Intravenous Leiomyomatosis of the Uterus.

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Abstract

Intravenous leiomyomatosis (IVL) is a rare neoplasm characterized by nodular masses of histologically benign looking smooth muscle cells growing within uterine or extrauterine venous system.The exact etiology is unclear and benign histological appearance of neoplastic smooth muscles can be deceptive since IVL might behave in a malignant fashion. Total abdominal hysterectomy and excision of any extrauterine tumor if technically feasible is the cornerstone of treatment. We report clinical, histological, and immunohistochemical features of a uterine IVL in a 48 year old lady who presented with menorrhagia. We also elaborate etiopathogenesis and conclude that knowledge about IVL is essential as it must be differentiated from malignant tumors to prevent overtreatment. Long term follow up is recommended in such cases.

Keywords : *Intravenous, leiomyomatosis, uterus.*

Introduction

Intravenous leiomyomatosis (IVL) is one of the several rare and unusual disorders of uterine smooth muscle proliferation characterized by quasimalignant behavior. In 1975, Norris and Parmley [(1)] defined it as a leiomyoma arising from the uterine venous wall or a uterine leiomyoma infiltrating intravenously and spreading into the venous cavity. The lesion affects women in varied age groups (23-80 years, median: 44 years), and there is no association with race, fertility or parity [2,3,4]. Preoperative diagnosis of IVL is difficult since symptoms and signs are not specific. It is usually established by intraoperative findings or post-operative pathological examination.

Although histologically benign, IVL may extend into inferior vana cava through uterine, pelvic or ovarian veins and can involve right-sided cardiac chambers and even the pulmonary artery causing various degree of vascular obstruction, which can be fatal. The cornerstone of treatment consists of complete excision of the tumor usually total abdominal hysterectomy (TAH), as well as an excision of any extrauterine tumor when technically feasible. We report a case of IVL in a 48 years old female who was diagnosed post-operatively.

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Case report

Clinical findings

A 48 year old female presented to gynecological out-patient clinic of Farwaniya Hospital with complaint of menorrhagia of 4 month duration. Local examination showed normal size, anteverted uterus which was confirmed by ultrasound. No extrapelvic mass was detected. General examination showed signs of anemia. Hematological work-up revealed low hemoglobin (54 gm/liter, normal 120-160 gm/liter), while other parameters were within normal limits. Biochemical investigations did not show any abnormality. She was given blood transfusion; anemia was corrected; and an endometrial sample was taken. It revealed simple hyperplasia of endometrium. There was no atypia. Hormonal treatment for hyperplasia failed to alleviate patient's complaint and a total abdominal hysterectomy was done.

Pathology

Grossly, the TAH specimen weighed 248 grams. Corpus uteri measured 8x8x5 cm while attached cervix was 3 cm in length. Cut surface showed a greyish white, nodular, rubbery to firm, worm like mass 4x3.5x3 cm in myometrium. No significant endometrial or cervical pathology was noticed. There were no parametrial masses or nodules.

Microscopically, there were moderately

cellular nodular masses of benign smooth muscle cells (smooth muscle actin and desmin positive) growing within channels lined by endothelium (confirmed by CD34 immunostain) (Figures 1, 2). Numerous vascular spaces were seen within the nodules. No significant atypia or coagulative necrosis was noticed. Mitotic count was less than 2/10 HPF. Endometrium was secretory in nature while cervix was unremarkable. A diagnosis of IVL was rendered and follow up was advised. The patient is doing well till date.

Discussion

IVL is rare and one of the intriguing benign smooth muscle tumors of the uterus which is well known for its unusual growth pattern. Its extrauterine extension, particularly within veins of the broad ligament has been reported in 80% of cases and in 10-40% of those, the tumor has reached the right side of heart [5,6,7].

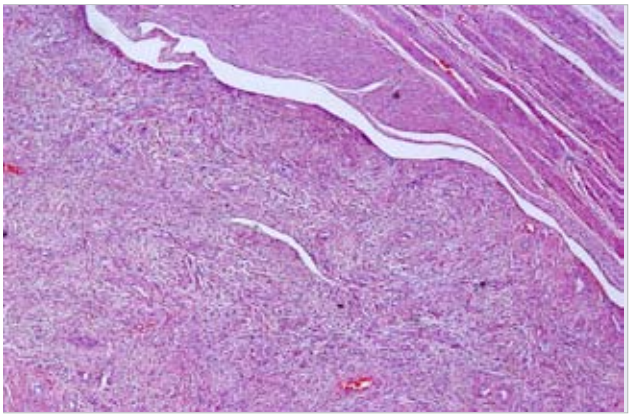

Fig. 1 : Intravascular smooth muscle tumor lined by endothelium (H&E x200).

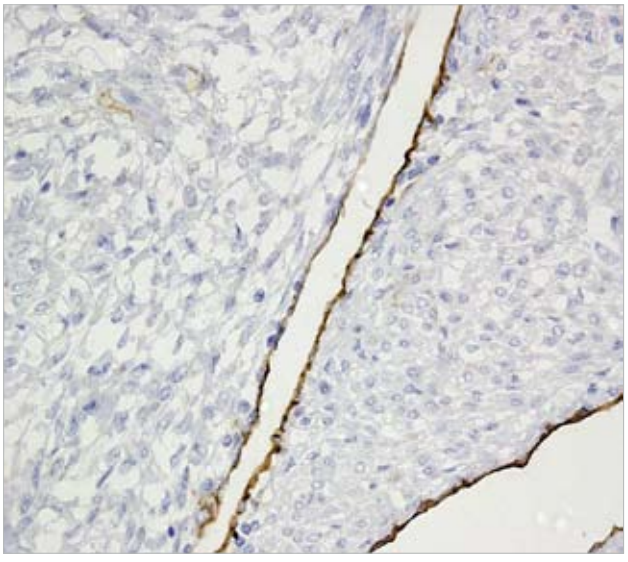

Fig. 2 : Tumor inside venous channel limited by endothelium, demonstrated by CD34 (DAB chromogen, x400).

Whether IVL is a primary tumor of the vessel walls or an intravascular extension of a primary uterine leiomyoma is still not clear. The first theory seems to be correct in those cases in which most or all of the tumor is within the vessels. The second theory explains cases with intravascular and extravascular lesions [1].

The diagnostic gross feature is the presence of one or more nodules or worm like extension of the tumor within myometrial or parametrial vessels. The present case was limited to myometrial vessels. Microscopically, the cardinal feature is the presence of endothelium covered protrusions of smooth muscle tumor in either venous or lymphatic vessels. Most cases are cytologically bland with mild or absent nuclear atypia and low mitotic index. Both features are typically demonstrated in our case. Morphologic variations on the usual smooth muscle theme (e.g., clear cells, fat, epithelioid cells) have been noted in intravascular leiomyomatosis [8].

Differential diagnosis include a) typical leiomyoma with artifactual retraction from surrounding myometrium, b) leiomyoma with perinodular hydropic change, c) low grade endometrial stromal sarcoma, and d) leiomyosarcoma with vascular invasion. Immunostain for endothelial marker is useful to confirm artifactual retraction as well as perinodular hydropic change. Low grade endometrial stromal sarcoma form single or multiple intramural masses that involve the endometrium in most cases. It may permeate the myometrium in irregular tongues. Myometrial as well as extrauterine veins and lymphatics frequently contain extensions of the tumor. However distinct features of smooth muscle origin on hematoxylin and eosin stain (i.e. fascicular growth pattern, thick walled blood vessels, and fusiform nuclei), and immunohistochemistry (smooth muscle actin and desmin positivity, and CD10 negativity) help to reach a correct diagnosis.

A mitotic index above 5/10 HPF is distinctly unusual in intravascular leiomyomatosis and tumor cell necrosis is not allowed. Because of

the paucity of cases with a mitotic index of 5 or more, that have been the subject of follow up study, the term uncertain malignant potential is appropriate for cases with bland histologic features but with a mitotic index of 5 to 15/10 HPF. Moderate to marked atypia and a mitotic index of more than 5 in an intravascular smooth muscle tumor is indicative of leiomyosarcoma [9] .

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 [10,11]. Furthermore, the neoplastic smooth muscle cells of IVL express estrogen & progesterone receptors and tumor growth appears to respond to hormonal manipulation [12,13]. Infact, some authors recommend bilateral oopherectomy since recurrence of disease is reported in patient's in whom ovaries were preserved [14]. In case of incomplete resection, systemic therapy with tamoxifen, or medroxyprogesterone should be applied [15]. For follow-up, patients should be submitted to ultrasound and magnetic nuclear resonance examination every 6 months [7,16] .

To conclude, IVL is 1) A rare and distinct benign smooth muscle tumor of the uterus which requires careful pathological evaluation since preoperative diagnosis is rarely made and differential diagnosis on histopathology from malignancy is important to avoid overtreatment. 2) Complete surgical excision is the treatment of choice, and antihormone therapy is used for incomplete/inoperable cases. 3) Follow up is mandatory.

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