revealed a mass extending from the right internal iliac vein to the right atrium; however, it was unclear whether this mass represented a thrombus or a tumor. Multiple cysts were observed in both kidneys (Figure 1A-4). The inferior vena cava was severely dilated (11 cm) (Figure 1A-5). Transesophageal echocardiography revealed a hyperechoic and mobile mass that filled 2/3 of the right atrium and protruded across the tricuspid valve throughout the cardiac cycle. Owing to the high risk of severe complications and death, a one-stage surgical strategy that combined cardiac and vascular procedures was planned to remove the mass. It should be mentioned that 28 days prior to the cardiovascular surgery, the patient underwent a total hysterectomy with bilateral salpingo-oophorectomy and resection of the vesical dome due to the previously mentioned adhesions. The right internal iliac vein was ligated with the mass inside, and the vesicoureteral fistula was repaired.

The removal of the intracardiac and intravascular masses was performed on October 30, 2009. The superior and inferior vena cava, the right atrium, and the two renal, iliac, and suprahepatic veins were exposed via a right thoracophrenolaparotomy in the fifth intercostal space (Figure 2A), after which the pericardium was opened with an inverted T-shaped incision (Figure 2B). Cardiopulmonary bypass was established by cannulating the ascending aorta, with venous drainage through the right atrium and the superior vena cava. Myocardial protection was provided by retrograde isothermic blood (32℃). The superior and inferior vena cava were longitudinally incised for exposure and complete eradication of the mass. In the first step, the intra-atrial extension of the mass was removed through a superior vena cava incision located 3 cm proximal to the closed right atrium (Figure 2C). An atriotomy was not performed because we were able to confirm beforehand that the intracardiac tumor was mobile and could be drawn out of the closed atrium without complications. In the second step, the intravascular extension of the mass was detached and removed through an inferior cava venotomy (Figure 2D) that extended caudally towards the iliac bifurcation. The excised mass measured approximately 31 cm in length (Figure 2E) and had no thrombi or areas of friable tissue. The histological examination revealed a benign tumor

No potential conflict of interest was reported.

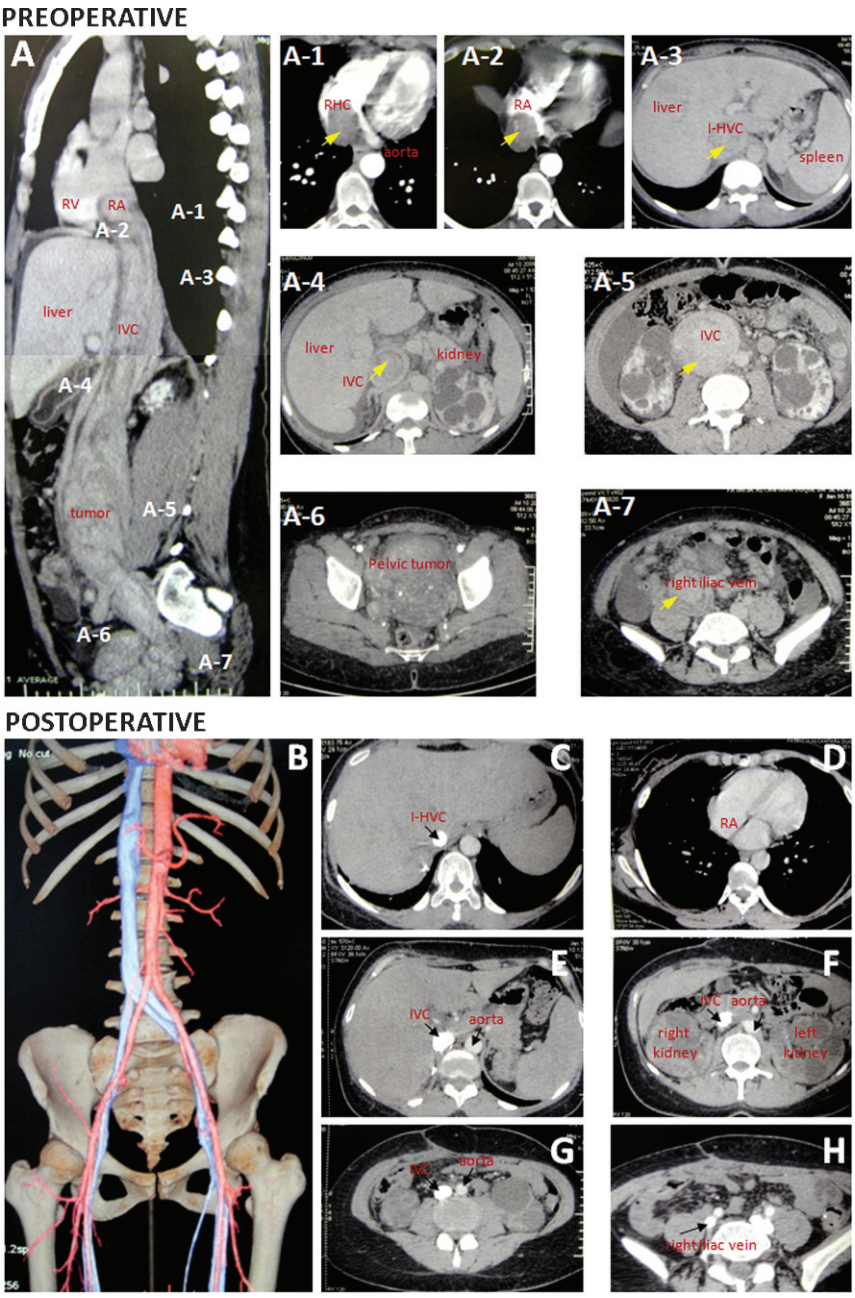

Figure 1 - (**A**) A preoperative sagittal computed tomography (CT) scan showing a mass (leiomyoma) extending from the right internal iliac vein to the right atrium. Figures A-1 to A-7 show the transverse CT scans of the areas indicated in A. (**A-1 and A-2**) The intracardiac tumor. (**A-3** to **A-4**) The intracaval tumor. Note that both kidneys presented with multiple cysts. (**A-5**) The severely dilated inferior vena cava (11 cm). (**A-6**) The multilobulated pelvic tumor with intense vascularization. (**A-7**) The intrailiac tumor. (**B-H**) The postoperative CT scans, showing absence of the tumor and a normal-diameter inferior vena cava. *I-HVC*, intrahepatic vena cava; *IVC*, inferior vena cava; *RA*, right atrium; *RHC*, right heart chambers; *RV*, right ventricle; *yellow arrow*, tumor localization; *black arrow*, vessel lumen.

compatible with an intravascular leiomyoma (Figure 2F). There were no extensive hyaline zones obscuring the underlying smooth muscle nature of the tumor, and complementary studies with myogenic markers (alpha-smooth muscle actin and desmin) were not required. All of the neoplastic cells were positive for progesterone and negative for estrogen.

At the end of the procedure, the suprahepatic segment of the inferior vena cava was repaired and clamped just above the liver. Next, the venous clamp was moved along the infrahepatic segment of the vessel, which was repaired towards the iliac bifurcation. The heart beat was restored, and the cardiopulmonary bypass was discontinued without complications. The total cardiopulmonary bypass time was 42 minutes, and the patient experienced no hemodynamic alterations after the procedure.

The postoperative course was uneventful, and a control computed tomography scan revealed no evidence of tumor (Figure 1B-H). The patient was discharged from our service on postoperative day six with a 15-day prescription for

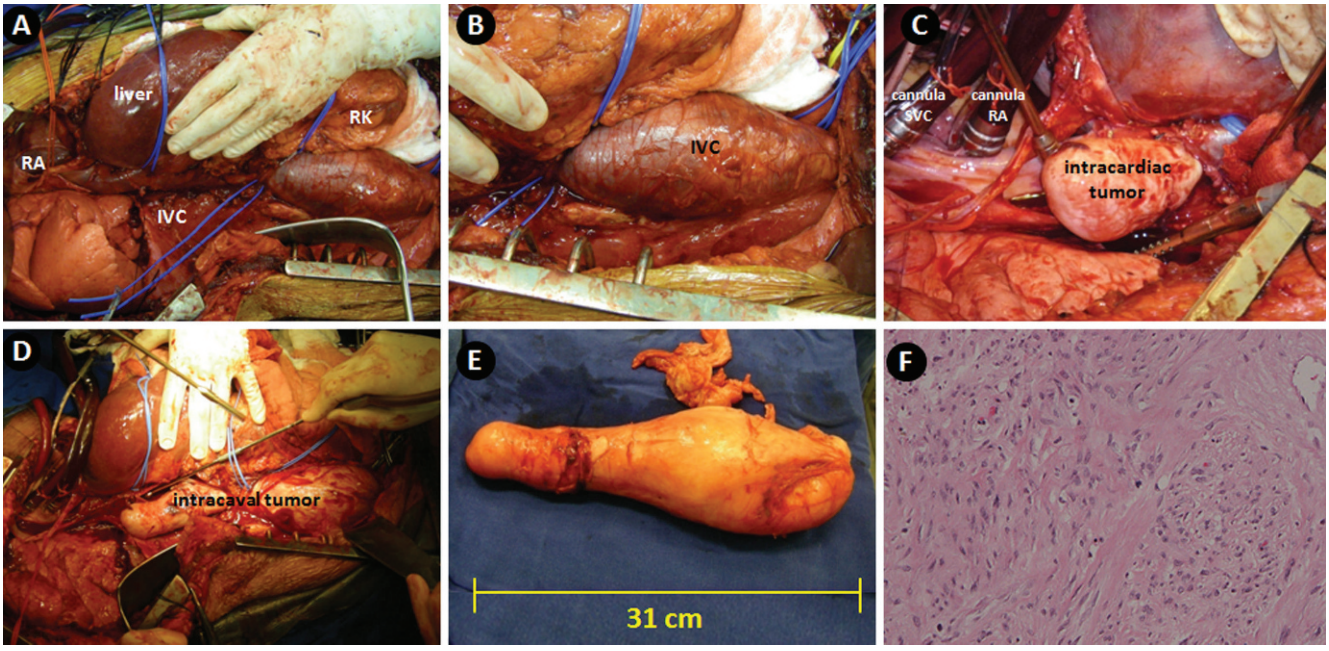

Figure 2 - (**A**) The right atrium and the superior and inferior vena cava were completely exposed through a right thoracophrenolaparotomy. (**B**) The pericardium was opened to access and cannulate the right atrium. (**C**) The intra-atrial extension of the tumor was removed through a superior cava incision located 3 cm proximal to the atrium. Note that the right atrium was not opened to achieve tumor exposure. (**D**) The intracaval extension of the tumor was completely detached from the vessel wall. (**E**) The specimen morphology. The excised tumor measured 31 cm in length and had no thrombi or areas of friable tissue. (**F**) A histological examination of a hematoxylin and eosin-stained tissue section (200X). The smooth muscle cells were predominantly organized into fascicles and occasionally into a plexiform pattern. The cells showed no abnormal mitotic activity, atypia, or necrosis, supporting the diagnosis of intravascular leiomyoma. *IVC*, inferior vena cava; *RA*, right atrium; *RK*, right kidney; *SVC*, superior vena cava.

low-molecular-weight-heparin (enoxaparin), to be followed by anti-vitamin K and tamoxifen (200 mg) for six months. The patient presented without any complications at 14 months postoperatively (the most recent consultation).

DISCUSSION

An intravascular leiomyoma is an insidious tumor, and extension into the right heart chambers can occur slowly, over many years (2-4,7-10). Our PubMed and Cochrane library literature search retrieved only 132 cases of leiomyoma with heart extension, many of which (~40%) have been described over the last 15 years. It is probable that recent advances in tumor diagnosis imaging and immunochemistry have resulted in an increased number of reports by facilitating the distinguishment between intravascular leiomyoma and other similar disorders, especially thrombi and malignant tumors (8). In addition, it is possible that the incidence of intravascular leiomyo is rising due to increased risk factors for developing hormone-dependent tumors (14). In general, intravascular leiomyomata affect premenopausal women, and the majority ($\pm$90%) are parous (4). (our patient was exceptional in being nulliparous).

The recent literature has recommended that an intravascular leiomyoma diagnosis be considered in all women presenting with deep vein thrombosis, a contrast-enhancing mass (visualized by computed tomography scan) within the vena cava or the right atrium, and unspecific symptoms associated with a history of pelvic surgery, hysterectomy, or uterine leiomyomatosis (15). A definitive intravascular leiomyoma diagnosis is confirmed by a histopathological analysis. A physical examination and adequate diagnostic imaging can rule out other potential diagnoses, allowing the physician to refer the patient for correct treatment. Nonetheless, the differential diagnosis between thrombus-in-transit and intravascular leiomyoma is not always clear by echocardiography or other imaging. In general, the features suggestive of a thrombus-in-transit include postoperative status, indwelling intravascular devices, immobility combined with other thromboembolism risk factors, and elongated mobile masses of a venous cast that have a ''popcorn'' appearance (16). By contrast, the classical appearance of an intravascular leiomyoma is an elongated mobile mass extending from the veins of the lower body, including the inferior vena cava and the azygos vein, that fills the vessel lumen and the right heart chambers and has multiple venous attachments (especially at the origin of tumor) (15-17).

The molecular mechanisms associated with the phenotypic and behavioral characteristics of an intravascular leiomyoma are not completely defined. There is evidence that hyaluronan, a non-sulfated proteoglycan from the extracellular matrix synthesized within the leiomyoma, can play a modulatory role in the kinetics of cell proliferation and the growth rate of the tumor (18,19). Recently, significant evidence has suggested a close relationship between intravascular and uterine leiomyomata. The neoplastic smooth muscle of an intravenous leiomyoma resembles that of a benign uterine leiomyoma and may include the same histological variants found in the uterus (5). Furthermore, both leiomyomata are genetically characterized by a balanced *t* translocation (12,14). involving the chromatin remodeling-gene *HMGA2* (20,21). The contribution of *HMGA2* to the intravascular leiomyoma phenotype remains under investigation.

Although it is nonmalignant, an intracardiac leiomyoma can lead to severe complications, including obstruction of the tricuspid valve, valvular regurgitation and diminished cardiac performance to the point of overt heart failure (7,15,22). Rarely, this tumor coincides with a benign metastasizing leiomyoma in the lung (5,23). A few cases of obstructive shock and sudden deaths have been reported in literature (5,24,25).

Since 1982, two surgical procedures have been performed to treat intravascular leiomyo with heart extension (3,4,9-13). The first requires completely removing the intracardiac and intracaval mass through a one-stage surgical approach, as in our case (3,4). The second involves an abdominal stage and a thoracic stage (11,12). The specific indications for each procedure are unclear and depend on the surgeon's experience and the preoperative status of the patient.

In many centers, including our own, one-stage surgery is the preferred operation for treating tumors with heart extension in patients with a clear preoperative diagnosis, good health conditions, and/or normal operative risks (3). By contrast, two-stage surgeries are typically planned for high-risk patients, including those with cardiopulmonary comorbidities, risk factors for major bleeding, and complications requiring repairing or resectioning the thoracic and abdominal structures; in the latter case, a one-stage surgery could result in a much longer operative time (3,10).

There are no guidelines for performing one-stage versus two-stage surgeries (13). Different surgical protocols have been applied to leiomyomata. For example, when planning a two-stage surgical protocol, no consensus exists on which component of the operation (abdominal or thoracic) should be performed first. In our opinion, the abdominal component should be performed before the thoracic due to the likelihood of encountering a dense adherence to the vascular wall at the origin of the tumor (by contrast, adherences along the upper path are often loose or nonexistent).

Regarding one-stage surgery techniques, our protocol consisted of the following specific features: 1) Surgical access was achieved through a right thoracophrenolaparotomy (single incision) rather than a median sternotomy plus laparotomy (two separate incisions), which has been used in several previous reports. Although unusual, our approach offered excellent exposure of the ascending aorta, the atrium, and the vena cava and its tributaries. 2) The right atrium was not opened to expose the intracardiac extension of the leiomyoma because we had previously confirmed that it was mobile and free from adhesions. When the tumor presents with cardiac adherences and compromises the morphofunctional integrity of the heart valves, an atriotomy is mandatory. 3) The cardiopulmonary bypass was established by cannulating the ascending aorta, with venous drainage through the right atrium and the superior vena cava. By contrast, some surgeons have opted for cannulating the right subclavian artery and the right femoral vein (3). 4) Myocardial protection was provided by retrograde isothermic blood rather than deep hypothermia, which has been used in previous reports. Recent studies have demonstrated that the isothermic approach used here provides more physiological myocardial metabolic activity than the hypothermic approach (i.e., the myocardium utilizes more oxygen and more glucose while producing less lactate) (26-28). We think that isothermia provides the same clinical benefits and eliminates the possible adverse effects of deep hypothermia and total circulatory arrest.

It is worth noting that surgically treating intravascular leiomyo with heart extension has a favorable prognosis. However, tumor recurrence can occur up to 15 years after the surgery. To prevent this complication, many authors, including our group, have recommended postoperative hormonal therapy with antiestrogens or aromatase-inhibitors, such as tamoxifen (23,29).

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Written informed consent was obtained from the patient to publish this case report and the accompanying images.

AUTHOR CONTRIBUTIONS

Morales MM conceived and designed the study, and was also responsible for the collection, analysis and interpretation of data, manuscript writing and final approval of the manuscript. Anacleto A was responsible for the analysis and interpretation of data and critical revision of the article. Leal JC, Carvalho S and Del'ArcoJ were responsible for the data collection.

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