

Retiform hemangioendothelioma: a rare lesion of the vulva

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Mingyue Zhang¹ , Xiaojiao Yin¹, Weikai Yao²,
Ning Liu¹ and Ying Yue¹

Abstract

Retiform hemangioendothelioma (RH) is a rare borderline-malignant vascular tumor with specific histological characteristics, usually occurring in the limbs and trunk. We report the case of a 63-year-old woman who presented with a painless, oval nodule that had been growing slowly on her left vulva for 3 years. Magnetic resonance imaging of the pelvic cavity revealed a 4.4 × 2.7 × 1.8-cm cystic lesion in the subcutaneous fat of the left vulva. Resection beyond the macroscopic border was performed. Pathology revealed vascular structures with elongated and narrow arborizing vascular channels that were arranged in a retiform pattern resembling rete testis tissue. Immunohistochemical endothelial staining was positive for CD31, CD34, and Friend leukemia integration-1 (FLI-1). The above features confirmed a diagnosis of RH. There was no local recurrence or metastasis during the 26-month follow-up. RH of the vulva is rare, and its diagnosis is supported by specific histological characteristics and immunohistochemical staining for CD31, CD34, and FLI-1. Wide surgical resection with tumor-free margins is important for a favorable prognosis.

Keywords

Retiform hemangioendothelioma, vulva, CD31, CD34, histology, Friend leukemia integration-1

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Introduction

Retiform hemangioendothelioma (RH) is a borderline-malignant vascular tumor with specific histological characteristics. The initial description of RH by Calonje et al. in 1994 included 15 cases.¹ The incidence of

¹Department of Gynecological Oncology, The First Hospital of Jilin University, Changchun, Jilin, China

²Department of Pathology, The First Hospital of Jilin University, Changchun, Jilin, China

Corresponding author:

Ying Yue, Department of Gynecological Oncology, The First Hospital of Jilin University, 1 Xinmin St, Changchun, Jilin 130021, China.

Email: yuey@jlu.edu.cn



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RH is very low, with lesions usually located in the limbs and trunk, and surgical excision with tumor-free margins is the standard treatment. RH occasionally relapses, but metastasis or death is rare. To date, fewer than 50 cases have been reported. We report the first case of RH occurring in the left labium majus, and review the literature relating to this rare vascular tumor.

Case report

A 63-year-old woman presented with a painless, oval nodule that had been growing slowly on her left vulva for 3 years. She had no relevant family history or previous radiotherapy. Physical examination revealed a well-defined, soft, non-tender, non-fixed, 5- × 3-cm mass in the left labium majus. The overlying skin appeared normal. The mass did not involve the vagina or rectum. The patient had no regional lymphadenopathy. Magnetic resonance imaging of the pelvic cavity showed a 4.4- × 2.7- × 1.8-cm cystic lesion in the subcutaneous fat space of the left vulva

(Figure 1). No positive signs were noted in routine laboratory examinations.

The lesion was initially mistaken for a lipoma. We performed surgery after obtaining the patient's consent. During surgery, the mass was characterized as having unclear margins and no obvious envelope. Wide resection beyond the borders was performed and the excised mass was fixed in formalin for histopathological examination. The mass measured 3.5 × 2.5 × 1.2 cm, was hazel-colored, solid, soft, delicate, and composed of vascular structures containing elongated and narrow arborizing vascular channels arranged in a retiform pattern resembling rete testis tissue (Figure 2a). The arborizing blood vessels had monomorphic cuboidal endothelial cells with characteristic prominent protuberant nuclei and scant cytoplasm, in a hobnail pattern (Figure 2b). Hyaline degeneration was observed in the perivascular interstitium.

Immunohistochemical endothelial staining was positive for CD31 (Figure 2c), CD34 (Figure 2d), and Friend leukemia

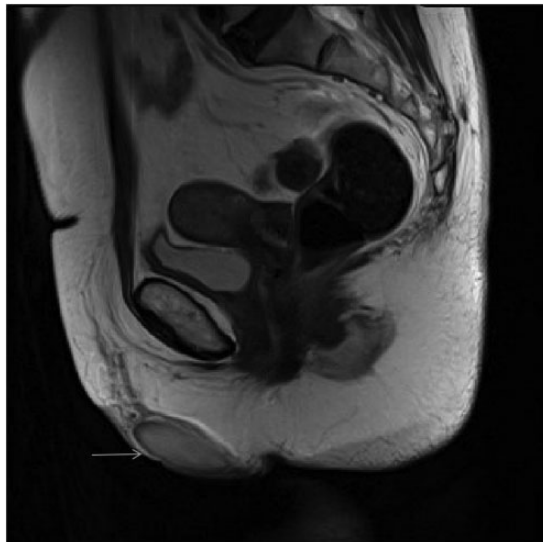


Figure 1. Magnetic resonance image showing the cyst with clear margins located in the subcutaneous fat space of the left vulva.

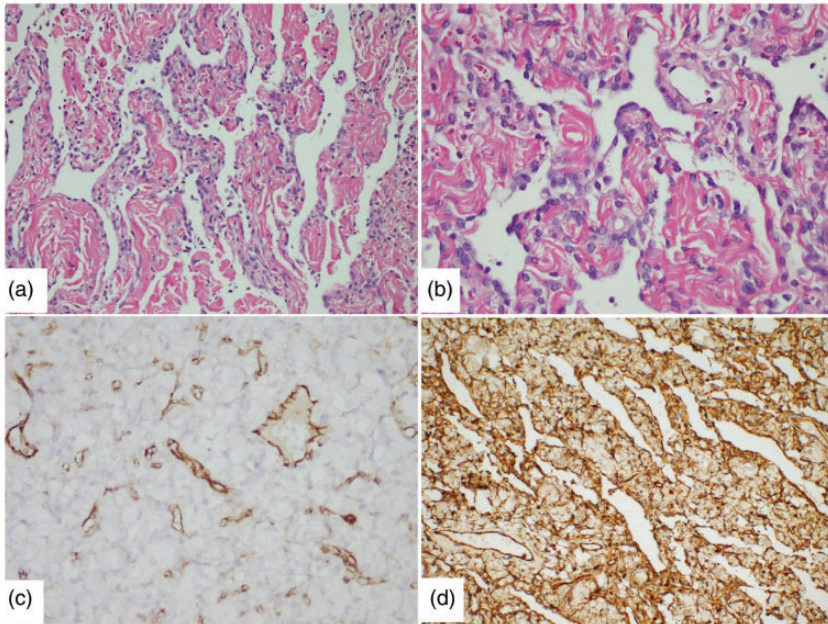


Figure 2. Histopathology and immunohistochemistry of the tumor. (a) Elongated and narrow arborizing vascular channels arranged in a retiform pattern (hematoxylin–eosin, original magnification $\times 200$). (b) Arborizing blood vessels had monomorphic cuboidal endothelial cells with prominent protuberant nuclei and scant cytoplasm (hematoxylin–eosin, original magnification $\times 400$). Immunohistochemical examination was positive for CD31 (c) and CD34 (d)

integration-1 (FLI-1). The cells were negative for pan-cytokeratin and desmin. The Ki-67 proliferation index was estimated at 1%.

A diagnosis of RH on the left labium majus was confirmed pathologically. The tumor had a negative margin, and no further treatment was recommended. There was no local recurrence or metastasis during the 26-month follow-up.

This case report conforms to the CARE guidelines.² This study was approved by the Pathology Department and Gynecological Oncology Department of The First Hospital of Jilin University, China (approval number: 2021-014). Written informed consent was obtained from the subject for treatment and for publication of this report.

Discussion

The cause of RH is obscure. Schommer et al.³ reported that RH tissues were associated with human herpesvirus 8 (Kaposi sarcoma-associated herpesvirus) infection in an initial and two subsequent tumors; however the small number of cases meant that the association could not be verified. Although some patients have a previous history of tumor and radiation therapy, there is no clear evidence associating RH with these factors.^{1,4} RH in the current patient had no obvious cause.

RH mostly occurs in young adults or children,⁵ with an age range of 6 to 78 years (median 35.5 years).^{1,6} The present patient was diagnosed at age 63 years. RH lesions are usually located on the limbs and occasionally on the trunk, with other

reports on the back, scalp, perineal area, medial canthus, earlobe, pleura, and jejunum.^{4,7-10} This is the first report of a lesion arising in the labium majus pudenda.

The course of illness can range from months to decades.¹¹ Most tumors are <5 cm in diameter, but a few have been >5 cm, and some have even had a diameter up to 30 cm³. RH mostly presents as exophytic or patchy skin lesions, but some tumors have pedicles.¹² Most are single nodules and plaques with no specific clinical symptoms, depending on the lesion site. Lesions on the pleura may present as dry cough, dyspnea, and pleural effusion,⁴ and RH in the jejunum may result in anemia.¹⁰

RH is often mistaken for other diseases upon initial presentation, and the present case was initially misdiagnosed as lipoma, which was mainly due to the absence of specific clinical manifestations and characteristic findings during clinical and laboratory examinations. Differential diagnoses of RH include Kaposiform hemangioendothelioma, epithelioid hemangioendothelioma, and Dabska's tumor. Kaposiform hemangioendothelioma is characterized by lobular infiltrates of capillaries and spindle endothelial cells associated with lymphatic vessels; epithelioid hemangioendothelioma comprises epithelioid endothelial cells within a distinctive myxohyaline stroma, with well-formed vessels lined by epithelioid endothelial cells with abundant eosinophilic cytoplasm; and Dabska's tumor consists of cavernous vascular spaces with very prominent intravascular papillae. The diagnosis is usually confirmed by preoperative biopsy or pathology after lesion resection. RH has also been detected by Ga-DOTA-tyr3-octreotide positron emission tomography-computed tomography.¹³ Blood and urine tests are not yet specific. Lymph node ultrasonography is usually more valuable than sentinel lymph node biopsy, given that degenerative hemangioendothelioma rarely metastasizes.⁷

Histopathologically, RH appears as characteristic elongated and narrow arborizing vascular channels that are arranged in a retiform pattern resembling rete testis tissue. The vascular endothelial cells show no obvious pleomorphism, with prominent protuberant nuclei and a characteristic tombstone or hobnail appearance. These cells have scant cytoplasm and mitotic figures are rare.⁵ Lymphocytes infiltrate around the tumor, in the lumen or stroma.

Histochemical staining of the endothelium includes CD31, CD34, factor VIII-related antigen, and D2-40. However, the presence of D2-40, which is often considered to be a lymphatic marker, is controversial. Parsons et al.¹⁴ considered RH to be a vascular entity without lymphatic differentiation, and D2-40 was rarely observed, while Tan et al.¹⁵ and Emberger et al.¹⁶ recorded the presence of D2-40, suggesting that RH might be a vascular neoplasm of lymphatic differentiation. However, more cases are needed to confirm this.

Surgical resection is the preferred treatment for RH, and a histopathologically tumor-free margin is important. Radiotherapy is also effective and can be used in patients with tumor sites that cannot be completely resected³ or in those who have tumor recurrence or lymph node metastasis. Combined radiotherapy and cisplatin chemotherapy has also achieved good results for tumors at unresectable sites.⁷ Nobeyama et al.¹⁷ reported on a patient who refused conventional treatment and was given a combination of pulsed dye laser, local corticosteroid injection, and external application of imiquimod cream. RH progressed slowly and showed no metastasis, suggesting that local control had some effect. The local recurrence rate after RH treatment is generally high (nearly 50%), but the rate of distant metastasis is low.¹

In conclusion, RH is a vascular tumor that may occur in any part of the body;

however, to the best of our knowledge, there have been no previous reports of vulval involvement. Here, we report the case of a woman with typical clinical and histomorphological features of RH. Postoperatively, the patient experienced no recurrence or clinical metastasis, further supporting the use of surgical resection as the preferred treatment for RH. A histopathologically tumor-free margin is important for a favorable prognosis.

Declaration of conflicting interest

The authors declare that there is no conflict of interest.

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ORCID iD

Mingyue Zhang  <https://orcid.org/0000-0003-2056-9571>

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