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Epithelioid Sarcoma of the Vulva in a 17-year-old Pregnant Woman

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Abstract

Epithelioid sarcoma of the vulva is an extremely rare neoplasm with aggressive behavior and poor outcome. Herein, we report a case of vulvar epithelioid sarcoma presenting in a 17-year-old very early in her pregnancy. The patient presented with an asymptomatic nodule of the right labia majora of 1-year duration. Computerized tomographic scans showed enlarged inguinal lymph nodes and numerous lung nodules. Positron emission tomography was performed and revealed no suspicious lesions for metastatic disease. The patient underwent local excision of her vulvar lesion. On the basis of morphology and extensive immunohistochemistry, the lesion was classified as epithelioid sarcoma. The patient was referred to radiation therapy and upon evaluation, she was found to be in her sixth week of gestation. The patient continued with her pregnancy and underwent a lymph node dissection, which was positive. We review the literature of only the well-documented cases extensively studied by immunohistochemical analysis. We summarize the clinical presentation, clinical impression, treatment modalities, and outcomes of these cases. On account of the rarity of this disease in the vulva, there is no clear consensus on treatment modalities, but it seems that early aggressive surgical resection is the treatment of choice, with the role of adjuvant therapy to be determined.

Keywords

epithelioid sarcoma; vulva; review

Sarcomas of the vulva account for less than 2% of vulvar malignancies. The predominant site of involvement is the labia majora followed by the Bartholin gland area, clitoris, and labium minus.¹ Primary epithelioid sarcoma (ES) of the vulva is an extremely rare tumor and only 20 cases have been reported in the English literature.^{2–18} The majority of these cases were described before immunohistochemistry (IHC) was validated for use in routine surgical laboratories and the diagnosis was based solely on morphology and electron microscopy, in which the findings are usually not very specific for ES.

Herein, we will review only the literature where cases were confirmed by IHC studies; this literature accounts for 8 cases.^{3–6} Our case has numerous interesting points worth publishing. It is the first case of ES to be reported in a patient of very young age (17 years). It is the second case reported in a pregnant woman and the first to be presented in very early pregnancy, which makes the treatment choices very limited and more challenging. It has aberrant expression for the endothelial marker CD31, which has not been reported before.

CASE REPORT

A 17-year-old African American female presented to Roswell Park Cancer Institute, Buffalo, NY, with an asymptomatic nodule involving the right vulva of 1-year duration. The patient noted an increase in the nodule size over the last month. However, she denied any abnormal vaginal bleeding, discharge, or abdominal pain. A physical examination revealed a 3 cm, firm nodule of the right labia, located at the 11-o'clock position. The patient underwent a local excisional biopsy with frozen section consultation to determine the nature of this lesion. In addition, chest, pelvic, and abdominal computerized tomographic scans were conducted. A Computerized tomographic scan of the pelvis showed enlargement of bilateral inguinal nodes. The right inguinal node measured 1.8 cm × 1.1 cm, which was interpreted by the radiologist as being representative of metastatic disease. There were multiple small nodules in the right and left lungs, suggestive of metastatic disease. Therefore, a positron emission tomographic scan was performed and revealed no metastatic disease to the lungs.

PATHOLOGIC FINDINGS

Grossly, the specimen consisted of a fragment of vulvar tissue in which a 3-cm well-circumscribed tan white nodule was identified. The cut surface was very firm and showed a homogenous white-tan tissue. The initial frozen section diagnosis was poorly differentiated squamous cell carcinoma. However, on the permanent sections, the diagnosis was changed. Microscopically, the tumor was very cellular. In some areas, the neoplasm demonstrated a granuloma-like arrangement with central geographic necrosis. The tumor was composed of a moderately cellular spindle to epithelioid cells with an infiltrative pattern of growth set in a collagenous background (Fig. 1). A high mitotic rate (>5 mitosis/10HPF) was seen. On IHC, the tumor cells were strongly and diffusely positive for AE1/3, epithelial membrane antigen (EMA), CD31, CD34, factor VIII, and vimentin (Figs. 2–4). They were negative for A103, Melan-A, HHV8, P63, cytokeratin (CK)5/6, CK7, and CK20. The morphology and IHC profiles were consistent with ES. However, on account of the strong expression of CD31 and factor VIII by tumor cells, the possibility of epithelioid angiosarcoma was higher and the case was sent to an expert for a second opinion who agreed with the diagnosis of ES.

The patient was advised of the risks involved in completing her pregnancy. However, she was committed to continuing her pregnancy and declined termination. She initially declined additional surgery and radiation therapy, but did agree to proceed with a bilateral inguinofemoral lymphadenectomy. A right and left groin lymph nodes dissection was performed, and revealed a metastatic tumor on her right groin lymph node measuring 3 cm × 2.5 cm. The patient was informed about the risk of radiation therapy to the developing baby. She is still undergoing consultation with her gynecologist and social worker to make a

decision on how to proceed: 2 months after initial diagnosis, the patient had still not reached a decision on her own. On account of her young age and the severity of the disease, a court hearing was planned to determine her rights. At 16 weeks gestation, the patient had still not received any additional therapy.

DISCUSSION

Epithelioid sarcoma is a rare soft tissue malignancy, which occurs in younger adults (mean age 26 years) with a male predilection, and generally involves the distal and proximal extremities.¹⁹ ES involving the vulva is exceptionally rare; only 20 cases are reported in the literature and a mere 8 out of these 20 cases have supportive IHC studies. The clinical and pathologic findings of the 8 cases are summarized in Table 1. The patients ranged in age from 23 to 57 years. Our patient (17 years old) is the youngest patient ever to be reported. The clinical impression varied, with Bartholin cyst being the most common impression, followed by fibroma, dermoid cysts, viral warts, and squamous cell carcinoma. The lesions generally presented as nodular masses ranging in size from 1.5 to 6 cm. ES is considered to be of unknown lineage and is often misdiagnosed as a benign lesion, especially as a benign granulomatous process. In these cases, two were initially misdiagnosed as hidradenoma papilliferum, and granulomatous inflammation with hyperplastic scarring. The interval between initial presentation and recurrence was 1 year for the former and nearly 7 years for the latter.^{4,7}

Morphologically, it is necessary to distinguish ES from other epithelioid-looking tumors such as epithelioid peripheral nerve sheath tumor, epithelioid leiomyosarcoma, epithelioid angiosarcoma, rhabdomyosarcoma, malignant melanoma, and poorly differentiated squamous cell carcinoma. IHC studies are very helpful in making this distinction. ES is positive for vimentin, keratin, EMA, CD34 (50% of cases), and muscles actin (HHF-35) (1/3 of cases). Epithelioid peripheral nerve sheath tumors are usually S-100+ and keratin–, malignant melanoma (S-100+, HMB45+), epithelioid leiomyosarcoma and rhabdomyosarcoma (muscle markers with negative keratin), and epithelioid angiosarcoma (keratin+, factor VIII+, CD34+, CD31+) and poorly differentiated squamous cell carcinoma (keratin+ and all endothelial markers–). IHC studies in our case demonstrated immunoreactivity for AE1/3, EMA, vimentin, CD34, CD31, and factor VIII. On account of the positivity of CD31, epithelioid angiosarcoma was present in our differential diagnosis. However, the characteristic morphology was consistent with ES. Positive staining for CD31 is exceptionally rare and may represent the first case reported, leading us to confirm that ES is in fact of unknown lineage and can express a number of immunomarkers.

In the past, the electron microscopic study showed a range of ultrastructural features wherein none were specific for ES, such as intercellular cytoplasmic interdigitations, ample cytoplasm with rough endoplasmic reticulum, intermediate-sized cytoplasmic filaments that lack condensation plaques, conspicuous Golgi complexes, and a moderate number of small, elongated mitochondria, lipid droplets, lysosomes, and glycogen.²

The cytogenetic studies of ES are very limited and have not revealed a specific alteration specific to these tumors. Various chromosomal deletions and gains, none of which were specific, were noted on 7p, 8q, 9p, 9q, 18q11, and 22q11.⁹

There are numerous factors that can predict poor prognosis. These include necrosis, vascular invasion, and mitotic index $>2/10$ HPF.²⁰ Clinically, locoregional lymph node involvement, a tumor size greater than 2 cm and deep localization are also poor prognostic factors. Metastatic disease of vulvar ES is common, with frequent involvement of the lungs and lymph nodes. Our patient had many poor prognostic factors: she presented with a lesion of 3 cm with necrosis, high mitotic index, and locoregional lymph node involvement.

Surgical resection with wide margins (>2 cm) is considered the mainstay of treatment. Adjuvant therapy, especially radiation therapy may be beneficial, but treatment should be considered on an individual basis. In pregnancy, treatment options are very limited, especially in our case in which the patient refused to terminate her pregnancy. Treatment for pregnant women with ES is unexplored, as this is the second reported case of ES occurring during pregnancy. In the earlier case, the patient presented at 36 weeks of gestation and treatment consisted of a radical hemivulvectomy 6 weeks post-partum followed by chemotherapy. In our case, the treatment is limited and local excision with bilateral inguinofemoral lymphadenectomy would be the course of treatment for our patient. In addition, we are confronted with another challenge in that the patient is not compliant and she was lost to follow-up just before any treatment could be given.

In conclusion, vulvar ES is a highly aggressive neoplasm with frequent locoregional and distant metastasis. Despite its rarity, both gynecologists and pathologists should be aware of its existence. The primary treatment modality remains extensive surgical resection with inguinal lymphadenectomy as early as possible in the disease course.

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FIGURE 1.

The tumor cells are epithelioid looking with abundant eosinophilic cytoplasm and round nuclei with prominent nucleoli (hematoxylin-eosin $\times 40$).

FIGURE 2.
Tumor cells are strongly and diffusely positive for total cytokeratin AE1/3 ($\times 40$).

FIGURE 3.
Tumor cells are strongly positive for CD34 ($\times 40$).

FIGURE 4.
Tumor cells are positive for CD31 ($\times 40$).

TABLE 1

Summary of the Clinical and Pathologic Findings in 8 Reported Cases

Author (y)	Age (y)	Size (cm)	Surgery	Chemotherapy/ Radiotherapy	Recurrent Site	Interval to Recurrence	Outcome (mo)	IHC								
								AE1/3	EMA	Vimentin	CD34	Desmin	SMA	CD31	S-100	Factor VIII
Weissmann et al (1990) ⁴	26	NA	Local excision	No/No	Local, lymph node, lung, liver, kidney	14mo	AWD 78	+	+	+	N/A	N/A	N/A	N/A	N/A	–
Guillou et al (1997) ⁵	57	5	Local excision	No/Yes	None	N/A	DOID 52	+	+	+	+	–	–	–	–	N/A
	49	3	Radical vulvectomy	No/Yes	None	N/A	NED 22	+	+	+	+	+	–	–	–	N/A
	45	6	Wide local excision	Yes/Yes	None	N/A	NED 21	+	+	+	–	+	+	–	–	N/A
Tjalma et al (1999) ⁶	23	1.5	Hemivulvectomy	No/No	None	N/A	NED 48	+	+	+	N/A	–	N/A	N/A	–	N/A
Kasamatsu et al (2001) ⁷	23	5.5	Local excision	No/No	Local, lymph node	17mo	NED 96	+	+	+	+	–	+	–	–	N/A
Moore et al (2002) ³	29	5.5	Hemivulvectomy	Yes/No	Lung	N/A	DOD 6.5	+	+	+	N/A	N/A	N/A	N/A	–	N/A
Altundag et al (2004) ⁸	51	3.5	Hemivulvectomy	Yes/Yes	Lung	4mo	DOD 6	+	+	+	+	–	–	N/A	N/A	N/A
Current Case (2008)	17	3	Local excision	No/No	None	N/A	AWD 2	+	+	+	+	–	–	+	–	+

AWD indicates alive with disease; DOD, dead of disease; DOID, dead of intercurrent disease; EMA, epithelial membrane antigen; IHC, immunohistochemistry; NED, no evidence of disease; SMA, smooth muscle actin.