

# Epithelioid leiomyosarcoma of the vulva: report of a rare case and literature review

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## Abstract

Leiomyosarcoma of the vulva is a rare soft tissue sarcoma that accounts for approximately 1% of all primary vulvar neoplasms, but it is the most common type of vulvar sarcoma. It usually originates from the smooth muscle within erectile tissue or blood vessel walls, the round ligament, the dartos muscle or the arrector pili muscle. No treatment algorithms have been established to date. Surgical resection is preferred for vulvar leiomyosarcoma. Currently, the recommended surgical method is extensive local resection with a safe surgical margin of at least 2 cm. The use of chemoradiotherapy for vulvar sarcoma remains controversial. This case report describes a 39-year-old female that underwent resection of a vulvar mass in January 2019. Postoperative pathological examination indicated that it was an epithelioid leiomyosarcoma. She presented with tumour recurrence after 43 days. Based on the diagnosis, radical right vulvectomy with a tumour margin of 2 cm was performed. The tumour margin was negative. The patient refused to undergo auxiliary radiotherapy and chemotherapy. The follow-up findings do not indicate any signs of recurrence. In order to avoid recurrence, vulvar epithelioid leiomyosarcomas should be completely resected with a margin of 2 cm at the time of first occurrence.

## Keywords

Diagnosis, sarcoma, treatment, vulvar cancer, vulvar neoplasms

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## Introduction

Primary vulvar sarcomas are rare and they account for 1–3% of malignant vulvar tumours.<sup>1</sup> Leiomyosarcomas are the most common histological type of vulvar tumour, although only approximately

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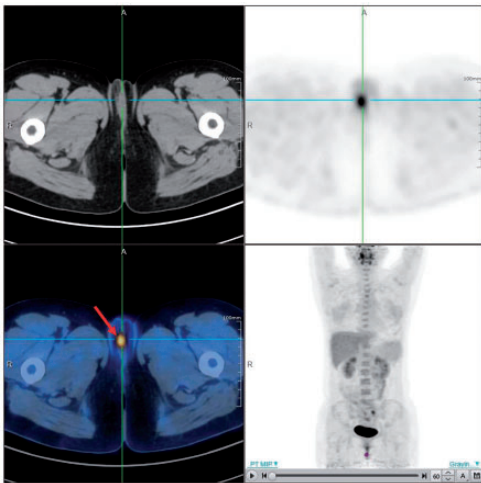
50 cases have been reported in the English literature and the highest prevalence is seen in patients between 35 and 50 years.<sup>2</sup> They occur most frequently in the labia majora, which is followed by, in decreasing order, the Bartholin gland area, clitoris and labium minus.<sup>3</sup> Vulvar leiomyosarcomas initially present as slow-growing lesions that generally originate from the smooth muscle within erectile tissue or blood vessel walls, the round ligament, the dartos muscle or the arrector pili muscle.<sup>4</sup> Additionally, they often present as painless subcutaneous nodules, and therefore, they are often diagnosed as benign lesions, especially when preoperative biopsy pathological assessments may indicate benign cytological changes.<sup>5</sup> This can lead to delayed diagnosis and ineffective treatment and, thus, a worse prognosis.

Currently, the diagnosis of vulvar leiomyosarcoma is dependent on pathological examination and immunohistochemical staining. The surgical treatment methods include extensive local resection, radical vulvectomy and/or inguinal lymph node resection; and it is important to ensure that the resection margin is negative. Tumour size and grade are important prognostic factors.<sup>6</sup> Additionally, low-grade locally recurring tumours require adjuvant radiotherapy.<sup>7</sup> However, the indicators for and outcomes of postoperative adjuvant chemoradiotherapy are unclear, as only a few case series and case reports on vulvar leiomyosarcomas have been published in the English literature. Additionally, clinical data and research are limited, and there are no guidelines or consensus pertaining to their pathogenesis, treatment and prognosis. This current case report aims to contribute to the data on this rare leiomyosarcoma by describing a case of vulvar epithelioid leiomyosarcoma and reviewing the relevant literature.

## Case report

A 39-year-old female patient had a slow-growing right vulvar mass for 3 months and had undergone vulvar mass resection at the Department of Gynaecology and Obstetrics, The Anji Hospital of Yushu County, Changchun, China on 20 January 2019. Postoperative pathology revealed the mass to be a malignant vulvar tumour, likely a mucinous liposarcoma. A pathological consultation at the Department of Pathology, The Second Hospital of Jilin University, Changchun, China revealed that the tumour could have developed from the mesenchymal tissue (sarcoma) and was characterized by nodular lesions, more mucus and inflammatory cell infiltration, epithelioid tumour cells, eosinophilic cytoplasm, a large number of myxoid vacuoles, mitosis and no necrosis. Immunohistochemical staining results were as follows: cytokeratin (CK [AE1/AE3]; +), epithelial membrane antigen (EMA; +), vimentin (+), glypican-3 (-), Sal-like protein 4 (-),  $\alpha$ -fetoprotein (-), CD34 (-), CD31 (+), S100 (-), CK7 (+), desmin (-), progesterone receptor (PR; +), CK8/18 (+), smooth muscle antibody (SMA;-), Ki67 (+20%), CD68 (-), oestrogen receptor (ER; +) and D2-40 (+). It was considered to be an epithelioid leiomyosarcoma after pathological consultation at the Department of Pathology, Peking Union Medical College Hospital, Beijing, China. The immunohistochemical results were as follows: EMA (+), CK7 (-), ER (+, 70%), carcinoembryonic antigen (-), Wilms tumour protein-1 (+), PR (+, 30%), vimentin (+), Ki-67 (index 25%), paired-box protein 8 (-), desmin (+), mammaglobin (-), SMA (-), S-100 (-), Myo-D1 (-), myoglobin (-), CD10 (-) and cyclin D1 (+). A physical positron emission tomography examination was performed in the Department of Radiology, The Third Hospital of Jilin University, Changchun,

China, which revealed thickened soft tissue behind the right labia majora, accompanied by increased glucose metabolism, excluding local tumour activity residue (Figure 1). The patient was admitted to the Department of Gynaecology and Obstetrics, The First Hospital of Jilin University, Changchun, Jilin Province, China on 8 March 2019. Physical examination revealed the following: the vulva had developed normally, a longitudinal scar about 3 cm long was present in the middle of the right labia majora (Figure 2), the vagina was unobstructed, the mucosa was moist and soft, the cervix was of normal size and the surface was smooth, and the uterus was of normal size and did not exhibit tenderness or any obvious abnormality (on palpation) in the bilateral accessory region. The quantity of vaginal secretion was normal and it was white in colour and odourless. Additionally, the abdomen was soft and did not exhibit tenderness or rebound



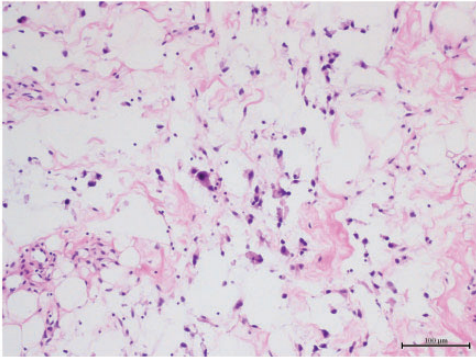
**Figure 1.** A positron emission tomography examination of a 39-year-old female patient that presented with a slow-growing right vulvar mass for 3 months and had undergone vulvar mass resection in January 2019 identified residual tumour on the right vulvar (red arrow). The colour version of this figure is available at: <http://imr.sagepub.com>.

tenderness. Radical vulvectomy was performed under general anaesthesia. Intraoperative frozen pathology and postoperative pathology specimens showed negative findings for the resection margins. Pathological consultation at the Department of Pathology, The Second Hospital of Jilin University, Changchun, China showed focal atypical cells in the subcutaneous fat and surrounding mucus; and on the basis of the first tumour's morphology, residual tumour (approximately 2 mm) was considered (Figure 3). The immunohistochemical results were as follows: vimentin (+) (Figure 4), CD34 (-) (Figure 5), CK (-) (Figure 6) and EMA (+) (Figure 7). No tumour was found at the resection margins. The patient refused adjuvant therapy after the operation. The patient is currently healthy and without evidence of recurrence 27 months after surgery.

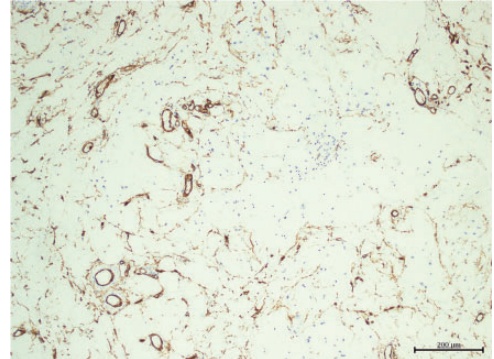
This study was approved by the Ethics Committee and Institutional Review Board of the First Hospital of Jilin University,



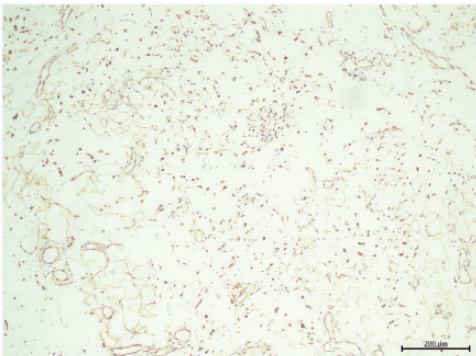
**Figure 2.** A physical examination of a 39-year-old female patient that presented with a slow-growing right vulvar mass for 3 months and had undergone vulvar mass resection in January 2019 identified a 3-cm longitudinal scar on the right vulva (red oval). The colour version of this figure is available at: <http://imr.sagepub.com>.



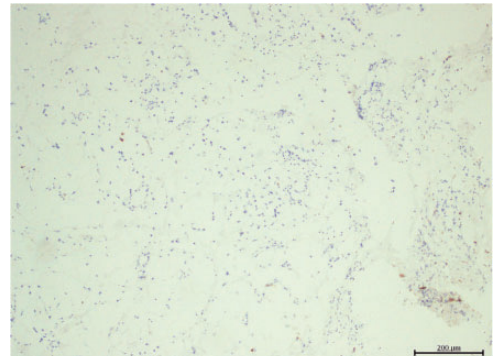
**Figure 3.** A representative photomicrograph of the residual tumour from a 39-year-old female patient that presented with a slow-growing right vulvar mass for 3 months and had undergone vulvar mass resection in January 2019 showing leiomyosarcoma cells in the subcutaneous fat and surrounding mucus suggestive of a vulvar leiomyosarcoma (haematoxylin and eosin; scale bar 100  $\mu\text{m}$ ). The colour version of this figure is available at: <http://imr.sagepub.com>.



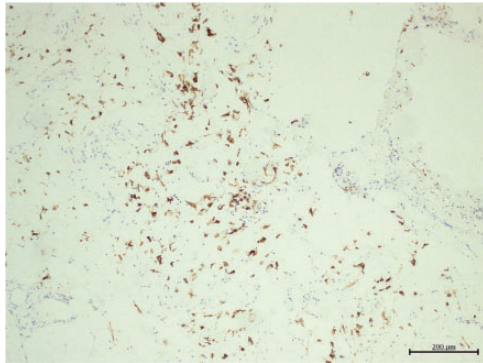
**Figure 5.** A representative photomicrograph of the residual tumour from a 39-year-old female patient that presented with a slow-growing right vulvar mass for 3 months and had undergone vulvar mass resection in January 2019 showing negative immunohistochemical staining for CD34 (haematoxylin and eosin; scale bar 200  $\mu\text{m}$ ). The colour version of this figure is available at: <http://imr.sagepub.com>.



**Figure 4.** A representative photomicrograph of the residual tumour from a 39-year-old female patient that presented with a slow-growing right vulvar mass for 3 months and had undergone vulvar mass resection in January 2019 showing positive immunohistochemical staining for vimentin (haematoxylin and eosin; scale bar 200  $\mu\text{m}$ ). The colour version of this figure is available at: <http://imr.sagepub.com>.



**Figure 6.** A representative photomicrograph of the residual tumour from a 39-year-old female patient that presented with a slow-growing right vulvar mass for 3 months and had undergone vulvar mass resection in January 2019 showing negative immunohistochemical staining for cytokeratin (haematoxylin and eosin; scale bar 200  $\mu\text{m}$ ). The colour version of this figure is available at: <http://imr.sagepub.com>.



**Figure 7.** A representative photomicrograph of the residual tumour from a 39-year-old female patient that presented with a slow-growing right vulvar mass for 3 months and had undergone vulvar mass resection in January 2019 showing positive immunohistochemical staining for epithelial membrane antigen (haematoxylin and eosin; scale bar 200  $\mu\text{m}$ ). The colour version of this figure is available at: <http://imr.sagepub.com>.

Changchun, China. The patient provided verbal informed consent for publication of the case report. The reporting of this study conforms to CARE guidelines.<sup>8</sup>

## Discussion

This present case report describes a female patient with vulvar epithelioid leiomyosarcoma that underwent resection for the primary tumour, but it recurred approximately 43 days later. The findings of this case contribute additional information to the literature, as this tumour is rarely reported and there is limited information on its diagnosis, treatment and prognosis.

The clinical presentation of vulvar leiomyosarcoma is typically vulvar discomfort, mass, pain, itching and ulceration, but it frequently presents as painless, progressively enlarging masses.<sup>6</sup> In the present case, the patient presented with a vulvar mass, but

did not report any pain, discomfort or itching. She underwent resection and she was finally diagnosed based on her postoperative pathological findings after resection of the primary tumour.

With regard to the immunohistochemical findings, most studies have confirmed that vimentin, CK and EMA are expressed by vulvar epithelioid sarcoma cells.<sup>9</sup> Furthermore, 50% of epithelioid sarcomas express CD34, while a smaller proportion of sarcomas express SMA, actin, neuron-specific enolase, S-100, CD99, desmin, neurofilament, CD56 and other markers.<sup>10</sup> The latest 2020 World Health Organization Classification of Tumours Female Genital Tumours indicates that desmin, smooth muscle actin and  $\alpha$ -caldesmon are most often positive.<sup>11</sup> In the current patient, the tumour was positive for vimentin, CK and EMA, but negative for desmin, CD34, SMA and S-100.

Surgical resection is preferred for leiomyosarcoma of the vulva. Currently, the recommended surgical method is extensive local resection with a safe surgical margin of at least 2 cm.<sup>12</sup> Due to its invasive nature, even if the surgical margin is negative, the local recurrence rate is 65–77%, which can even go up to 85%.<sup>13</sup> Moreover, recurrence is often multifocal and mostly occurs within 1 year after initial treatment.<sup>13</sup> In particular, vulvar sarcomas have a high lymph node metastasis rate of 22–45%.<sup>13</sup> In the early stage of prophylactic lymphadenectomy, no local lymphadenopathy is observed, but lymph node metastasis is detected in 75% of the patients.<sup>14</sup> A previous study showed that inguinal lymph node dissection did not improve the survival time of patients.<sup>9</sup>

The application of chemoradiotherapy for sarcoma vulvae remains controversial.

A previous report considered leiomyosarcoma of the genital as a low-grade malignant tumour and recommended post-operative adjuvant radiotherapy and/or chemotherapy for patients with an insufficient surgical margin, residual tumour and high-level tumour (G2–G3).<sup>15</sup> Another report recommended that adjuvant radiotherapy could reduce the local recurrence rate and improve the survival time of vulvosarcoma.<sup>16</sup> Even if the surgical margin was negative, high-dose radiotherapy at the surgical site was still of adjuvant value and the radiotherapy range included the primary foci and regional lymph nodes.<sup>16</sup> However, despite these reports,<sup>15,16</sup> there is very little evidence for the benefits of radiotherapy and chemotherapy, conducted simultaneously or sequentially. In the present case, the patient refused to undergo postoperative chemoradiotherapy, but there has been no recurrence as per the data from the last follow-up. Future studies on large samples need to be conducted to understand the potential benefits and indicators of adjuvant therapy in the form of chemotherapy or radiotherapy.

Tumour size and grade are important prognostic factors. A previous study described performing surgery and radiotherapy on 24 cases of epithelioid sarcoma and the 5-year survival rates of patients with a tumour diameter  $<5$  cm and  $\geq 5$  cm were 77% and 39%, respectively, with the differences being significant.<sup>17</sup> Some researchers believe that high-grade tumours, margin-positive status and a tumour diameter  $>5$  cm are indicators for adjuvant radiotherapy.<sup>18</sup> Other factors that may influence the prognosis of vulvar sarcoma include vascular invasion, tumour necrosis, polyploidy of tumour cells, high mitotic figures, age of the patient and multiple recurrence of the tumour.<sup>9</sup>

However, due to the low incidence of this cancer, there is not enough evidence from large clinical samples to confirm these findings. The patient in the present case was 39 years old and the tumour diameter was 3 cm. Therefore, she underwent only right half vulvar resection, with a negative resection margin and refused adjuvant treatment.

At present, genomic data on vulvar sarcomas are limited. A previous study analysed seven cases of epithelioid sarcoma and the results showed that the common site with increased DNA replication was 22q; and the expression of the interleukin-2 receptor located at 22q was detected, suggesting that it may be involved in the occurrence of epithelioid sarcoma.<sup>19</sup> In the present case, unfortunately, genomic studies were not performed because of limited time and resources. Genomic studies on this cancer could help identify genomic markers, which would be useful for timely and accurate diagnosis of vulvar sarcomas.

In conclusion, vulvar sarcomas are often misdiagnosed preoperatively and their diagnosis is typically based on a combination of clinical manifestations, histopathological findings and immunohistochemical findings. The treatment strategy mainly involves surgical resection with a negative margin and adjuvant treatment in the form of chemoradiotherapy, which is determined according to the histological type, tumour size, degree of differentiation, patient age and medical complications. However, the efficacy of chemoradiotherapy remains uncertain due to the low incidence of this carcinoma. Therefore, further studies on a larger number of clinical samples are needed to confirm which diagnostic markers and treatment indicators would allow for efficient, timely and accurate diagnosis and management.

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## Author contributions

Honghe Lan and Guifeng Jia were the patient's surgeons. Guifeng Jia reviewed the literature and contributed to drafting the manuscript. Honghe Lan reviewed the literature and contributed to drafting the manuscript. Wei Chai and Fengyan Gong were responsible for the revision of the manuscript for important intellectual content. All authors issued final approval for the version to be submitted.

## Declaration of conflicting interest

The authors declare that there are no conflicts of interest.

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