Case Report

Cardiovascular Ultrasonographic Features and Clinical Findings for Intravenous Leiomyomatosis: A Case Report

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Abstract

Introduction: To summarize the vascular ultrasonographic features of intravenous leiomyomatosis (IVL) and assess the role of this method for the accurate diagnosis of patients with IVL. The current study was carried out in Shandong provincial hospital affiliated to Shandong university and Shandong medical imaging research institute, Shandong university of Jinan, Shandong province, P.R. China in 2017.

Case Presentation: The 9 samples of IVL were collected from patients undergone surgery from July 2007 to December 2016 in the department of gynecology of the hospital. The clinical data, vascular ultrasonographic findings, and histologic results were retrospectively reviewed. Six patients underwent computed tomography (CT) and 3 patients were examined by magnetic resonance imaging (MRI). Clinical symptoms included lower extremity edema, chest congestion, and syncope. Any pelvic masses found were identified. On ultrasonography, the internal iliac vein, common iliac vein, and the inferior vena cava (IVC) were all involved with dilated veins and isoechoic masses noted in all 9 patients. The right ovarian vein was involved in 2 patients, and in 3 patients, masses had emerged in the IVC and spread into the right atrium, at times intruding into the tricuspid orifice during diastole. All 9 patients underwent a 1-stage thoracoabdominal surgical procedure. There was no documented recurrence of the masses in 7 patients and in the remaining 2 patients; solid pelvic masses were detected 3 or 6 months after the surgery. No intravascular masses were detected.

Conclusions: Ultrasonography is performed to evaluate the features and path of extension of IVL. Patients diagnosed with uterine leiomyoma or hysterectomy were at greater risk of developing IVL. Vascular ultrasound could be used as an additional diagnostic tool for IVL screening and diagnosis in patients at an early age.

Keywords: Leiomyomatosis, Uterus Neoplasms, Intravascular Ultrasonography, Computed Tomography, Magnetic Resonance Imaging

1. Introduction

Intravenous leiomyomatosis (IVL) is a rare smooth muscle neoplasm derived from either the walls of the uterine vessels or the uterine leiomyoma, in some instances infiltrating and extending into the venous system (1). Although IVL is histologically benign, the tumor has the potential to be clinically aggressive due to its massive intraluminal growth. In most cases, IVL is limited to the pelvic veins, and in rare instances, may extend through the inferior vena cava (IVC) to the right heart chambers (causing intracardiac leiomyomatosis (ICL) (2)). Further intracardiac spread into the main pulmonary artery is potentially life-threatening. In addition, several uncommon cases of IVL with pulmonary and lymph node involvement are described (3-5). The pathological mechanism of IVL development, however, remains unclear.

Preoperative imaging of IVL is crucial. Precise information on the extent of the tumor and its relationship with adjacent tissue helps to guide the surgery and assess the morbidity of the patient. When the various currently available options are considered, a non-invasive imaging technique to diagnose IVL is helpful. These methods include ultrasonography, venogram, magnetic resonance imaging (MRI), and computed tomography (CT), and each possesses characteristics that question its appropriateness for the routine diagnosis of IVL. Conventional venogram is invasive and involves catheter cannulation and radiation exposure; direct contrast CT venography also involves irradiation.
tion and the potential problem of a contrast reaction and resulting complications (3).

Three-dimensional MRI is increasingly used to diagnose IVL, and provides better soft tissue-contrast resolution and faster imaging sequences, but is saddled with several problems, as Gui et al., (4) documented, including the inability to use the modality in patients with internal metallic hardware (e.g., cardiac pacemaker) and more artifacts. CT, despite its advantages of presenting the full scale of an invasive tumor, unfortunately exposes the patient to radiation. Cardiac ultrasonography, which is useful to evaluate intravascular and intracardiac tumors, requires specialized training, and therefore, needs to be conducted by an experienced technician. In summary, vascular ultrasonography may represent the safest and most practical method to diagnose IVL.

Vascular ultrasonography is not used as commonly as echocardiography, CT, or MRI to evaluate IVL (5). In general, ultrasonography may be problematic: it is operator-dependent, bowel gas obstruction is a frequent hindrance, and assessment of the deep structures of the abdomen and pelvis is not always ideal (3). There is little information in the literature regarding the employment of vascular ultrasonography, specifically to evaluate IVL, although the assessment of the vessels in this disease is performed using other imaging modalities such as CT angiography (4). For some patients, ultrasonography of the vessels might be the preferable option, compared with other imaging modalities. However, the fact that vascular ultrasonography does not involve the risk of radiation exposure (as CT imaging does) or the risk of a reaction to contrast agent or their complications, makes vascular ultrasonography a potentially valuable adjunct in the evaluation of the extent of IVL lesions through imaging (6).

No imaging modality can differentiate between benign and malignant tumor prior to surgery because IVL often mimics the growth patterns of more aggressive neoplasms (7), extending into the vena cava and heart. Therefore, a histological diagnosis is essential to make this distinction. In addition, early diagnosis and comprehensive assessment prior to surgery are crucial for clinical management given the postsurgical complications documented with IVL. These complications include unplanned reoperation, disseminated intravascular coagulopathy, large blood loss leading to massive transfusion, and even patient mortality (3).

The current study aimed at summarizing the vascular ultrasonographic features of IVL and assessing the role of this method for the accurate diagnosis in patients with IVL. The results may provide guidance on the early diagnosis and therapy of IVL and insight into the pathological mechanisms underlying this complicated disease.

2. Case Presentation

2.1. Sample Collections

The current study was conducted in Shandong provincial hospital affiliated to Shandong university and Shandong medical imaging research institute, Shandong university of Jinan, Shandong province, P.R. China in 2017. A comprehensive analysis was conducted on 9 cases of IVL undergone surgery from July 2007 to December 2016. Data were obtained from medical and pathological records, and included age, symptoms at presentation, medical history, ultrasonographic findings, and histological results. All procedures performed in the studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and the 1964 Helsinki declaration and its later revisions or comparable ethical standards.

2.2. Measurements and Interventions

The GE Vivid 7 Dimension sonography system (GE Healthcare, USA) with a linear array transducer (7.5-12 MHz) and 3.5 MHz for pelvic vessels was used in the current study. The venous system of the lower extremities of all the patients was examined, with a focus on the internal iliac vein, iliac vein, and inferior vena cava. Echocardiography was conducted when necessary. Six patients underwent CT of the chest and abdomen, and 3 patients were examined using MRI. The reasons these additional imaging modalities were not used on all the patients was not clear from the medical records.

A linear array probe was used on the lower extremity body surface from the level of the inguinal ligament to the ankle. Two-dimensional ultrasonography of the common femoral vein, superficial femoral vein, deep femoral vein, and popliteal vein was performed to observe the intravascular presence of the solid mass echo, noting the compressibility of the vein with probe pressure. Color doppler flow imaging (CDFI) was used to confirm the existence of a flow signal. A convex array probe was used to find any pelvic masses and evaluate their shape, size, border, internal echo, and blood flow dynamics. In addition, the surrounding adjacent structures, particularly the peripheral veins, were carefully examined. Among the 9 patients, 6 were evaluated using CT angiography, while the others were examined using contrast-enhanced MRI; the scan range extended from the level of the ascending aorta to the inguinal ligament.

3. Results

The age of the 9 patients ranged from 40 to 57 years (mean age: 46.8 years). All the patients had a history of
uterine leiomyoma, and 8 had previously undergone a hysterectomy; the remaining patient was not known to be pregnant at the time of diagnosis. The recorded clinical symptoms included lower extremity edema (all 9 patients), chest congestion (3 patients), and syncope (1 patient). Pelvic masses were found in all patients, and 1 patient had uterine leiomyomas. The vascular ultrasonographic findings of each patient are listed in Table 1.

The internal iliac vein, common iliac vein, and inferior vena cava were observed in all patients. Vascular ultrasound showed that the normal echo of the venous lumen was now only slightly echoed or replaced with solid echo, extending mostly in a long strip along the length of the vascular cavity. The internal echo was either uniform or uneven, often accompanied by expansion of the venous lumen. The dimensions of the lesions ranged widely. The origin of the lesion, either the iliac vein or the ovarian vein, was the primary location and key to diagnosis. CDFI revealed that not all patients with inferior vena cava leiomyoma had arterialized flow within the lumen. The appearance of arterialized flow was related to the level of activity of smooth muscle cell proliferation. The greater the activity, the more obvious this flow became.

Vascular ultrasonography showed dilated veins and isoechoic masses initially extending from the ipsilateral internal iliac vein to the common iliac vein, and subsequently to the IVC (Figure 1). The right ovarian vein (ROV) was involved in 2 patients, and there were several masses in the ROV that extended into the IVC. In 3 of the 9 patients, masses were noted emerging in the IVC before spreading to the right atrium and the tricuspid orifice during diastole. CDFI was employed to detect the arterial blood flow signal in the masses in the lumen of the iliac vein and IVC in 5 patients. The blood flow velocity ranged from 21 to 45 cm/second. No blood flow signal was noted in the remaining 4 patients.

The 9 patients underwent a 1-stage thoracoabdominal surgical procedure with pelvic mass resection and removal of the IVL pedicle. In addition, the patient with multiple uterine leiomyomas also underwent a total hysterectomy and bilateral salpingo-oophorectomy. The pathology report confirmed the diagnosis of IVL.

There was no documented recurrence of the masses in 7 of the 9 patients. In the other 2 patients, solid pelvic masses were detected 3 or 6 months after the surgery, but no intravascular masses were observed. In 2 cases, a 2-stage procedure was conducted to remove the tumors. The post-operative histology confirmed the diagnosis of IVL recurrence.

4. Discussion

Intravenous leiomyomatosis is a rare histologically benign intravascular tumor of uterine origin, and the most commonly affected patients are premenopausal and multiparous females aged 20 to 70 years, with a mean age of 45 (8). The clinical course of the disease is variable and is determined by the position and scale of the neoplasm. Symptoms include lower abdominal pain, irregular menses, lower extremity edema, dyspnea, chest pain and syncope, pelvic bulk, or even sudden death. However, patients may also be asymptomatic (1, 9, 10). If abnormal uterine bleeding occurs, anemia may be a prominent feature in the laboratory results. Electrocardiographic abnormalities may be secondary to systolic dysfunction, cardiac valve involvement, or tumor emboli, among other reasons.

IVL is estrogen-dependent. The estrogen receptor concentration of the patients is ten times higher than normal, which indicates the close association of estrogen with IVL growth.

Two theories regarding the origin of IVL are proposed. The first theory suggests that the neoplasm originates from the vascular wall, and the second proposes that vascular invasion is caused by the uterine leiomyoma projecting into the adjacent venous channel.

IVL can follow 2 distinct pathways into the systemic venous circulation (11): extension via the uterine vein or the ovarian vein. The uterine vein is the principal pathway and can extend through this vessel into the internal iliac veins, the common iliac veins, and finally into the IVC. In contrast, growth in the right ovarian vein can extend directly into the IVC; whereas growth in the left ovarian vein can extend into the left renal vein before reaching the IVC. In the 9 enrolled patients with IVL, the traversed pathways were consistent with the ones reported in previous reports. In 7 of the 9 patients, masses extended from the iliac vein into the IVC through the uterine vein, reaching the right side of the heart in three patients. In the remaining 2 patients, masses reached the heart through the ovarian vein. Therefore, the iliac vein and IVC, and the branches of the IVC such as the ovarian vein and renal vein, were necessarily included in the vascular ultrasonographic examination.

The 9 patients were histopathologically proven after surgery to have IVL. The ultrasonographic evidence should alert clinicians to the possibility of IVL in such patients. The typically long and serpentine masses grow from the iliac or ovarian veins and into the IVC, and can even breach the right side of the heart, particularly in patients previously undergone a hysterectomy or with uterine leiomyoma. Any pelvic masses discovered simultaneously were removed, and assessed for the presence of the arterial blood flow signal. In addition to ultrasonography, CT and
Table 1. Vascular Involvement Characteristics of Patients with IVL

| Patients | Lower Limb Veins | External Iliac Vein | Internal Iliac Vein | Common Iliac Vein | Other Veins | Inferior Vena Cava | Right Atrium |
|----------|------------------|---------------------|---------------------|-------------------|-------------|-------------------|-------------|
| 1        | -                | -                   | +                   | +                 | -           | +                 | -           |
| 2        | -                | -                   | +                   | +                 | -           | +                 | -           |
| 3        | -                | -                   | +                   | +                 | -           | +                 | -           |
| 4        | -                | -                   | +                   | +                 | -           | +                 | -           |
| 5        | -                | -                   | +                   | +                 | + (ROV)    | +                 | -           |
| 6        | -                | -                   | +                   | +                 | + (ROV)    | +                 | -           |
| 7        | -                | -                   | +                   | +                 | -           | +                 | -           |
| 8        | -                | -                   | +                   | +                 | -           | +                 | -           |
| 9        | -                | -                   | +                   | +                 | -           | +                 | -           |

Abbreviations: -, Not involved; +, Involved; ROV, right ovarian vein.

MRI were used for their multiplanar capabilities and large fields of view.

Few studies used vascular ultrasonography to assess IVL in the vasculature. Several used echocardiography to evaluate the extension of IVL into the heart chambers (10, 12, 13), but most of them did not specifically focus on the pathway through the vasculature of tumor spread from the uterine vessels or wall.

The differential diagnosis of IVL primarily includes leiomyosarcoma, atrial myxoma, right-sided heart thrombus or embolus, and metastases resulting from IVC invasion, e.g., renal cell carcinoma, hepatocellular carcinoma, adrenal cortical carcinoma, and lymphoma (1). These diseases do not have to be based on a history of uterine leiomyoma. Leiomyosarcoma, which can be also found in males (14), arises from the wall of the IVC (12). The vascular ultrasonographic findings show irregular masses, rarely blocking the lumen completely, with limited range of lesion (primarily in one-third of the IVC cases); generally, the iliac and common iliac veins are not affected. At the early stages of the disease, it is difficult to differentiate between such various tumors.

Atrial myxoma is the most common primary heart tumor. It is usually located only in the atria and does not affect the IVC (13). In terms of central vein thrombosis, iliofemoral vein thrombosis is common, in some patients with extension into the distal section of the IVC. Moreover, an intravenous thrombus displays no blood flow signal. Metastasis with IVC invasion usually develops when there is a history of a primary tumor, and the extent of the lesion is much smaller than that of IVL. A further diagnosis that should be considered can be benign metastasizing leiomyoma (BML) (9). BML is characterized by uterine leiomyoma in young adulthood, with pulmonary metastasis occurring during the pre-menopausal period (10). Pulmonary nodules or masses provide the most significant evidence of BML, and the final diagnosis depends on histopathology.

Successful therapy for IVL depends on total surgical excision of the tumor. It is demonstrated that removal provides the optimal mid- and long-term prognosis (15). Also, the surgical procedure should include bilateral salpingo-oophorectomy in addition to the removal of the intravenous tumor extension. Furthermore, anti-estrogenic drugs are used pre- and post-operatively to reduce the tumor burden and control residual tumors (16). Lastly, ultrasonography is performed 1 month, 3 months, or 6 months after IVL surgery to evaluate the patients’ prognosis.

However, the current study had several limitations. First, it was a retrospective review, and some patients not being evaluated in sufficient detail. This may have resulted in the collection of insufficient information regarding the features of IVL. Second, the variable vascular ultrasonographic characteristics of this rare tumor might be underestimated, given the breadth of findings in the current study. Stronger and more detailed criteria to classify such lesions may be needed in future studies. Lastly, the sample size of 9 patients was small. The disease was rare that affected the number of cases found, even retrospectively. Therefore, it may be difficult to generalize the findings based on such a small sample of patients.

In a word, the current study described the pathological characteristics of IVL by performing a comprehensive analysis on 9 cases of IVL. The clinical and vascular ultrasonographic characteristics, including the echocardiographic features of the tumors, were described in details. The results showed the vascular and dynamic flow characteristics of the tumor, features that could play a vital role in the diagnosis and surgical plan for this disease. Patients with uterine leiomyoma or the ones undergone a hysterectomy were found to be at increased risk of developing IVL. Vascu-
Figure 1. The vascular ultrasonographic findings of patient 1: A, the vascular ultrasonographic and CT angiographic findings of patient 5; B, the vascular ultrasonographic and CT angiographic findings of patient 7; C, the CDFI findings of patient 3; A, the solid hypoechoic masses extending from R1IV to R1IV; B, a large tubular mass in R0V that extends into IVC; C, the IVC dilated with elongated cord-like masses within the lumen of IVC, extending into right atrium, and D, shows that plenty of blood flow signals are detected in the masses in IVC, and the spectrum of arterial blood flow is measured by pulse doppler, with systolic peak velocity 38 cm/second.

Lar ultrasound could be used as an additional diagnostic tool for IVL screening and diagnosis in patients at an early age.

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Footnote

Competing Interests: The authors declare no conflict of interest.

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