Clinical Case Report

Medicine®

OPEN

Intravascular epithelioid hemangioendothelioma of the femoral vein diagnosed by contrast-enhanced ultrasonography

A care–compliant case report

Luying Gao, MD, Yahong Wang, MD, Yuxin Jiang, MD, Xingjian Lai, MD, Ming Wang, MD, Jianchu Li, MD*

Abstract

Rationale: Intravascular epithelioid hemangioendothelioma (EHE) is a rare endothelial tumor with an intermediate grade of malignancy. We present a case of one woman affected by EHE of the femoral vein. Contrast-enhanced ultrasonography played a role in diagnosing EHE and helped differentiate it from thrombosis. To our knowledge, this is the first reported contrast-enhanced ultrasonography of intravascular EHE in the imaging literature.

Patient concerns: A 46-year-old woman presented to our hospital due to pain and swelling in her right lower limb since 5 years prior to her presentation.

Diagnoses: The patient was misdiagnosed as having thrombosis by ultrasound. Contrast-enhanced ultrasonography showed solid lesions with visible blood supply, suggesting angiogenic tumors.

Interventions: The patient was treated by complete surgical removal of the mass and postoperative radiotherapy. Pathological examination confirmed the diagnosis of EHE.

Outcomes: During follow-up, there were no signs of local or distant relapse.

Lessons: Intravenous EHE may be misdiagnosed as thrombosis by ultrasound and contrast-enhanced ultrasonography can help make the differential diagnosis.

Abbreviations: CDFI = color Doppler flow imaging, EHE = epithelioid hemangioendothelioma, FDG = 18F fluoride deoxyglucose, IFN = interferon, MRI = magnetic resonance imaging.

Keywords: contrast-enhanced ultrasonography, femoral vein, intravascular epithelioid hemangioendothelioma

1. Introduction

Epithelioid hemangioendothelioma (EHE) is a rare angiogenic tumor originating from vascular endothelial or pre-endothelial cells. It is an aggressive tumor with pathological and biological characteristics that lies between benign hemangioma and malignant hemangiosarcoma. It can occur in soft tissue, bones, and internal organs, and about half of EHE are primary vascular.[1] Images are significant for its preoperative diagnosis, which is used as guidance for therapeutic scheme and further treatment. However, the differential diagnosis of intravenous EHE is usually difficult and often misdiagnosed as thrombosis by images. We reported a case of EHE in the femoral vein diagnosed by contrast-enhanced ultrasonography.

2. Case report

A 46-year-old woman presented to our hospital due to pain and swelling in her right lower limb since 5 years prior to her presentation. Her medical and family history revealed no other major medical problems. Five years ago, the patient appeared with the right lower extremity swelling after long-standing, and the swelling gradually aggravated accompanied with thigh soreness pain. In February 2015, a round mass was reached in inguinal region, 1 × 2 cm, tough, unmovable, tenderness, no ulceration, and no sense of volatility. Ultrasound showed a hypoechoic mass (2.0 × 1.2 cm) in the right common femoral vein with no obvious blood flow signal, suggesting right common femoral thrombosis (Figs. 1 and 2). Patient was not treated, and the symptoms gradually aggravated. In June 2016, with 3.0 to 9.0 MHz probe, ultrasound showed a hypoechoic mass (2.2 × 1.1 cm) in the right common femoral vein with no obvious blood flow signal, suggesting angiogenic tumors or thrombosis. With transvaginal 4.0 to 8.0 MHz probe, ultrasound showed a hypoechoic mass (2.2 × 1.1 cm) in the right common femoral vein with arterial waveform pattern blood signal, suggesting angiogenic tumors. Contrast-enhanced ultrasonography (intravenous injection of Sonovue, 1.0 mL) showed that the microbubble quickly entered the mass, and the contrast agent filled the

Editor: N/A.

LG and YW contributed equally to this work and should be considered co-first authors.

This study was supported by a grant from Peking Natural Science Foundation (No. 7162159).

The authors have no funding and conflicts of interest to disclose.

Department of Ultrasound, Chinese Academy of Medical Sciences, Peking Union Medical College Hospital, Beijing, China.

* Correspondence: Jianchu Li, Department of Ultrasound, Peking Union Medical College Hospital, 9 Dongdansantiao, Beijing, China (e-mail: jianchu.li@163.com).

Medicine (2017) 96:49(e9107)

Received: 17 August 2017 / Received in final form: 3 November 2017 / Accepted: 8 November 2017

http://dx.doi.org/10.1097/MD.0000000000009107

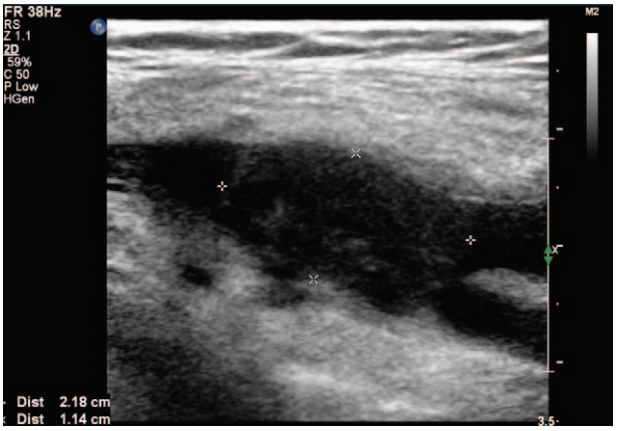

Figure 1. Sonography showed a hypoechoic mass (2.0 × 1.2 cm) in the right common femoral vein.

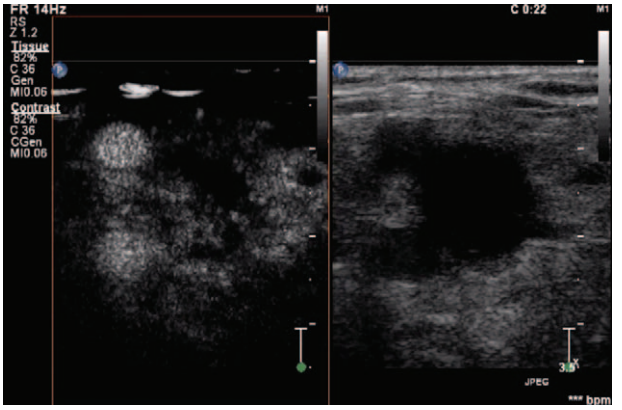

Figure 3. Contrast-enhanced ultrasonography (intravenous injection of Sonovue, 1.0 mL) showing that the microbubble quickly entered the mass in the arterial phase.

mass in arterial phase, which is earlier than the venous lumen; with uneven enhancement and local strengthening, the contrast slowly exited, suggesting angiogenic tumors (Fig. 3). Resection of the tumor was then performed, and the mass was attached to the posterior wall of the common vein. Immunohistochemical analysis showed that the cells stained positively for CD31, CD34, vimentin, and smooth muscle actin, and negatively for AE1/AE3, CAM5.2, and Desmin. The Ki67 showed that the proliferation rate of the tumor cells was >5%. Pathological examination confirmed a diagnosis of EHE. Postoperative radiotherapy was delivered to the patient, high-risk area around the original tumor area, dose 50.4 Gy, 28 times; tumor bed area, dose 60.2 Gy, 28 times. In February 2017, ultrasound indicated that no obvious abnormalities were shown in the right common femoral vein, and the patient was still closely followed up. Informed consent was obtained in accordance with the institutional guidelines.

3. Discussion

EHE originated from the endothelium.[2] Weiss and Enzinger[1] first described 14 patients with EHE, and EHE acted as an intermediate entity between benign hemangioma and high-grade angiosarcoma, with the potential to metastasis or recurrence. Mentzel et al[3] found that metastasis occurred in 20% to 30% of EHE patients, and the overall risk of death was up to 17%.

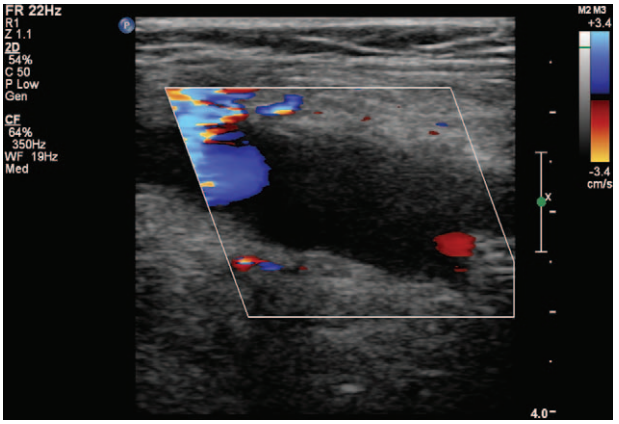

Figure 2. CDFI showing no obvious blood flow signal in the mass. CDFI = color Doppler flow imaging.

Primary vascular EHE accounted for about 50% of reported cases. They were from blood vessels,[4] usually small- to medium-sized veins, such as the femoral, iliac, or jugular veins, but also larger vascular structures, such as the aorta or the vena cava. Clinical presentation was variable, depending on the size and location of the tumor. Usually, clinical manifestations of EHE were painless mass in peripheral blood vessels, causing symptoms and signs of deep vein occlusion, ranging from the limb edema, weakness, and ischemia to venous thrombosis syndrome.[5]

It is often difficult to make the right diagnosis at an early stage. Ultrasonography is useful to define the morphology and vascularization of these masses and to evaluate blood flow, usually showing luminal defects and changed hemodynamics.[6] However, imaging features of EHE lack specificity and can be similar to thrombosis,[7] so a differential diagnosis of thrombosis needs to be made. Firstly, as to venous thrombosis, blood flow cannot be detected in the solid lesion. When the vein is partly revascularization, the color flow signal can be detected with venous blood flow signal.

Therefore, the distribution of blood vessels, especially the arterial blood flow signal, in the mass have a high value for differentiating tumors from thrombi. Many articles indicate the ultrasound diagnostic criteria for venous thrombosis, and the main features include: abnormalities of intravenous compressibility; abnormalities of Doppler color flow; a band of strong echo; the diameter changes abnormal with Valsalva action. Although prospective studies have demonstrated that ultrasound diagnosis of proximal venous thrombosis has a high sensitivity (>95%) and specificity (>95%), but various types of venous thrombosis diagnostic criteria, including primary diagnostic criteria and secondary diagnostic criteria, were not assessed for blood supply,[8–12] which may lead to misdiagnosis of conventional ultrasound. Only when there are no internal nourishing blood vessels in the mass, it can be more definitive diagnosis of venous thrombosis.[13] In this case, with a Philips IU 22 3.0 to 9.0 MHz probe, no clear blood flow was detected in the mass, so in the first time, the case was misdiagnosed as deep vein thrombosis by ultrasound. A transvaginal 4.0 to 8.0 MHz probe can show the blood flow within the mass, suggesting that other probes, such as L12–5 or intracavitary probe, may be more sensitive to blood flow. More importantly, ultrasound contrasts allowed visualization of blood vessels with diameters as small as about 40 μm,[14] which correspond to precapillary and postcapillary vascular systems, and studies have shown that deep vein systems can be

visualized in 40 to 350 seconds by ultrasound contrasts.[15] Contrast-enhanced ultrasonography showed intravenous solid lesions with visible arterial blood supply, suggesting angiogenic tumors. Secondly, the tumors are mostly localized lesions with vascular wall enlargement. With acute thrombus, the diameter of vein is usually increased, while with subacute and chronic venous, the diameter of vein thrombosis usually decreased. In addition, the muscle pump weakened and venous return weakened make thrombosis deposit near the venous valve. The structure of adjacent tissue is clear. The tumors are mostly localized lesions, sometimes with metastasis or vascular invasion, and these characteristics can help differentiate from thrombus. As mentioned above, the arterial blood supply in the embolus is the most reliable imaging feature for the diagnosis of angiogenic tumors, suggesting that ultrasound contrast is a more ideal noninvasive examination method than conventional ultrasound. In addition to morphological features, magnetic resonance imaging can give additional information on the involvement of surrounding soft tissues and cleavage planes.[16] Lately, studies showed that in EHE, uptake of 18F fluoride deoxyglucose increased.[17]

Surgery is the primary method of treating primary vascular EHE, and prosthesis or autologous vascular replacement can be used to rebuild the blood vessels.[18] A few patients have been treated with chemotherapy, often in the metastatic setting, but response to chemotherapy seems to be low. Because of the endothelium origin of EHE and the good response to interferon alpha therapy,[19] recent treatments have focused on the use of antiangiogenic drugs.[20] Bevacizumab is a monoclonal antibody against vascular endothelial growth factor that appears to be effective and well tolerated for metastatic or locally advanced angiosarcoma and epithelioid hemangioma.[21] Taking into account the high incidence of local recurrence and moderate radiation sensitivity of EHE, radiotherapy in some high-risk cases was used as adjuvant therapy with good effect. In addition, few cases of spontaneous regression of EHE have been reported.[8]

Primary vascular EHE is rare, and published articles are almost case reports. We reported contrast-enhanced ultrasonography pattern of EHE to improve physician's understanding of contrast-enhanced ultrasonic manifestations of EHE.

References

[1] Weiss SW, Enzinger FM. Epithelioid hemangioendothelioma: a vascular tumor often mistaken for a carcinoma. Cancer 1982;50:970–81.
[2] Deyrup AT, Tighiouart M, Montag AG, et al. Epithelioid hemangioendothelioma of soft tissue: a proposal for risk stratification based on 49 cases. Am J SurgPathol 2008;32:924–7.
[3] Mentzel T, Beham A, Calonje E, et al. Epithelioid hemangioendothelioma of skin and soft tissues: clinicopathologic and immunohistochemical study of 30 cases. Am J Surg Pathol 1997;21:363–74.
[4] Minyi Y, Xintian H, Weimin L, et al. Intravascular epithelioid hemangioendothelioma. Int Angiol 2011;30:181–4.
[5] Reix T, Sevestre H, Sevestri-Pietri MA, et al. Primary malignant tumors of the venous system in the lower extremities. Ann Vasc Surg 1998;12: 589–96.
[6] Louail B, Vautier-Rodary R, Gondry-Jouet C, et al. Value of imaging in early diagnosis of peripheral veintumors. J Radiol 1998;79:1387–91.
[7] Osawa S, Saito A, Shimizu H, et al. A case of intravascular epithelioid hemangioendothelioma occurring 14 years after coil embolization for an extracranial internal carotid artery aneurysm. J Vasc Surg 2012;55:230–3.
[8] Scarvelis D, Wells PS. Diagnosis and treatment of deep-vein thrombosis. CMAJ 2006;175:1087–92.
[9] Zwiebel WJ, Pelerito JS. Introduction to vascular ultrasonography. 5th ed. Singapore: Elsevier 2004;205:450–7.
[10] Lensing AW, Prandoni P, Brandjes D, et al. Detection of deep-vein thrombosis by real-time B-mode ultrasonography. N Engl J Med 1989;320:342.
[11] Mattos MA, Londrey GL, Leutz DW, et al. Color-flow duplex scanning for the surveillance and diagnosis of acute deep venous thrombosis. J Vasc Surg 1992;15:366.
[12] Monreal M, Montserrat E, Salvador R, et al. Real-time ultrasound for diagnosis of symptomatic venous thrombosis and for screening of patients at risk: correlation with ascending conventional venography. Angiology 1989;40:527.
[13] Castelli P, Caronno R, Piffaretti G, et al. Epithelioid hemangioendothelioma of the radial artery. J Vasc Surg 2005;41:151–4.
[14] Lassau N, Koscielny S, Opolon P, et al. Evaluation of contrast-enhanced color Doppler ultrasound for the quantification of angiogenesis in vivo. Invest Radiol 2001;36:50–5.
[15] Spiss V, Loizides A, Plaikner M, et al. Contrast Enhanced Ultrasound of the lower limb deep venous system: a technical feasibility study. Med Ultrason 2011;13:267–71.
[16] Treglia G, Ceriani L, Paone G, et al. Multifocal epithelioid hemangioendothelioma of the lower limbs detected by 18F-FDG PET/MRI. Clin Nucl Med 2015;40:352–4.
[17] Muñoz A, Diaz-Perez JA, Romero-Rojas AE, et al. Report of 2 cases of primary epithelioid hemangioendothelioma of the external iliac vein. Vasc Endovascular Surg 2013;47:474–8.
[18] Niemelä M, Mäenpää H, Salven P, et al. Interferon alpha-2a therapy in 18 hemangioblastomas. Clinical Cancer Res 2001;7:510–6.
[19] Calabrò L, Di Giacomo AM, Altomonte M, et al. Primary hepatic epithelioid hemangioendothelioma progressively responsive to interferon-alpha: is there room for novel anti-angiogenetic treatments? J Exp Clin Cancer Res 2007;26:145–50.
[20] Agulnik M, Yarber JL, Okuno SH, et al. An open-label, multicenter, phase II study of bevacizumab for the treatment of angiosarcoma and epithelioid hemangioendotheliomas. Ann Oncol 2013;24:257–63.
[21] Cronin P, Arenberg D. Pulmonary epithelioid hemangioendothelioma: an unusual case and a review of the literature. Chest 2004;125:789–93.