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Intracardiac extension of intravenous leiomyomatosis in a woman with previous hysterectomy and bilateral salpingo-oophorectomy: A case report and review of the literature

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Abstract Intravenous leiomyomatosis (IVL) is a rare tumor, characterized by benign smooth muscle growth inside veins. The tumor arises from the uterine venous wall or uterine leiomyomas and is usually confined to the pelvic cavity. However, on rare instances, it may extend into the cardiac cavity (*Pathol Annu* 1988;23 Pt 2:153–158), and the pulmonary system (*Arch Gynecol Obstet* 2001;264:209–210). Treatment consists of surgical removal of the tumor, cessation of ovarian function and avoidance of estrogen replacement therapy (*Gynecol Obstet Invest* 2004;58:168–170). We present a case of intravenous leiomyomatosis with extension from IVC to RA, RV and PA, with an unusually rapid course of progression in the absence of estrogen (TAH-BSO, without concomitant hormonal therapy).

1. Introduction

Intravenous leiomyomatosis (IVL) is a rare tumor, characterized by benign smooth muscle growth either from within venous walls or uterine leiomyomas. Though typically confined to the pelvic cavity, they may spread along vessels and extend right up to the cardiac cavities, causing significant cardiovascular symptoms [1]. First reported in 1907 [2], IVL with cardiac extension is seen in up to 10% of cases, and is often misdiagnosed as a primary cardiac tumor or a venous thrombus in transit [3]. Right atrial and ventricular involvement has been reported in 30% and 70% of cases respectively [4]. Extension or

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embolization into the pulmonary artery (PA) system is very rare, and has been reported in less than 5% of cases [5]. Thus far, there have been 11 cases of PA extension reported in the English language literature [6]. Standard treatment consists of complete surgical removal, with cessation of ovarian function and avoidance of post-operative estrogen replacement therapy, as estrogen and progesterone receptors have been detected in the nuclei of IVL cells [7].

We present a case of IVL with cardiac involvement with extension to the PA, with an unusually rapid course of development in the absence of exogenous estrogen.

2. Case presentation

A 58-year-old woman was referred to our institution after routine computed tomography (CT) of the chest, abdomen, and pelvis for follow-up. Her history was significant for hypertension, dyslipidemia, depression and hypothyroidism. Her medications included ramipril 2.5 mg PO OD, rosuvastatin 20 mg PO OD, levothyroxine 0.088 mg PO OD, venlafaxine 100 mg PO OD and lamotrigene 200 mg PO OD. She was a life-long non-smoker, and did not consume alcohol. Her surgical history included a total abdominal hysterectomy with bilateral salpingo-oophorectomy (TAH-BSO) five years prior, for endometrial bleeding. Pathology confirmed intravenous leiomyomatosis. She did not receive any concomitant hormonal therapy, and was followed with routine imaging, which was unremarkable after three years post-surgery. Seventeen months after her last follow-up, she underwent repeat routine CT of her abdomen and studies, which showed new filling defects in the main PA, right main PA, with extension into the segmental arteries of the right lower lobe. Proximally, the filling defect extended into her right atrium (RA) and ventricle (RV), with extension into the inferior vena cava (IVC) up to the level of her gonadal veins. She was asymptomatic, and was referred for surgical management.

On examination, her blood pressure was 127/80 mmHg and heart rate, 96 bpm. Her physical exam (abdomen, lower limb, neurological exam) was unremarkable and laboratory data were all within normal limits. Chest x-ray was unremarkable, and ECG showed sinus rhythm. Transesophageal echocardiogram (TEE) revealed a highly mobile variegated mass extending from the IVC to the RA, RV and PA (Fig. 1). CT confirmed the findings, and demonstrated a right adnexal mass with extension to the gonadal vein (Fig. 2). Coronary angiography was normal and showed the conus supplying two independent mobile masses with tumor blush visible. The extensive mass was removed via thoracotomy and laparotomy with no complications. Post-operative TEE was normal, and she was discharged home in stable condition.

3. Pathology

The explanted gray-white and blue mass had a variegated shape measuring 6.5 × 5.5 cm at the cardiac end, with a narrow 55 cm tube extending from it. The mass is nodular with no discernible capsule between the nodules. The "tube" measured 3.0 cm in diameter at one end, and narrows to 0.6 cm at its most distal end (Fig. 3).

Histological examination revealed a tumor composed of cords and bundles and masses of spindle cells with features of neoplastic smooth muscle cells with no direct involvement of the endocardial surface of the blood vessels or the cardiac chambers (Figs. 4–5), except at the right atrium. Immunohistochemistry was positive for smooth muscle cells (SMActin), consistent with intravenous leiomyomatosis (Fig. 4). Staining for estrogen receptors showed strong signaling, with 80–90% of cells being positive, while progesterone receptor staining showed strong positivity (70–80%). The core of the tumor as well as the residual tumor was positive for both receptors (Fig. 6).

4. Discussion

We present a 58-year-old Caucasian woman who had uterine leiomyomatosis and was found, on serial imaging during follow-up, to have IVL growth extending up to her PA. She had undergone a TAH-BSO 5 years prior, for uterine IVL which was not followed by hormone replacement therapy (HRT).

IVL is a rare benign tumor characterized by the growth of smooth muscle cells within the venous system. It is most commonly seen in premenopausal women with an average age of 44 years [1]. In the majority of cases, only the pelvic veins are involved; however, in rare instances, tumor growth may extend into the IVC, with cardiac extension in up to 10% of cases [3]. Since its first description, there have been multiple cases reported in the English language literature. Wu *et al.* reviewed 77 cases of IVL with intracardiac extension from 1900 to 2008 [8], and since then, there has been an additional 14 cases. These findings are summarized in Table 1.

Although the etiology of IVL is unknown, there are two widely accepted theories on its development. Knauer [9] hypothesized that the tumor originates from smooth muscle cells within the vessel wall, while Sitzenfry [10] proposed that its invasion into the veins from a uterine source leads to IVL development. Though the pathogenesis has not been thoroughly studied, Fukuyama *et al.* examined the mechanism of IVL development in one case, and found extension of CD34 antibody staining from the myoma which advanced into the lining of the vein [11]. This finding has not been replicated in other studies and its