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Intravascular leiomyomatosis: an exceptional entity

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Summary

Intravenous leiomyomatosis (IVL) is a rare benign condition characterized by the proliferation of smooth muscle cells originating from either the uterine venous wall or a uterine myoma. This leiomyomatosis extends most frequently to pelvic vessels, but also occasionally into the inferior vena cava and right cardiac chambers. Preoperative diagnosis is difficult and it should be suspected in the presence of cardiac or pelvic masses in women who have undergone hysterectomy or myomectomy previously. The treatment is hysterectomy, normally associated with a bilateral oophorectomy and removing the mass or metastasis if any. The post-surgical follow-up should be performed at long term and include exploration and imaging, either ultrasound or MRI. The association of antiestrogenic drugs can be useful for disease control, especially in cases where oophorectomy is not performed and the tumor cannot be removed completely.

Key words: Intravascular leiomyomatosis; Intravenous leiomyomatosis; Cardiac tumor; Pelvic mass.

Introduction

Intravenous leiomyomatosis (IVL) is a rare disease first reported in 1896 by Birsh-Hirschfield [1] and later defined by Norris and Parmley in 1975, with a series of 14 cases [2]. It is a benign lesion histologically characterized by proliferation of intravascular endothelial smooth muscle cells of the myometrial vessels [3].

Despite the benign histology, these tumors have an aggressive behavior such as an oncological condition. They can produce metastatic dissemination by vascular invasion, affect pelvic vessels, inferior vena cava, renal veins, adrenal veins, and even the right cardiac chambers, and more rarely left cardiac chambers and pulmonary artery [4]. Clinical manifestations depend on the location and size of the lesions and can produce from pelvic pain to sudden death in extreme cases [4].

Diagnosis is usually made with the analysis of the surgical specimen or it could occasionally be suspected during surgery. However, preoperative diagnosis is complex and should be suspected in the presence of concomitant tumors in the pelvis and right cardiac chambers; or pelvic tumor in a patient who has undergone a hysterectomy for uterine fibroid [5]. The authors report four cases diagnosed in their hospital between 1990 and 2013.

Cases Report

Case 1

A 42-year-old woman had a hysterectomy with bilateral salpingectomy for fibroid uterus. The histological analysis revealed the presence of uterine intravascular leiomyomatosis with extension to extrauterine vessels. Immunohistochemistry revealed a marked positivity to progesterone receptors and weaker against estrogen receptors. One year after surgery the patient experienced abdominal pain and the abdominal ultrasound revealed a multilobulated tumor of ten cm in maximum diameter. During surgery, a multilobulated mass occupying the pelvis and a right ovarian tumor about four cm in size was visualized and excision of the mass and right oophorectomy was performed.The histologic examination of the specimen indicated smooth muscle cell proliferation compatible with a diagnosis of extrauterine intravascular leiomyomatosis. The postoperative course was uneventful and a treatment with GnRH analogues was established.

Case 2

A 40-year-old woman underwent a simple hysterectomy for fibroid uterus reaching belly button at the expense of several solid formations. The histological diagnosis was intravascular leiomyomatosis. Eleven years after the first surgery, the patient had an episode of acute urinary retention. A urography was performed, which confirmed a delayed elimination of the contrast in the right kidney and bilateral uretero-hydronephrosis. Abdominopelvic CT showed a pelvic tumor of 11 cm, which suggested an ovarian cystodenocarcinoma that produced a grade-IV hydronephrosis. With the suspected diagnosis of ovarian cystadenocarcinoma, an exploratory laparotomy was performed, and, during surgery, a cystic mass occupying the pelvis was observed, which was removed with the ovaries, which had a normal appearance. In the analysis of the surgical specimen, a proliferation of highly vascular smooth muscle cells was observed. It showed a muscle differentiation (positive actin) presenting estrogen and progesterone receptors. The ovaries showed no pathology and diagnosis was of relapse of the intravascular leiomyomatosis. During four years of follow up, the patient has no sign of recurrence.

Case 3

A 42-year-old woman, with previous myomectomy 13 years prior, went to the emergency room for pain in left chest radiating to the arm. The chest X-ray showed bilateral parahilar nodules with

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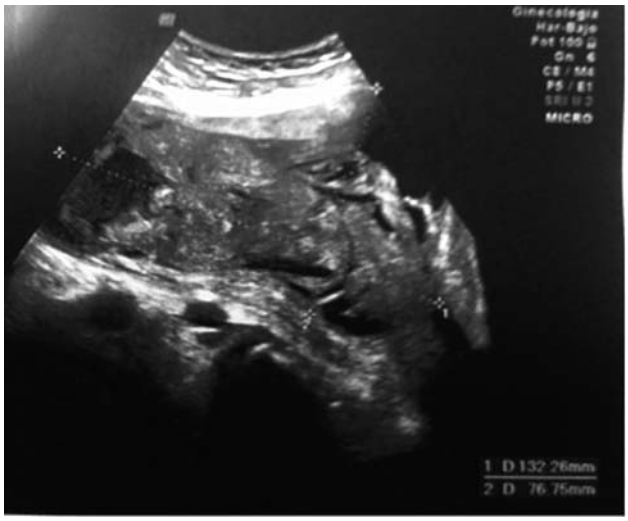

Figure 1. — Ultrasound scan of the uterine tumor. Heterogeneous mass with mixed echogenicity is apparently in the interior of the endometrial cavity.

regular contour. Bronchoscopy found no data of interest. A thoracotomy was performed and intraparenchymal multiple nodes, one of more than five cm and the remaining of 0.5 to one cm in diameter were found. Histological analysis described a smooth muscle proliferation without criteria of malignancy. Subsequently, gynecological examination and ultrasound were performed with result of fibroid uterus and normal adnexa. With the diagnosis of pulmonary metastases from uterine leiomyoma, the authors performed the same treatment as for metastatic leiomyosarcoma. Three cycles of chemotherapy (vincristine, actinomycin D, and cyclophosphamide) were introduced without acceptable variations in the size of metastases from a radiological point of view. Behind them, a surgical treatment consisting of total hysterectomy with bilateral oophorectomy was performed.

Case 4

A 37-year-old woman was admitted to the hospital with a history of metrorrhagia. Physical examination revealed an enlarged uterus size. In ultrasound a heterogeneous mass of 132 x 76 mm that suggested the presence of a degenerated myoma was visualized (Figure 1). The authors decided to perform an abdominal hysterectomy preserving adnexa, blood transfusion prior to surgery was necessary, as the analysis performed preoperatively showed anemia with hemoglobin of 4.9 g/dL. Surgery was performed without complications and the postoperative course was satisfactory so the patient was discharged after five days of admission, with hemoglobin of 8.3 g/dL that required treatment with oral iron therapy. One month after surgery, the patient was examined and was totally asymptomatic. Furthermore, echocardiography to discard extrauterine involvement was requested, which was normal. She is currently awaiting the second follow up at six months after surgery.

Discussion

Intravascular leiomyomatosis is a rare neoplastic disease, which is characterized by intravenous growth of histologically benign smooth muscle cells. In cases of IVL, the extrauterine extension can reach 80%, especially in the vessels of the broad ligament, with up to 10-40% of cases with cardiac involvement [6]. The main problem is in the difficult diagnosis prior to surgery; the clinical suspicion of this condition remains complicated. However this clinical condition is unspecific and it could present as abdominal pain, symptoms of heart failure, and may even debut as a pulmonary embolism [4, 7]. Sometimes the diagnosis is made during the same surgical procedure, observing invasion of uterine vessels [8]. Other times it could present as a recurrent tumor in the pelvis or in the cardiovascular system, in a patient who has undergone a hysterectomy in the past.

Regarding imaging techniques, the role of computed tomography with contrast is important, which allows to assess the extent of the lesion through the venous system and right cardiac chambers, making a proper planning of surgery possible [8]. MRI may also be useful, presenting as advantages a higher resolution for the soft tissues and the ability to assess blood flow through the affected vessels [9].

The histologic differential diagnosis includes typical leiomyoma with an artifact retraction surrounding myometrium, leiomyoma with vascular invasion, leiomyoma with hydropic changes, and endometrial stromal sarcoma of low-grade [5]. The suspected imaging diagnosis and the histological diagnosis are not always clear. In fact, in the first case the authors present, the diagnosis of myoma that was performed after pelvic recurrence. It is essential to integrate clinical information with imaging tests when suspecting this pathology. Even so, the preoperative diagnosis is complicated. Symptoms of recent heart failure or pelvic masses after performing a hysterectomy are clues that should lead us to suspect this condition, seeking a better extension study by imaging, to facilitate the planning of surgery. In the present series of cases none was suspected before surgery.

The operative approach requires careful consideration with the aim of radical resection of the tumor, including extrauterine mass being forced performing hysterectomy, and according to some authors, bilateral oophorectomy, as it is a tumor hormone-dependent and estrogen can produce stimulation and growth of tumor [5, 10, 11]. After surgery, the patient should receive adequate long-term follow up, because there are cases that have been described as recurrence up to 43 years after hysterectomy [12]. Some authors recommend MRI and ultrasound every six months, and in the case of finding any sign of recurrence, cardiac involvement may be investigated by echocardiography [5]. In the present center, these patients are followed every six months for the first five years, with ultrasounds and exploration. After the fifth year, annual follow ups are made.

In cases where no complete removal of the tumor is obtained or is not operable, adjuvant treatment with antiestrogen therapy can be useful [9-11]. Of the four cases presented, only the first patient started treatment with GnRH analogues, because in the second and in the third

cases bilateral oophorectomy was performed. In the last case, given the age of the patient, the authors evaluated the risk-benefit of therapy antiestrogenic, and so far, it has been chosen to closely monitor without adjuvant treatment.

Adjuvant therapies such as radiotherapy and chemotherapy were administered on established protocols. With the use of different agents, doses and duration of administration, it is difficult to assess the impact of treatment. Preoperative chemotherapy and radiotherapy may control micrometastases, shrink the tumor, prevent progression and prevent recurrences, even if failed to improve long-term survival [13]. In the third case, the administration of chemotherapy did not improve pulmonary radiographic findings. In conclusion, intravascular leiomyomatosis of the uterus is a rare disease, with potential to produce distant metastases, the diagnosis is usually histological and requires close follow up after surgery to identify a possible recurrence.

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