Taiwanese Journal of Obstetrics & Gynecology 60 (2021) 132–135

Contents lists available at ScienceDirect

Taiwanese Journal of Obstetrics & Gynecology

journal homepage: www.tjog-online.com

Case Report

Vulvar epithelioid sarcoma: A case report with literature review

Joseph J. Noh [a], Jung-eun Jeon [a], Hera Jung [b], Hyun-Soo Kim [b], Yoo-Young Lee [a], Chel Hun Choi [a], Jeong-Won Lee [a, *]

[a] Department of Obstetrics and Gynecology, Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, South Korea
[b] Department of Pathology and Translational Genomics, Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, South Korea

ARTICLE INFO

Article history:
Accepted 25 November 2019

Keywords:
Gynecologic neoplasms
Radiotherapy
Sarcoma, epithelioid
Surgery, gynecological
Vulva neoplasms

ABSTRACT

Objective: To report a case of vulvar epithelioid sarcoma, a rare type of tumor that has been reported in 37 cases in the English literature to date.
Case report: We report three cases of vulvar epithelioid sarcoma, proximal type. Wide excisions of the mass were performed with margins free of tumor in all three cases.
Conclusion: Due to its low incidence, there are no evidence-based diagnostic algorithms or published recommendations for treatment. Locoregional lymph node involvement, vascular invasion, tumor size larger than 2 cm, deep localization, presence of necrosis, and a high mitotic index are known as poor prognostic factors. Adjuvant radiotherapy is advisable in the presence of a high-grade tumor or positive margins. The beneficial effect of adjuvant chemotherapy is not well established. Treatment decisions should be made based on the individual case presentation and pathology evaluation.

Introduction

Epithelioid sarcomas are rare malignant soft tissue tumors of unknown histogenesis. Proximal-type epithelioid sarcoma differs from its distal counterpart by having predilection to arise in the deep soft tissue of the proximal extremities such as the pelvic soft tissue and it has a more aggressive clinical course. We report three cases of vulvar proximal epithelioid sarcoma treated by wide excisions and adjuvant radiotherapy or chemotherapy. We also summarized the current understandings of this rare type of disease.

Case presentation

Case 1

A 29-year-old nulliparous woman with no past medical history was referred to our institution for evaluation of left vulvar mass. The mass first appeared a year ago and grew in size to about 4 cm. A 4-cm solitary, firm, non-ulcerated, flesh-colored mass was seen on the left labium majora adjacent to the urethral meatus (Fig. 1(A)). Abdominopelvic computed tomography (CT) and pelvis magnetic resonance imaging (MRI) revealed a well-defined oval mass involving left vulvar subcutaneous tissue and it was measured 5 cm in long axis. Positron emission tomography – computed tomography (PET-CT) showed 18F-fluorodeoxyglucose (FDG) uptake at the left vulva site, suggestive of malignancy (Fig. 1(B)). She underwent wide excision of left vulvar mass. The mass was excised with all margins free of tumor, and there was about 1 cm distance between tumor lesion and the excised margin in all directions. On gross examination, an ill-defined irregular mass of 4.6 × 2.5 cm was located in subcutaneous tissue and was 0.8 cm distant from the nearest radial resection margin. Histological examination revealed infiltration of large monomorphic tumor cells with multinodular growth pattern. The tumor cells had eosinophilic cytoplasm, large nuclei and prominent nucleoli, showing epithelioid features (Fig. 1(C)–(D)). The number of mitotic counts was 8 per 10 high power fields (HPFs). Immunostaining showed positivity for epithelial membrane antigen (EMA), cytokeratin and CAM5.2. The loss of nuclear INI-1 expression was also observed (Fig. 1(E)). The patient received a total of 50 Grays of adjuvant radiotherapy in 25 fractions targeting the left perineum that included the left inguinal and external iliac lymph nodes. She has remained free of disease for 24 months after the operation until the time of the publication of this report.

* Corresponding author. Department of Obstetrics and Gynecology, Samsung Medical Center, Sungkyunkwan University School of Medicine, 81, Irwon-ro, Gangnam-gu, Seoul, 06351, South Korea. Fax: +82 2 3410-0630.
E-mail address: garden.lee@samsung.com (J.-W. Lee).

https://doi.org/10.1016/j.tjog.2020.11.020

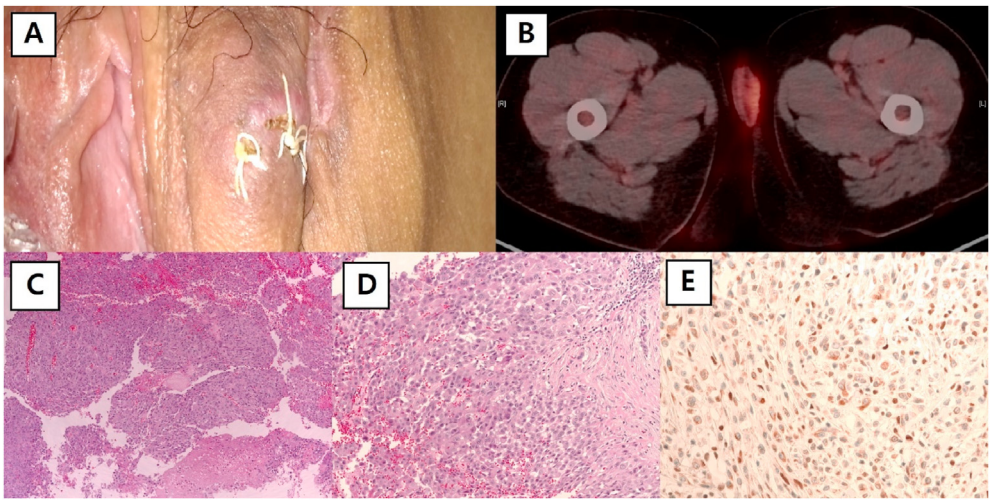

Fig. 1. **(A)** Gross appearances of the lesion in Case 1. A 4-cm solitary, firm, non-ulcerated, flesh-colored mass was seen on the left labium major adjacent to the urethral meatus without pain, itching or irritation over the lesion. Suture materials after punch biopsy are seen; **(B)** Positron emission tomography – computed tomography (PET-CT) showing hypermetabolic left vulva site, suggestive of malignancy; **(C)** Representative photomicrograph showing intermediate cellularity and marked pleomorphism (100×); **(D)** Increased mitotic rate (8 per 10 high power field; 200×); **(E)** Loss of INI-1 expression (200×).

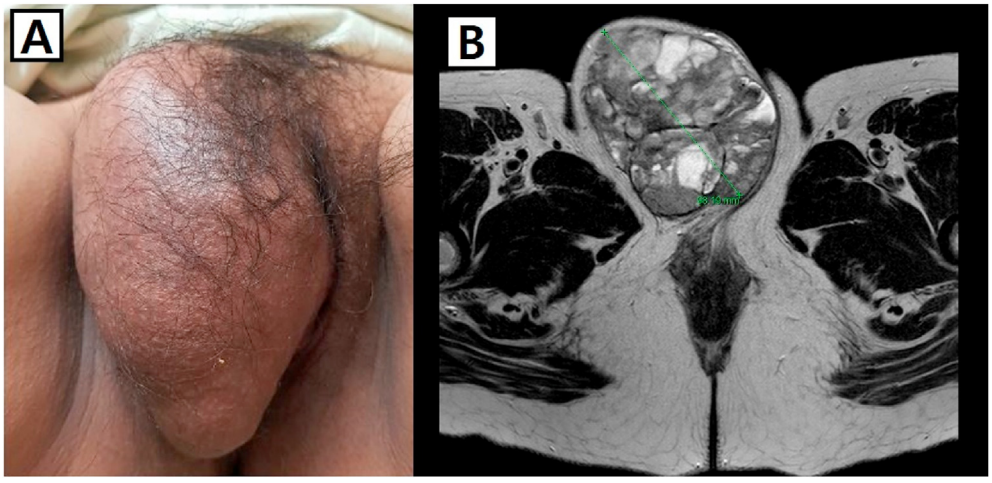

Fig. 2. **(A)** A 10-cm solitary, soft, non-ulcerated, flesh-colored mass was seen on the right labium major; **(B)** Pelvis MRI axial T2 of Case 2 showing a well-defined oval mass involving right vulvar subcutaneous tissue, which was measured at about 10 cm in long axis.

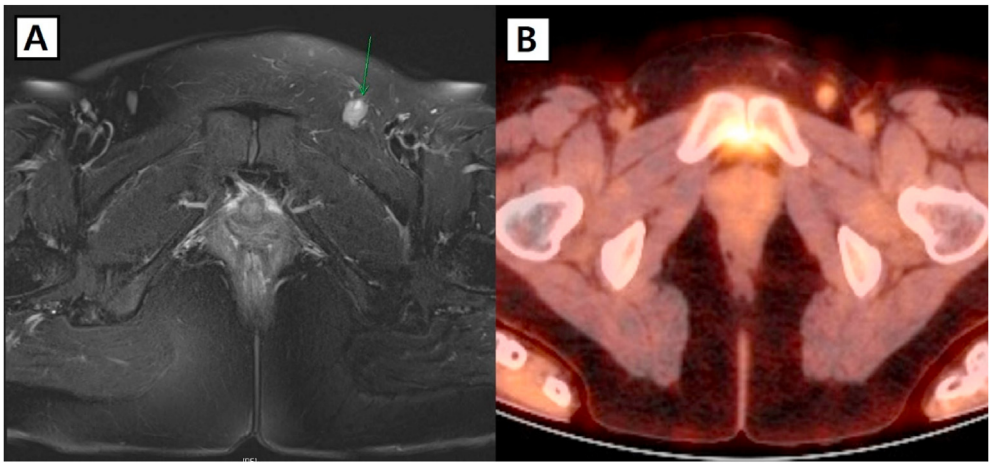

Fig. 3. **(A)** A 1.5 cm enlarged lymph node seen in the left inguinal area in pelvis MRI; **(B)** The same enlarged lymph node with hypermetabolic image on PET-CT was observed, which could not exclude malignancy.

Table 1
Clinical data of the vulva epithelioid sarcoma reported between 1972 and 2018.

Characteristics	Data (N = 37)
Median patient age (range)	34 (17–80)
Site – No. (%)	
Labium majora	21 (57%)
Vulva	9 (24%)
Pubis	2 (5%)
Clitoris	1 (3%)
Other pelvic organs	6 (16%)
Mean size of the mass in centimeters (range)	5.1 (0.9–30.0)
Symptoms – No. (%)	
Asymptomatic	5 (14%)
Symptomatic	
Mass	18 (49%)
Pruritis	1 (3%)
Irritation	1 (3%)
Pain	4 (11%)
Inability to walk	1 (3%)
Not described	10 (27%)
Surgical procedures performed – No. (%)	
Local excision	14 (38%)
Wide local excision or radical excision	22 (59%)
No surgery	1 (3%)
Lymph node dissection – No. (%)	
Ipsilateral lymph node dissection	4 (11%)
Bilateral lymph node dissection	5 (14%)
Lymph node dissection not performed or not described	28 (76%)
Immunohistochemistry positivity – No. (%)	
Cytokeratin	21 (57%)
Vimentin	22 (59%)
EMA	18 (49%)
CD34	11 (30%)
Desmin	2 (5%)
SMA	1 (3%)
CD99	1 (3%)
NSE	2 (5%)
p53	3 (8%)
Factor VIII	1 (3%)
CD31	1 (3%)
Ki-67	1 (3%)
Immunohistochemistry negativity – No. (%)	
S100	17 (46%)
Desmin	10 (27%)
CEA	2 (5%)
HMB45	5 (14%)
Factor VIII	2 (5%)
EMA	1 (3%)
SMA	4 (11%)
CD31	7 (19%)
CD34	3 (8%)
CD99	2 (5%)
Melan-A	1 (3%)
HHV8	1 (3%)
p63	1 (3%)
Cytokeratin 5/6	2 (5%)
Cytokeratin 7	1 (3%)
Cytokeratin 20	1 (3%)
CD163	1 (3%)
INI-1 staining – No. (%)	
Loss of INI-1 staining	6 (16%)
No information regarding INI-1 staining	31 (84%)
Adjuvant treatment – No. (%)	
Radiotherapy	8 (22%)
Chemotherapy	3 (8%)
Concurrent chemoradiotherapy (CCRT)	2 (5%)
Clinical outcome – No. (%)	
No evidence of disease after treatment	21 (57%)
Recurred	14 (38%)
Died of disease	14 (38%)
No information	1 (3%)
Site of recurrence – No. (%)[a]	
Lymph nodes	8 (57%)
Local recurrence	4 (29%)
Lung	5 (36%)
Others	2 (14%)
Median intervals to recurrence in months (range)	6.5 (1–48)

[a] Percentage calculated out of recurred cases only.

Case 2

A 35-year-old woman in her second pregnancy at the gestational age of 30 3/7 week was referred to our institution for evaluation of right vulva mass. The mass first appeared about 5 years ago. A10-cm soft, non-ulcerated, flesh-colored mass was seen on the right labium majora (Fig. 2(A)). Pelvis MRI revealed a well-defined oval mass of 10 cm in long axis (Fig. 2(B)). All tumor markers including carcinoembryonic antigen (CEA), cancer antigen (CA) 19-9, CA 125 and squamous cell carcinoma (S.C.C.) tumor antigen (TA) 4 were within normal limits. The patient underwent right vulvectomy with wide excision and elective cesarean delivery at the gestational age of 32 6/7 week. The excised mass was about 9.0 × 8.0 cm with intermediate cellularity and moderate pleomorphism. The number of mitotic counts was 10 per 10 HPFs. More than 50% of tumor contained necrosis. The resection margins were negative for malignancy with the closest margin of 0.1 cm. Immunostaining demonstrated strong positivity for cytokeratin, focal positivity for CD34 and p53 and negativity for S-100 and Pan-TRK. Nuclear INI-1 expression was completely absent in the tumor cells. The diagnosis of vulvar epithelioid sarcoma with FNCLCC (Fédération Nationale des Centres de Lutte Contre Le Cancer) grade 3 was made. After the operation, she underwent chest CT and PET-CT, in which multiple variable size discrete nodules in the lungs were seen. She was initially scheduled to receive intensity-modulated radiotherapy (IMRT) with systemic chemotherapy with adriamycin and cisplatin. However, she developed hemoptysis with severe cough immediately after the operation. The follow-up chest CT taken one month after the operation showed increased numbers and sizes of pulmonary metastatic lesions. She was unable to receive IMRT due to the rapid progression of the disease. She received doxorubicin and olaratumab palliative chemotherapy once and we transferred her to hospice for further care.

Case 3

A 24-year-old nulliparous woman was referred to our institution for evaluation of left palpable inguinal mass. She had already undergone wide vulvar excision two years ago at a local institution and was diagnosed as having vulvar epithelioid sarcoma, proximal type with FNCLCC grade 2. Immunostaining of the resected mass from the previous operation revealed that the tumor cells were positive for cytokeratin and EMA but negative for CD34. The resection margins were negative in all directions. She did not receive any adjuvant treatment. However, about 1.5 cm movable and hard mass started to develop in the left inguinal area two years after the operation. Abdominopelvic and chest CT did not show any evidence of recurrence except for the left inguinal mass (Fig. 3(A)). PET-CT revealed a hypermetabolic lymph node enlargement in the left inguinal area, which could not exclude malignancy (Fig. 3(B)). The result of ultrasound-guided biopsy of the mass was consistent with metastatic epithelioid sarcoma and it showed positivity in cytokeratin and the loss of INI-1 expression. She underwent left inguinal lymph node excision, laparoscopic left ovary transposition and left pelvic lymph node dissection. She is scheduled to undergo radiotherapy on left inguinal and pelvic lymph nodes.

Discussion

Epithelioid sarcoma, a rare soft tissue malignancy, was first described by Enzinger in 1970 [1]. The mean age of diagnosis is reported to be around 35 years old, similar to other sarcomas [2]. Among all vulvar malignancies, epithelioid sarcoma comprises approximately 1% [2]. Proximal epithelioid sarcomas of vulva have been reported in only about 37 cases in the English literature

(Table 1). Due to its rarity, it is frequently misdiagnosed as benign lesion such as infectious granuloma, fibrous histiocytoma, dermoid cyst or squamous cell carcinoma [3]. The most common initial symptom is slowly growing painless mass. The proximal type tends to be more aggressive characterized by rapid expansion of the tumor, elevated local recurrence even after surgery with negative margins and propensity for early metastasis.

These rare tumors are diagnosed mostly by biopsy. The reported cytological smears of epithelioid sarcoma show a dissociated population of large, atypical neoplastic cells with bi-nucleated or multinucleated cells, vesicular nuclei, abundant cytoplasm and a rhabdoid appearance [5]. Microscopic appearance ranges from plump spindle cells to large polygonal cells with eosinophilic cytoplasm [5]. Its resemblance to epithelioid or squamous cells makes diagnosis challenging [5]. Immunohistochemical staining usually reveals cytoplasmic immunoreactivity for cytokeratin, vimentin, and EMA, whereas S-100 and CD31 staining are usually negative. Epithelioid sarcoma commonly displays membranous positivity for EMA, in contrast to other majority of soft tissue sarcomas, which show nonspecific cytoplasmic EMA expression. About 50% of the cases express CD34 [6]. The characteristic immunophenotype of epithelioid sarcoma is the loss of nuclear immunoreactivity for INI-1 [7]. This loss of INI-1 protein is related to biallelic inactivation of the tumor suppressor gene *SMARCB1/INI1*, which is located at chromosome 22q11.2 [7].

The mainstream treatment is surgical removal of the lesion with wide margins greater than 2 cm [8]. Many authors prefer local wide excision to radical vulvectomy [9]. Inadequate margins have been associated with an increased risk of local recurrence. However, local recurrence despite negative surgical margins is common. It has been reported that distant metastasis eventually occurs in up to 60% of cases and often takes place within 6 months after surgery [3,6]. Locoregional lymph node involvement, vascular invasion, tumor size larger than 2 cm, deep localization, presence of necrosis, and a high mitotic index in excess of 2/10 HPFs are also known as poor prognostic factors [3,4]. Locoregional lymph node dissection for staging should only be considered when they are clinically suspicious or enlarged, because there is no evidence of the beneficial effect of lymph node resection on local or distant relapse rate [1].

Adjuvant radiotherapy is advisable in the presence of a high-grade tumor or positive margins. The beneficial effect of adjuvant chemotherapy is not well established, but is recommended in cases of disseminated disease. Agents with the most documented cytotoxic effect are doxorubicin, dacarbazine, ifosfamide, cyclophosphamide, etoposide, vincristine, and methotrexate [10]. Doxorubicin is described as the most active single agent for patients with soft tissue sarcomas with overall response rates of 15–35%, followed by dacarbazine with response rate of 16% [10].

In future, gene therapy targeting the genetic pathway in tumorigenesis of this aggressive neoplasm may provide a better prognosis. *SMARCB1/INI1* gene acts as a tumor suppressor gene. Previous studies found that inactivation of *SMARCB1/INI1* played a crucial role in tumorigenesis of epithelioid sarcoma and immunochemistry studies revealed that a significant number of cases have inactivated *SMARCB1/INI1* [7]. Target therapy restoring *SMARCB1/INI1* gene function could provide new therapy in epithelioid sarcoma [5].

Owing to the low incidence of these tumors at this location, there are no evidence-based diagnostic algorithms or published recommendations for treatment. More clinical characteristics of this rare type of disease should be collected as well as its response to various types of treatment modalities.

Declaration of competing interest

The authors of this publication disclose that there are no relevant financial, personal, political, intellectual or religious interests to declare. The terms of this arrangement have been reviewed and approved by Samsung Medical Center in accordance with its policy on objectivity in research.

References

[1] Enzinger FM. Epitheloid sarcoma. A sarcoma simulating a granuloma or a carcinoma. Cancer 1970;26(5):1029–41.
[2] Ulutin HC, Zellars RC, Frassica D. Soft tissue sarcoma of the vulva: a clinical study. Int J Gynecol Cancer 2003;13(4):528–31.
[3] Chase DR, Enzinger FM. Epithelioid sarcoma. Diagnosis, prognostic indicators, and treatment. Am J Surg Pathol 1985;9(4):241–63.
[4] Prat J, Woodruff JM, Marcove RC. Epithelioid sarcoma: an analysis of 22 cases indicating the prognostic significance of vascular invasion and regional lymph node metastasis. Cancer 1978;41(4):1472–87.
[5] Han CH, Li X, Khanna N. Epithelioid sarcoma of the vulva and its clinical implication: a case report and review of the literature. Gynecol Oncol Rep 2016;15:31–3.
[6] Hasegawa T, Matsuno Y, Shimoda T, Umeda T, Yokoyama R, Hirohashi S. Proximal-type epithelioid sarcoma: a clinicopathologic study of 20 cases. Mod Pathol 2001;14(7):655–63.
[7] Hornick JL, Dal Cin P, Fletcher CD. Loss of INI1 expression is characteristic of both conventional and proximal-type epithelioid sarcoma. Am J Surg Pathol 2009;33(4):542–50.
[8] Bos GD, Pritchard DJ, Reiman HM, Dobyns JH, Ilstrup DM, Landon GC. Epithelioid sarcoma. An analysis of fifty-one cases. J Bone Joint Surg Am 1988;70(6):862–70.
[9] Gallup DG, Abell MR, Morley GW. Epithelioid sarcoma of the vulva. Obstet Gynecol 1976;48(1 Suppl). 14S-7S.
[10] Antman KH. Chemotherapy of advanced sarcomas of bone and soft tissue. Semin Oncol 1992;19(6 Suppl 12):13–20.