Proximal-type epithelioid sarcoma of the mons pubis: report of a case

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Summary

Introduction: Proximal-type epithelioid sarcoma (PES) represents an extremely rare and aggressive form of soft tissue neoplasm, typically presenting as a painless subcutaneous nodule in the trunk often located in the genital area. *Case report:* A 46-year-old female was subjected to the excision of a growing soft tissue mass in the mons pubis that, at histology, was identified as PES. The tumor showed an extreme aggressiveness involving subsequently adjoining structures and lymph nodes despite subsequent wide surgical resections during the following months. *Discussion:* Gynecologists should pay careful attention to all soft tissue masses of the perineal area or external genitalia. It is important to know the possible genital localization of PES which, although rare, is an aggressive high-grade soft tissue tumor with a deceitful behavior, poorly sensitive to chemotherapy and radiotherapy. Surgery, though wide and demolitive, often fails to obtain the necessary radicality.

Key words: Sarcoma; Epithelioid sarcoma; Soft tissue neoplasms; Female genitalia.

Introduction

Proximal-type epithelioid sarcoma (PES), also called large-cell type [1], represents an extremely rare form of epithelioid sarcoma differing from the distal counterpart for an aggressive pattern of local recurrence despite negative margins and a stronger propensity for early metastasis [2, 3]. Epithelioid sarcoma is commonly cited as example of ungradable sarcoma [4, 5], due to the failure in capturing the essential histological information of this rare disease. If the distal form is infrequent, even much rarer is the proximal-type, with the perineum as a quite frequent location both in men and women. Particularly the vulvar site has been described [6].

The symptoms can be different according to the site of the neoplasm [7, 8], but PES typically presents between the 3rd and 5th decade of life as a painless subcutaneous nodule in the trunk (mainly located in the pelvic area, perineus, external genitalia) [3, 9].

This tumor shows sheets of large cells with prominent nucleoli resembling a poorly differentiated carcinoma [1], and immunohistochemical analysis is important for the correct diagnosis [10, 11].

Despite radical surgery, the prognosis for this tumor is generally poor and the role of adjuvant therapy remains unclear owing to the deficiency of evidence.

Case Report

The patient, a 46-year-old Caucasian female, who underwent laparoscopic uterine myomectomy one year before at our Gynecological Clinic, presented to our Department with a painless growing soft tissue mass in the mons pubis. The lesion, noticed three weeks before as a small pimple, was 5.5 x 4 cm at presentation. Considering it as a probable soft tissue sarcoma, we avoided a biopsy and the lesion was excised.

On cut sections, the lesion was ill defined, with multinodular confluent whitish masses, often with necrosis. The lesion extended to the deep margins. At histology, the neoplasm disclosed a granuloma-like pattern with nodules of epithelioid cells and frequent central necrosis. Clusters of lymphocytes and also follicles were present (Figure 1a) mainly peripherally, but also intermixed. On high power view, sheets of large cells, mainly rounded polygonal with amphophilic cytoplasm, enlarged vesicular nuclei, and prominent central nucleoli were observed. The tumor, resembling a poorly differentiated carcinoma, disclosed discohesive cells at the border of the nodules. Keratin stain (MNF116) was positive in some cells (Figure 1b); vimentin was widely positive. Other immunohistochemical markers were tested (AE1, AE3, CAM5-2,CK7 negative; EMA focally positive; CD34, CD56, CD79a negative; S100, MB45, NSE, chromogranin, synaptophisin, negative; lymphocytes were mainly CD20 positive). Hemorrhage and necrotic changes were common. Margins, mainly the deep ones, were positive. The patient underwent specialistic supervision and a final diagnosis of PES was made.

Ten days later, since the surgical margin was positive, the patient underwent superior radical vulvectomy (preserving the clitoris, labia minora and majora and fourchette) and bilateral superficial and deep crural inguinal lymphadenectomy. The histological findings demonstrated the presence of several neoplastic foci – less than 3 mm in diameter – infiltrating the subcutaneous tissue close to the right resection margin; all 16 crural inguinal lymph nodes were negative.

During the following ten months the patient underwent five surgical resections performed by different surgeons at our Gynecological Clinic and later also at a General Surgery Service. Surgeons noticed a particular aspect of the margins, described as scattered "white spots" suggesting neoplastic infiltration and, despite subsequent cutting, a clean margin result is often not easy to reach. When apparently disease-free, the local

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Table 1. — *Timing of surgical excisions and main findings*.

Sequence of surgery	Site/resection	Histology	Margins	Tumour spread or neural invasion	Vascular, lymphatic
February	Mons pubis mass (5.5 cm)	Confluent nodules (5 x 4 cm)	+	Subcutis	–
February	Radical superior vulvectomy	Small foci (max 0.3 cm)	+	Subcutis	Lymph nodes: 16 neg
March	Local enlargement	–	–	–	–
May	Inner right tight nodule: 6 x 5.5 cm	Confluent multiple nodules	+	Infiltrating striated muscle	Lymph nodes: 1 pos 10 neg
May	Resection of: Inner right tight: 4 x 3 cm	Confluent multiple nodules	+	Infiltrating striated muscle	Vascular and neural invasion
	Inner left tight: 3 x 2.5 cm	Confluent multiple nodules			
December	Resection of: Right tight: 7 x 5 x 4 cm	Multiple nodules (max 0.3 cm)	+	Infiltrating striated muscle	Vascular and neural invasion
	Labia minora	–	–	–	–
	Gracilis muscle margin	–	–	–	–
January	Resection of: Abdominal wall: 10.5 x 9.5 cm	3 nodules (max 5.2 x 2.5 cm)	+	Subcutis, striated muscle invasion	Vascular and neural invasion
	Pubic tubercle	–	–	–	–
	Partial omentectomy	–	–	–	–

recurrence of the sarcoma negated the radicality of the surgery (Figure 1c-f).

The tumor demonstrated an extreme aggressiveness involving subsequently adjoining structures as the fascial sheet, nerves and vascular wall, with extension to the genital, inguinal and thigh muscles and, finally, also the abdominal wall (Figure 1c-f). Despite this, lymphatic involvement, generally limited, was evidenced only histologically, with an isolate micro metastasis found in one of the 11 removed lymph nodes.

Table 1 reports timing of surgical excisions and main histological findings and Figure 1c-f shows tumor spread in relapses.

In association with surgery, the patient underwent adjuvant polychemotherapy with epirubicin and ifosfamide, but after six cycles the treatment was suspended due to the worsened clinical condition. This therapy was integrated with pelvic and inguinal radiotherapy (45 Gy in 5 fractions).

Computerized tomography, performed after three months, showed the presence of hypervascularized foci in the abdominal wall, inguinal area, anterior region of both thighs and a coarse neoplastic area surrounding the bladder.

Considering the severe clinical condition, only palliative with antalgic therapy was possible, and the patient died two months later.

Discussion

This case underlines the relevance of paying careful attention to all soft tissue masses, in particular painless, even if the lesion does not show particular suspicious features. Epithelioid sarcoma is an uncommon aggressive high-grade soft-tissue tumor [12], typically appearing as a subcutaneous or deep dermal mass in distal portions of the extremities of adolescents and young adults [6, 13], whereas the proximal-type grows up in proximal parts of middle-aged and older people.

Correct histological diagnosis can be difficult considering the extreme rareness of the disease. Small superficially located tumors with nodular pattern are likely to be mistaken for an inflammatory process as necrotizing infectious granuloma. Some epithelioid sarcomas are hard to distinguish from a wide array of epithelioid-appearing malignant soft tissue neoplasms and poorly differentiated carcinomas [14-16]. The number of pathologists dealing with female genital disease, that can be named as expert in this particular kind of sarcoma is limited, and the main referential texts of gynecologic pathology do not even mention PES among the possible vulvar lesions or they only cite it [17]. For this reason it is essential to have at disposal a highly qualified histopathological center with experience to avoid incorrect diagnoses that can lead to wrong therapeutic decisions. Immunohistochemical examination provides a contribution to the diagnosis, but the pathologist's specific experience in the field of soft tissue sarcoma is fundamental. Epithelioid sarcoma usually expresses epithelial membrane antigen, vimentin and cytokeratins, and is often positive for CD34, but several other antigens can be expressed. The ultrastructure displays epithelial and mesenchymal features including myofibroblastic differentiation. In addition, many cases display chromosomal abnormalities in the 22q region, but this can not be considered as specific [10, 18].

The mainstay of treatment in case of proximal-type epithelioid sarcoma is surgery and a radical resection is necessary as in all high-grade soft tissue sarcomas [19]. Extensive operations were performed in our case by different expert surgeons, but often surgery results only apparently radical and insufficient to improve prognosis, considering the extreme aggressiveness and the deceitful behavior of the disease.

Patients often develop multiple local recurrences with subsequent metastases in 30-50% of the cases [20]. As described, our case well exemplifies the propensity of PES to disseminate in a centripetal way, at first with local spread towards the aponeurosis and tendon sheaths, and successively infiltrating also vessels, nerves and the lymphatic system.

Fig. 1a

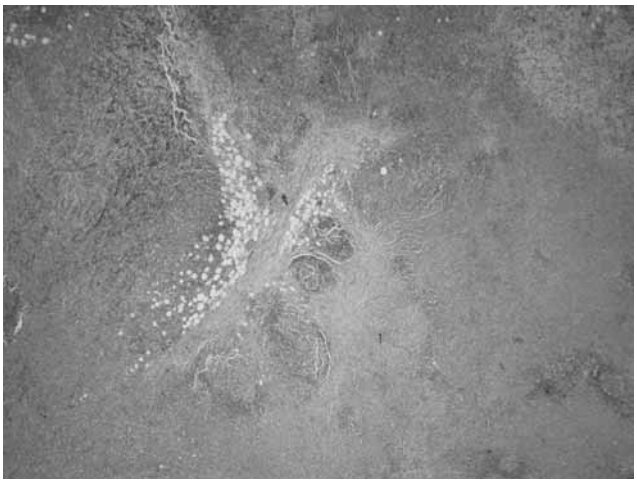

Fig. 1b

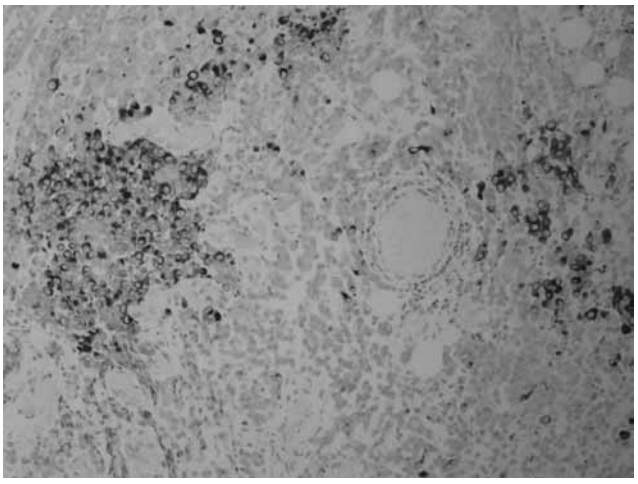

Fig. 1c

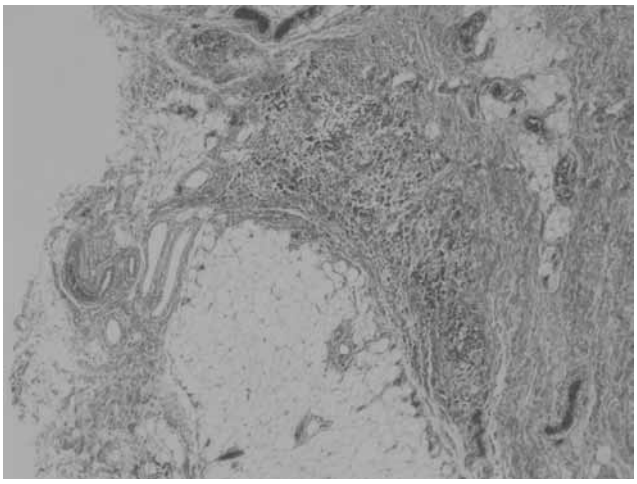

Fig. 1d

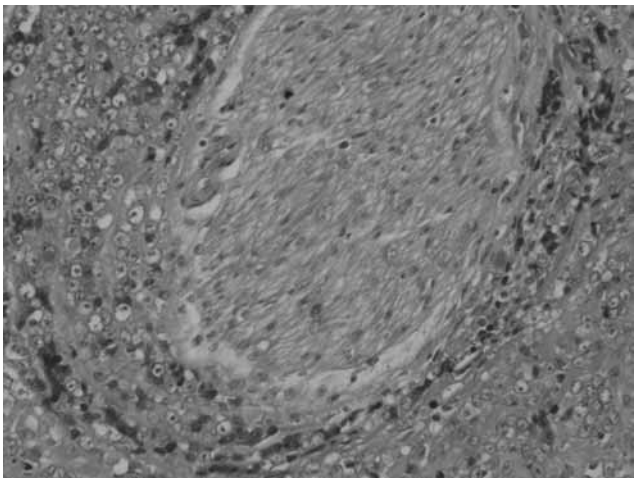

Fig. 1e

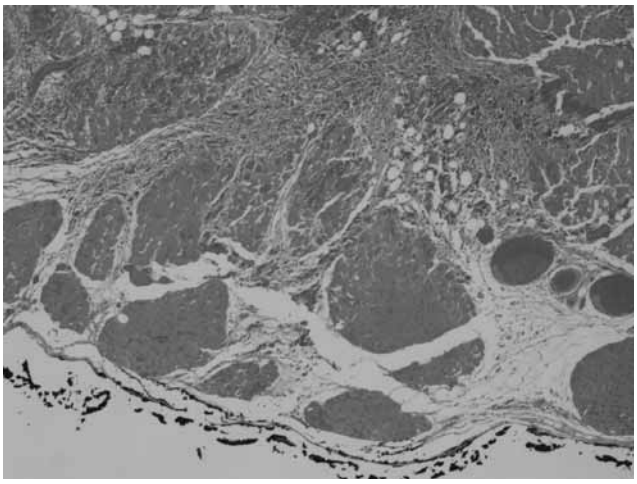

Fig. 1f

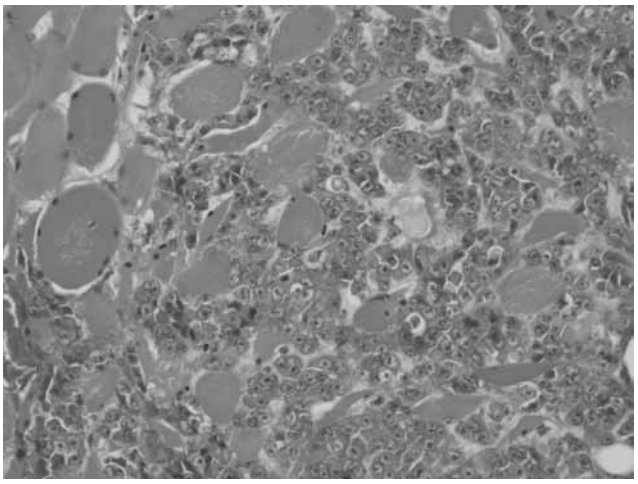

Figure 1. — a) First biopsy: multinodular pattern; aggregates of lymphocytes in follicles (H&E 12.5x).
b) First biopsy: at immunohistochemistry scattered groups of cells are positive for cytokeratins (MNF116 100x).
c) First surgical enlargement. Scattered microscopic foci (< 3 mm) of discohesive neoplastic cells, mainly in the deep right margin (H&E 31x).
d) Fifth surgical enlargement: neoplastic cells with large vescicular nuclei and prominent nucleoli surrounding and infiltrating a neural trunk (H&E 200x).
e) Last surgical excision: neoplastic cells infiltrating the muscle of the abdominal wall close to the resection margin (marked by India ink) (H&E 25x).
f) Detail of Figure 1e (H&E 200x).

Considering the insidious behavior of PES, the gold standard would be to ensure, with the first surgical approach, the best level of radicality, avoiding the necessity of a following intervention to enlarge the margins of resection. Some authors underline that the execution of needle or excision biopsy, with a diagnostic aim, can be dangerous considering the high risk of neoplastic cells spreading; this concept, important in all oncological surgery, is actually essential in case of high-grade sarcoma [5]. Moreover the literature reports that epithelioid sarcoma in cytology specimens shares many features with other neoplastic and non-neoplastic conditions and that the relatively low specificity in the classification is the main limitation of fine needle aspiration biopsy [21, 22].

Taking into account the difficulty for the surgeon to identify the limits of the mass and the underhanded way of spreading, the necessity to perform wide demolitive surgery as soon as possible is evident. Mass extirpation with wide margins (> 2 cm) should be integrated by locoregional lymphadenectomy, although, as in our case, the lymph nodes are usually involved later.

It is also important to underline that radical intervention, which should be fundamental as the first approach, is not common in case of unsuspected trivial small masses, all the more considering the absence of elements capable of addressing suspected malignancy.

Chemo- and radiotherapy were performed without effect, confirming that adjuvant therapy presents limited efficacy to control both local relapse and metastases [5]. Nevertheless, adjuvant radiation therapy is recommended in soft-tissue sarcoma, while the efficacy of chemotherapy is still unclear and only a few drugs result effective, even if only partially: anthracycline, ifosfamide, dacarbazine [5].

Few cases of this rare sarcoma localized in the female genital area have been described until now; a recent review considers about 20 cases of vulvar localization described in the literature [3]. The low clinical experience in dealing with this kind of pathology can lead to diagnostic errors due to the rareness of the disease and to lack of knowledge about soft tissue sarcoma in the scientific background of the gynecologist.

Considering the possible localization of PES in the genital region, though rare, awareness of the existence of this entity and knowledge of its deceitful behavior are important for a quick and correct management. Gynecologists should keep in mind PES as a possible differential diagnosis when a subcutaneous mass of the perineal area or external genitalia is observed during a visit [22, 23].

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