

## CASE REPORT

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### Declaration of ethical aspects

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# Proximal type epithelioid sarcoma of the vulva

## Sarcoma epitelioid de tipo proximal de vulva

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### ABSTRACT

Epithelioid sarcoma is a rare type of mesenchymal tumor. Proximal-type epithelioid sarcoma of the vulva is an extremely rare malignant tumor of the soft tissues with frequent recurrences due to its aggressive behaviour. Because its characteristics are similar to other benign lesions, this leads to diagnostic and therapeutic delays. Histologic features of this tumor include prominent epithelioid cells and the appearance of rhabdoid features with marked nuclear atypia. Due to its low incidence, there are no evidence-based diagnostic algorithms or published recommendations for treatment. The prognosis is generally poor. A case of proximal type epithelioid sarcoma of the vulva is presented.

**Key words:** Vulva, Epithelioid sarcoma, Vulvar neoplasms.

### RESUMEN

El sarcoma epitelioides es un tipo raro de tumor mesenquimal. El sarcoma epitelioides de tipo proximal de vulva es un tumor maligno extremadamente raro de los tejidos blandos, con frecuentes recurrencias por su comportamiento agresivo. Debido a que sus características son similares a otras lesiones benignas, esto lleva a retrasos diagnósticos y terapéuticos. Las características histológicas de este tumor incluyen células epitelioides prominentes y aparición de rasgos rhabdoides con marcadas atipias nucleares. Debido a su baja incidencia, no existen algoritmos diagnósticos basados en la evidencia ni recomendaciones publicadas para el tratamiento. El pronóstico es generalmente malo. Se presenta un caso de sarcoma epitelioides de tipo proximal de vulva.

**Palabras clave.** Vulva, Sarcoma epitelioides, Neoplasia de la vulva.

### INTRODUCTION

Malignant soft tissue tumors of the vulva are infrequent, with primary sarcomas accounting for 1% to 3% of cases<sup>(1)</sup>. Epithelioid sarcomas are rare malignant soft tissue tumors with unknown histogenesis. The proximal type arises from deep soft tissues of the extremities and soft tissues of the pelvis, perineum and genital area, with a more aggressive clinical course and high recurrence rate, which differentiates it from its distal counterpart<sup>(2)</sup>. It usually appears as a relatively small and generally painless tumor, which can lead to confusion with benign lesions, leading to diagnostic and therapeutic delays<sup>(2,3)</sup>. Currently there are less than 50 reported cases of vulvar localization. A case of proximal type epithelioid sarcoma of the vulva is presented.

### CASE REPORT

This was a 30-year-old female patient, nulliparous, who consulted for presenting painless tumor in the right vulvar region, which increased in size in approximately 20 months. On clinical examination, a tumor of approximately 9 centimeters in diameter, cystic in appearance, smooth, well-circumscribed, adherent to deep planes, painless and non-ulcerated in the posterior region of the right labium majus and involving the adjacent soft tissues was found. Speculscopy and vaginal examination showed that the lesion extended to the lower right third of the vaginal wall. There was no erythema, bleeding, discharge or other abnormalities on physical examination or bilateral palpable inguinal lymphadenopathy.

Abdomino-pelvic computed tomography showed a well-defined oval tumor affecting the subcutaneous tissue on the right side of the vulva. It measured 9 centimeters in its longitudinal axis, with cutaneous thickening and some bilateral inguinal nodes of small volume; the largest measured 5 millimeters in diameter in the right inguinal area. All tumor markers (carcinoembryonic antigen, CA19-9 and CA125) were within normal limits. The patient underwent fine needle biopsy under local anesthesia and the specimen was sent for pathologic evaluation. Sections showed firm, whitish nodular tissue compatible with sarcomatous tissue. In view of the findings, the patient was scheduled for tumor resection.

During surgery, a yellowish white, encapsulated, multilobulated tumor was observed within the soft tissue of the perineum. The tumor was excised with wide margins in all directions. There was no evidence of local invasion. The surgery was concluded without complications.

Pathologic examination revealed a lobulated tumor 8 centimeters in diameter with no evidence of hemorrhage, fibrous or myxoid tissue within. Resection margins were negative for malignancy in all directions, with the closest margin at 18 millimeters. Microscopic evaluation showed that the lesion was well circumscribed with several focal nodules within the margins. Proliferation of epithelioid, moderately pleomorphic cells with eosinophilic cytoplasm, thick, pleomorphic, eccentric nuclei with prominent nucleoli was evident. These were accompanied by cells with denser cytoplasm, with rhabdoid features and other multinucleated giant cells. Focally admixed osteoclastic giant cells were also found, as well as foamy histiocytes. There was no evidence of necrosis and mitotic figures were 5 by 10 high power fields in most areas. Immunohistochemical staining showed that the epithelioid component was strongly positive for epithelial membrane antigen (EMA) and negative for INI-1, keratin, CD34, SMA, and desmin. Immunostaining for CD34, S-100 protein only was focal. Considering the findings, the diagnosis of proximal vulvar epithelioid sarcoma was made.

The patient was discharged on the third day. Although she was referred to the medical oncology service, she refused any further adjuvant treatment. To date, the patient's evolution is unknown.

FIGURE 1. MICROSCOPIC IMAGE OF THE TUMOR. A) PROLIFERATION OF EPITHELIOID CELLS WITH INTENSE INTRACELLULAR STAINING. B) SCATTERED LARGE EPITHELIOID TUMOR CELLS WITH VESICULAR NUCLEI AND SOME SPARSE MITOTIC FIGURES.

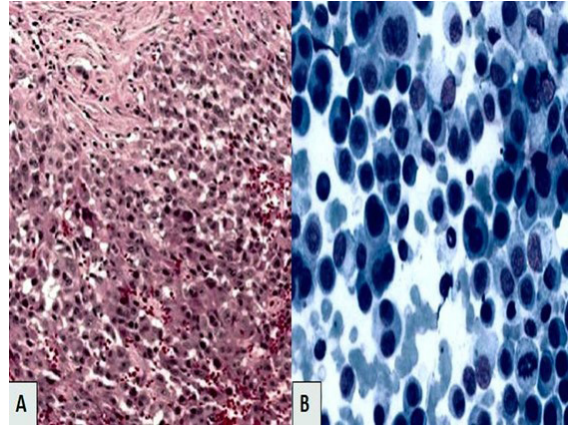
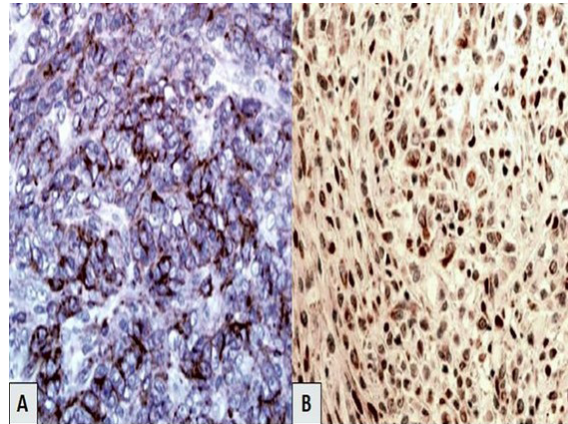


FIGURE 2. IMMUNOHISTOCHEMICAL STAINING. A) POSITIVE FOR EPITHELIAL MEMBRANE ANTIGEN (EMA). B) NEGATIVE FOR INTEGRASE INTERACTOR 1 (INI-1).



## DISCUSSION

Epithelioid sarcoma is a very rare and potentially aggressive mesenchymal neoplasm of soft tissues. It has a nodular or multinodular pattern along fascial structures and tendons with slow growth<sup>(1,4)</sup>. There are two histological types. The distal (or classic) is the most frequent and appears in extremities (especially hands and wrists)<sup>(5)</sup>. The proximal (or axial) type arises from soft tissues in proximal areas (pelvis, perineum, genitals), with very different histological characteristics. It has a more aggressive behavior, with rapid expansion, high frequency of local recurrence, even after resection with wide margins, and a higher frequency of early metastases compared to the distal type<sup>(6)</sup>.

The most common initial symptom of proximal epithelioid sarcoma is that of a painless tumor



of variable size, with slow growth that appears on the chest wall, axilla, inguinal region, thighs and perineum of young adults and women of reproductive age<sup>(1)</sup>. The labia majora are the most frequent site of appearance in the vulva, both superficial and deep tissues, and it manifests as a nodular or multinodular tumor<sup>(7)</sup>. It can be confused with benign conditions such as infectious granuloma, fibrous histiocytoma, Bartholin's cyst, fibroma, lipoma or teratoma, causing delays in diagnosis and treatment<sup>(4,8)</sup>.

Histopathologic evaluation is the only useful and accurate diagnostic method. The macroscopic appearance of proximal epithelioid sarcoma is variable, but it generally appears as a whitish, firm tumor with several well-demarcated satellite nodules and, occasionally, foci of necrosis and/or hemorrhage<sup>(9)</sup>. Microscopically it presents prominent epithelioid cells with sarcomatoid-rhabdoid features and marked cytoplasmic and nuclear atypia<sup>(10)</sup>. The resemblance of epithelioid cells with squamous cells makes differential diagnosis difficult<sup>(3)</sup>. Therefore, immunohistochemistry is useful for the differentiation of these tumors. Epithelioid sarcoma is frequently positive for EMA (85% of cases) and CD34 (50% of cases), in contrast to most soft tissue sarcomas which show nonspecific cytoplasmic expression to these stains<sup>(11)</sup>. They are also negative for S100, CD313 and desmin staining<sup>(6)</sup>. The characteristic immunophenotype of epithelioid sarcoma is loss of nuclear immunoreactivity for INI-1. This is related to biallelic inactivation of the tumor suppressor gene SMARCB1/INI1, which is located on chromosome 22q11.2<sup>(11)</sup>.

Epithelioid sarcoma of the proximal vulvar type should be distinguished from other neoplastic tumors such as primary/metastatic poorly differentiated carcinoma, malignant extrarenal rhabdoid tumor, rhabdomyosarcoma, malignant melanoma, synovial sarcoma, extraskelletal myxoid chondrosarcoma, leiomyosarcoma, desmoplastic small round cell tumor and rhabdomyosarcoma, by histopathological, immunohistochemical and molecular features<sup>(9,12)</sup>.

The treatment of proximal vulvar epithelioid sarcoma is not well defined, but surgical resection with margins greater than 2 centimeters is recommended, similar to the treatment of ex-

tragenital epithelioid sarcoma<sup>(2,13)</sup>. The extent of free margins is the main risk factor for local recurrence, due to the possibility of the presence of satellite lesions around the primary tumor<sup>(2,14)</sup>. Some investigators also recommend resection of suspicious inguinal lymphadenopathies, but there is no evidence that demonstrates any beneficial effect in reducing the frequency of recurrences<sup>(8)</sup>.

Studies on the effects of adjuvant treatment after surgical resection in reducing the risk of tumor recurrence or improving survival do not provide clear evidence either<sup>(12,13)</sup>. Radiotherapy should only be used in patients with high-grade tumors or inadequate surgical margins. It has been described that the recurrence rate is 14% in treated patients compared to 70% in untreated patients, accompanied by a decreased mortality rate (9% compared to 50%)<sup>(12)</sup>. Chemotherapy has been used in different schemes and combinations, which makes it difficult to establish comparisons and conclusions, so it is only recommended in cases of disseminated metastatic disease<sup>(13)</sup>. The most studied cytotoxic agents are doxorubicin, dacarbazine, ifosfamide, cyclophosphamide, etoposide, vincristine and methotrexate<sup>(15)</sup>.

The prognosis of patients with proximal type epithelioid sarcoma is generally unfavorable, due to the high frequency of local recurrence and early metastasis. The 5-year survival rate of patients with proximal tumors is worse than that of distal types, which is between 50% and 80%<sup>(5)</sup>. Those patients with tumors larger than 3 centimeters in diameter, vascular invasion, elevated mitotic index greater than 2 per 10 high power fields, deep location and/or focal necrosis have worse prognosis<sup>(2,13)</sup>. Metastases frequently appear in approximately 60% of cases from satellite lesions of the primary tumor or regional lymph nodes, often within 6 months after surgery<sup>(6)</sup>.

In conclusion, proximal epithelioid sarcoma of the vulva is a rare tumor that presents diagnostic challenges due to its similar appearance to other benign lesions. To date, there is no specific therapeutic approach for this type of lesion. The suggested treatment is total resection of the tumor with wide margins. Due to the high rates of local recurrences and distant metastases, follow-up of cases is necessary.



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