Intravenous Leiomyomatosis of the Uterus

A Report of Three Cases

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Three cases of intravenous leiomyomatosis (IVL) of the uterus, a rare benign smooth-muscle tumor, are described. A preoperative diagnosis of IVL was not made in any of the patients, all of which presented with a pelvic mass with the presumptive diagnosis of leiomyoma. Surgical exploration confirmed the presence of uterine mass and two of the three cases showed extra-uterine extension into the ovarian or uterine veins. Histological examination demonstrated a fascicular pattern of bland spindle-shaped smooth-muscle cells, which extended to veins inside the myometrium or to extrauterine veins. This was confirmed by immunohistochemical stain for desmin and factor VIII. Despite their histological benignity, these lesions have a tendency to metastasize and are closely related to the conditions called “benign metastasizing leiomyoma” and “intracaval mass and cardiac extension”. The primary treatment of IVL is hysterectomy and excision of any extrauterine tumor, when technically feasible. Anti-estrogenic therapy has been suggested as potentially useful in controlling of unresectable tumor. According to the literature, the follow-up must be long and periodic postoperative ultrasonic or magnetic nuclear resonance imaging studies may be useful in detecting growth of residual intravascular tumor. (Pathology Oncology Research Vol 4, No 1, 44–47, 1998)

Introduction

Intravenous leiomyomatosis (IVL) is a rare benign smooth-muscle tumor that is defined as an extension of grossly visible smooth muscle into vascular spaces or growth of microscopic tongues of benign smooth muscle cells into vessels beyond the confines of a leiomyoma.

The lesion was first described by Birch-Hirschfield in 1896, according to Clement and Mullings. About one hundred cases have now been reported. IVL has been described in women 23 to 80 years of age, with most patients being middle-age (median: 44 years). There has been no demonstrable association with race, fertility or parity. The symptoms and signs are like those of ordinary leiomyoma. The correct preoperative diagnosis of IVL is difficult. It is usually established by intraoperative findings or postoperative pathological examination. According to Clement, IVL is more common than the number of reported cases suggests, because in an unknown proportion the diagnosis is overlooked by the pathologist. The presence of typical leiomyomas, which coexist in most cases of IVL, may divert attention from the intravascular tumor, mainly in cases in which no extrauterine extension is noted.

Despite its cytohistological benignity, IVL has a metastatic potential because of vascular invasion. Most of the tumors arise in the uterus and grow into the lumen of uterine veins, but some may extend through the pelvic or ovarian veins into the inferior vena cava and reach the right side of the heart. Rarely, the patient’s initial symptoms are related to the cardiac involvement: congestive heart failure, dyspnea and syncope. Our report describes three patients with the postoperative pathological diagnosis of IVL.
Case Reports

Case 1

M.H.L., 38 years old, G3P1A2, was treated for symptoms of pelvic pain, hyperpolymenorrhea and dysmenorrhea for 4 months. Physical examination indicated an oversize uterus, which was confirmed by ultrasonography: 126x56x60 mm, irregular contours, heterogeneous texture, presenting various hypochoic nodular images; other organs and large vessels were normal. Twenty-two months after the first diagnosis ultrasonography showed a uterus of 129x80x54 mm with multiple hypochoic images, the largest of which was in the subserosa of the left uterine horn. A total hysterectomy and left oophorectomy were performed. The pathological gross examination revealed a myomatous uterus with compact whitish nodules located intramurally, in the submucosa and the subserosa; close to the left ovary there was a friable blood-filled area, 60x50x40 mm, suggestive of degenerated myoma. Microscopy showed hypercellular myomas with focal areas of infiltration in the periphery, low mitotic rates, without atypias. Vascular invasion was observed in the myometrium outside the limits of the leiomyoma and extending to the ovarian vessels. Diagnosis was intravenous leiomyomatosis with vascular extension to the vessels of the myometrium and ovary, associated with multiple leiomyomas of the uterine corpus. The patient has been followed for two years, without recurrences.

Case 2

M.S.E., 47 years old, G5P5A0, was treated for hyperpolymenorrhea and dysmenorrhea for 5 years. Physical examination showed an oversized uterus, which, on ultrasonography, measured 170x113x102 mm, with regular contours and homogeneous echotexture. A fist-sized nodule was palpated on the left wall of the uterus. Uterine curettage revealed a hyperplastic endometrium with normal glands, with normal myometrium. Pathological examination revealed a myoma located intramurally, with degenerative changes. The patient was referred for further evaluation. A total hysterectomy was performed. The pathological examination revealed a myomatous uterus with multiple nodules located intramurally, in the submucosa and subserosa; close to the left ovary there was a blood-filled area, 60x50x40 mm, suggestive of decomposed myoma. Microscopy showed hypercellular myomas with focal areas of infiltration in the periphery, low mitotic rates, without atypias. Vascular invasion was observed in the myometrium outside the limits of the leiomyoma and extending to the ovarian vessels. Diagnosis was intravenous leiomyomatosis with vascular extension to the vessels of the myometrium and ovary, associated with multiple leiomyomas of the uterine corpus. The abdominal organs and large vessels were normal. The patient was submitted to curettage with histopathological diagnosis of proliferative endometrium. Total hysterectomy was performed. During section of the right uterine vein a solid mass measuring 1 cm in diameter was observed inside the vessel with the appearance of leiomyoma. Pathological examination revealed various myomas in the uterus, some of them related to vascular spaces (Figure 1). Microscopically, there were fusiform smooth muscle cells inside venous channels limited by endothelium. Diagnosis was intravenous leiomyomatosis. The patient has been followed for one year after the surgery, without recurrences.

Case 3

S.M.M.M., 50 years old, G5P3C2A0, was treated for hyperpolymenorrhea for 6 months. She had received uterine curettage 2 months previously at another service with a histopathological diagnosis of secretory endometrium. Physical examination and ultrasonography showed uterus of 155x84x77 mm, with heterogeneous texture, presenting solid nodular images in the myometrium; other organs and large pelvic and abdominal vessels were unaltered. The patient underwent total hysterectomy. On histopathological examination, microscopic tongues of muscular tissue were seen in venules of the myometrium outside the limits of the myomas. Diagnosis was intravenous leiomyomatosis associated with uterine leiomyomas. The patient did not present any recurrence two years after the surgery.

Discussion

Intravenous leiomyomatosis (IVL) is also known as a smooth-muscle tumor with unusual growth pattern.6 Its extraterine extension, particularly within veins of the broad ligament, has been reported in 80% of the cases and, in 10 to 40 % of those, the tumor had reached the right side of the heart.2-6, 19

Extraterine extension may be diagnosed intraoperatively or on gross examination of the hysterectomy specimen. In other cases it only becomes evident on revision many years after hysterectomy, because of recurrent tumor in the pelvis, in the cardiovascular system or, rarely, associated with solitary metastases, as in benign metastasizing leiomyoma.

The diagnostic gross feature is the presence of one or more nodules or wormlike extensions of tumor within myometrial or parametrial vessels. Leiomyomas are often present, but occasionally all tumor is intravascular, without a gross nodule.

Only one of our three cases was noted by the surgeon as an extraterine nodule inside a uterine vein. The other two were diagnosed only by microscopic examination. However, one of them had extraterine extension to the ovarian veins.
Figure 2. Smooth muscle tumor inside venous channel limited by endothelium, demonstrated by factor VIII-related antigen (arrow).

Microscopically, IVL is characterized by endothelium-coated plugs of benign smooth muscle cells within myometrial vessels or lymphatics. The intravascular tumor resembles a typical leiomyoma or it may be a leiomyoma variant, such as cellular, atypical, epithelioid, myxoid, etc. Mitotic figures are rare but as many as 4 in 10 high power fields have been reported.6

Differential diagnosis includes: a) typical leiomyoma with artifactual retraction from the surrounding myometrium; b) leiomyoma with vascular invasion; c) leiomyoma with perinodular hydropic change; d) low-grade endometrial stromal sarcoma. Stains for endothelium antigens such as factor VIII or Ulex europaeus may be useful to confirm the absence of endothelial cells in artifactual retractions.

That is also the case in leiomyomas with perinodular hydropic change that may give a false impression that the nodules are lying within vessels. The leiomyoma with vascular invasion is a typical leiomyoma or a leiomyoma variant with microscopic intravascular growth to the tumor that is clinically inconsequential in most patients.6 However, some authors3,6 believe that it may represent a precursor of IVL.

The low-grade endometrial stromal sarcoma forms single or multiple intramural masses that involve the endometrium in most cases. It may permeate the myometrium in irregular tongues. Myometrial as well as extraterine veins and lymphatics frequently contain extensions of the tumor. It is worth noting that the presence of a fascicular growth pattern, thick-walled blood vessels and fusiform nuclei indicate a smooth muscle origin. Although immunohistochemical stains have limited value in the differential diagnosis, desmin is more frequent in the smooth muscle cell than in the endometrial stromal cell.15

Our three cases were desmin-positive and the endothelium cells were demonstrated by factor VIII-related anti-
gen (Figure 2). Two of our three cases were not grossly recognizable and this fact indicates that IVL is probably underdiagnosed, due to failure to appreciate the early stages of tumor development and inadequate sampling of all uterine leiomyomas.

The treatment of IVL is basically surgical. There is general agreement that hysterectomy and resection of all extra uterine masses should be performed. Even for pelvic and abdominal vessels and cardiac involvement, surgical tumor resection has been reported as successful.7,9,14,28 Some authors also propose bilateral oophorectomy119 to help avoid growth of tumor tissue stimulated by estrogenic action. Anti-estrogenic drugs, as tamoxifen, danazol and gestrinone, GnRh agonist and progesterone have been used for inoperable tumors. Marcus et al11 in 1994 tried to stop intravascular tumor growth through actinic oophorectomy using 2100 cGy, with no success.

For the follow-up, patients should be submitted to ultrasonic and magnetic nuclear resonance examination every 6 months.17,19,20 In case any abnormality is noticed in pelvic or abdominal vessels, transesophageal echocardiogram is indicated10 to investigate cardiac involvement.

References

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