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Original contribution

Intravenous leiomyomatosis of the uterus
A clinicopathologic study of 18 cases, with emphasis on early diagnosis and appropriate treatment strategies

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Summary Intravenous leiomyomatosis is a rare variant of leiomyoma that could result in death. Early and accurate diagnosis and appropriate treatment strategies play a dominant role in good prognosis. Eighteen cases of Intravenous leiomyomatosis , along with clinicopathologic data, were retrieved from our database. Most of the patients who ranged in age from 33 to 54 years (median, 44 years) presented with a pelvic mass or abnormal uterine bleeding. The diagnosis was confirmed by a immunohistochemical staining for smooth muscle actin, CD34, and Ki67. Surgical exploration confirmed the presence of a uterine mass (mean size, 5.08 cm). Wormlike plugs were identified within the broad ligament in 5 cases. The tumor penetrated to the inferior vena cava in 1 case. Histologic variants were noted in 33.33% (6/18) of our cases, which were classified as cellular intravenous leiomyomatosis (3 cases) and intravenous leiomyomatosis with papillary-like contour (1 case) and with fat metaplasia (2 cases). The 18 cases are made up 0.097% of all genital smooth muscle tumor cases of the hospital. The ratios of intravenous leiomyomatosis with uterine leiomyoma, with adenomyosis, with uterine leiomyoma and adenomyosis were 38.89% (7/18), 11.11% (2/18), and 27.78% (5/18), respectively. Follow-up information was available for 16 patients, with a follow-up duration of 26 to 104 months (mean, 55 months). Three cases (16.67%) recurred in patients younger than 40 years (33, 34, and 37 years). We propose that young patients undertake hysterectomy and unilateral salpingo-oophorectomy if they do not have any birthing requests. The cases of intravenous leiomyomatosis were underestimated because early diagnosis was easily missed. It is important to adequately sample all uterine leiomyomas and carefully examine the soft tissue on either side of the lower uterine segment below the peritoneal reflection to identify early-stage intravenous leiomyomatosis.

1. Introduction

Intravenous leiomyomatosis (IVL) is a rare neoplasm characterized by a histologically benign-looking smooth muscle cell tumor mass growing within the uterine and

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extrauterine venous system. Although histologically benign, IVL may penetrate the inferior vena cava (IVC), reach the right heart chambers, or extend to the right pulmonary artery; hence, threats to life could recur within a relatively short time span [1,2]. We reviewed all the literature included by PubMed from 1959 to August 2010 and found that 298 cases of IVL were reported in the English literature. Our report represents the second largest series; the first largest series of 22 cases of IVL was reported in 1994. Case reports comprised the bulk of the literature. In 45% of the 298 reported cases, the tumor has either penetrated to the inferior vena or reached the right atrium. Early diagnosis of IVL has received little attention in the reported literature. Early and accurate diagnosis and appropriate treatment strategies are important to patient outcome. The current study is performed to clarify these important questions pertaining to this disease.

2. Materials and methods

2.1. Patients

Eighteen cases of IVL were retrieved from the files of the Department of Pathology at the Tianjin Central Hospital for Gynecology and Obstetrics between January 2002 and July 2008. All clinicopathologic data were collected from the patients' records. All specimens were formalin-fixed and processed for paraffin embedding, and sectioned and stained with hematoxylin and eosin. Eighteen tumors were reassessed by veteran pathologists. One case (case3), misdiagnosed as cotyledonoid dissecting leiomyoma of the uterus, was reclassified as IVL because of recurrence on follow-up. The Ki67 labeling index was used to evaluate cell proliferation in the cases including areas of high cellularity and mitotic activity within the tumors. Only those intravenous smooth muscle tumors with a mitotic figure count of 1 or fewer per 10 high-powered fields (HPFs) and without cytologic atypia were considered to represent IVL. Finally, 18 cases were reconfirmed by immunohistochemical staining for smooth muscle actin (SMA) and CD34. An attempt was made to follow up each patient.

2.2. Immunohistochemical studies

The primary antibodies were mouse monoclonal antibody raised to human CD34 (dilution 1/100; clone no. QBEnd/10), SMA (1/100; clone no. 1A4), and Ki67 (1/100; clone no. 7B11). These primary antibodies were purchased from Zhongshan Golden Bridge Biotechnology Co Ltd, Beijing, China. Heat-induced epitope retrieval in citrate buffer (0.01 mol/L; pH 6.0) was applied to all slides before immunohistochemical staining. Staining with primary antibodies against SMA, CD34, and Ki67 was performed on formalin-fixed, paraffin-embedded tissues using the SP-9000 kit (Zhongshan Golden Bridge Biotechnology Co Ltd). For negative controls, the primary antibody was replaced with a phosphate-buffered saline solution (0.01 mol/L; pH7.2-7.4). The immunoreactivity of Ki67 was evaluated as a Ki67 labeling index [3], a percentage of positively stained cells per

Table 1 Clinical features of 18 cases of IVL

Case	Age (y)	Presentation	Treatment	Follow-up (mo)
1	54	Menorrhagia	TAH and BSO	104 NED
2 [a]	33	Pelvic mass	Myomectomy	22, myomectomy again, then lost to follow-up
3 [a]	37	Pelvic mass	TAH	76, BSO (39 after TAH)
4	41	Pelvic mass; amenorrhea	TAH	77 NED
5	47	Pelvic mass	TAH and LSO	73 NED
6	47	Dysmenorrhea	TAH and BSO	70 NED
7	42	Menorrhagia; pelvic mass	Subtotal hysterectomy	Lost to follow-up
8	38	Pelvic mass	TAH	58 NED
9	52	Pelvic mass	TAH and BSO	Lost to follow-up
10	48	Menorrhagia; pelvic mass	TAH	56 NED
11 [a]	34	Pelvic mass	TAH	51, BSO (15 after TAH)
12	41	Dysmenorrhea	TAH	34 NED
13	47	Pelvic mass	TAH	34 NED
14	40	Pelvic mass	TAH	33 NED
15	42	Pelvic mass	TAH and BSO	29 NED
16	50	Pelvic mass	TAH and BSO	27 NED
17	50	Menorrhagia	TAH	27 NED
18	46	Pelvic mass	TAH	26 NED

Abbreviations: TAH, total abdominal hysterectomy; BSO, bilateral salpingo-oophorectomy; LSO, left salpingo-oophorectomy; NED, no evidence of disease.
[a] A recurrent case.