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Apocrine carcinoma of the vulva. Case report and review of literature

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Summary

Objectives: To report a case of apocrine adenocarcinoma of the vulva and introduce the sentinel node dissection as a method to diagnose it. *Materials and Methods:* Description of a case of a 77-year-old woman with histological diagnostic of apocrine adenocarcinoma of the vulva and literature review of the 16 cases published from 1954 to nowadays. *Results:* Treatment of vulvar apocrine carcinoma is controversial given its low incidence and the small number of cases which have been reported. *Conclusion:* Selective sentinel lymph node biopsy may provide a valid option in selected patients to decrease their clinical complications.

Key words: Apocrine carcinoma; Vulva; Sentinel node biopsy.

Introduction

Vulvar neoplasms represents 4% of all tumors found in the genital tract. The primary adenocarcinoma of the vulva is a very rare entity and it is classified into three categories: sweat gland carcinomas, extramammary Paget's disease, and primary breast carcinoma of the vulva.

Through this paper the authors would like to introduce a case of apocrine adenocarcinoma of the vulva which is an extremely rare tumor; to this day few cases have been reported worldwide.

Materials and Methods

A literature review of the 16 cases that have been reported of apocrine adenocarcinoma of the vulva from 1954 to date are included. The research databases of Medline, Scielo, Pubmed, and Cochrane Library were searched using the words "apocrine vulva cancer". In each of the cases the description included: study author, country of origin, age, description of clinical lesion, TNM tumor classification, and treatment. The age range of these patients were between 34 and 89 years, resulting in an average age of 63.5. Patients were classified into three groups: without local and distant metastasis (group 1), locoregional metastasis (group 2), and distant metastasis (group 3).

In the first group (Table 1) the authors found seven cases, four treated with local excision, two with hemivulvectomy, and one with hemivulvectomy and bilateral lymphadenectomy. In the second group (Table 2) the authors found five cases, one treated with radical vulvectomy and adjuvant radiotherapy, two cases treated with hemi and complete vulvectomy and bilateral lymphadenectomy, one with radiotherapy, and finally a case without reported treatment. In the third group (Table 3) the authors found four cases, one treated with hemivulvectomy, bilateral lymphadenectomy, radiotherapy, and adjuvant chemotherapy; one treated only with adjuvant chemotherapy; another one with palliative treatment; and one exceptional case treated only with tamoxifen therapy with complete response.

Case Report

A 77-year-old woman with family history of mother with endometrial cancer and daughter with breast cancer. Her personal history was positive for arterial hypertension and she was operated for appendicitis, tonsillitis, narrowing of the spinal canal, and lower right member liposarcoma subsequently treated with chemotherapy. Age of menarchia: 12, gravida 6, para 5, age of menopause: 40. The patient was referred to the present center with the diagnosis of erithematous formation in the introitus. On vulvar examination a warty, rigid consistency, erithematous and nonulcerated lesion of 3×1.5 cm involving minor right labia was noticeable. Vagina and cervix appeared atrophic and bimanual examination was normal. No inguinal nodes were palpated.

Transvaginal ultrasound revealed an anteverted uterus with normal shape and size, with linear endometrial midline, without pathological adnexal findings, and no ascites. Extension study abdominopelvic contrast CT scan was performed with no evidence of hepatic lesions and without pelvic or retroperitoneal lymph node involvement.

Complete local excision of the lesion was performed. Histologic examination described a primitive apocrine adenocarcinoma of the vulva including negative surgical margins and without perineural and lymphovascular invasion (Figures 1, 2, and 3). The adenocarcinoma cells expressed epithelial membrane antigen (EMA) (Figure 4), cytokeratin (CK)7, CK 19, carcinoembryonic antigen (CEA) (Figure 5), and showed Ki 67 index of 20% (Figure 6). Estrogen and progesterone receptor analysis was negative. Given the uncommon histopathological nature, the case was discussed within a multidisciplinary oncologic group which decided to widen the security resection margins, associated with sentinel node dissection and complete vulvectomy with

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Table 1. — *Literature review of 7 case reports of apocrine adenocarcinoma of the vulva without local or distant metastasis.*

Study	Country	Age	Clinical lesion	TNM	Treatment
Pelosi *et al.* 1991	Italy	40	Tender nodule, left labium minus, painful	T1N0M0	Local excision
Robson *et al.* 2008	U. Kingdom	65	2 cm	T1N0M0	Local excision
Robson *et al.* 2008	U. Kingdom	59	2 cm	T1N0M0	Local excision
Robson *et al.* 2008	U. Kingdom	56	0.8 cm	T1N0M0	Local excision
Hou *et al.* 2010	China	34	Mass in right labia majora, 1 cm	T1N0M0	Right VT
Kajal *et al.* 2013	Canada	67	Enlarging left vulvar lesion thought to be cystic	T1N0M0	Left VT
Ota *et al.* 2002	Japan	58	Hard, 7 mm, left labia majora	T1N0M0	Left VT + LGND

VT: vulvectomy; HT: hemivulvectomy; BGND: bilateral groin nodal dissection; LGND: left groin nodal dissection; RT: radiotherapy; QT: quimioteraphy; TNM: classification tumor size – lymph nodes - distant metastasis.

Table 2. — *Literature review of 5 case reports of apocrine adenocarcinoma of the vulva with locoregional metastasis.*

Study	Country	Age	Clinical lesion	TNM	Treatment
Nazário *et al.* 1989	Brazil	58	2 cm, solid, right labium minus, bleeding	T1N2M0	Radical VT + RT
Khaled *et al.* 2008	Canada	89	Ulcerated mass, involved left labia majora, clitoris and mons	T2N2M0	Complete VT + LGND
Stueben *et al.* 2012	USA	72	1 cm, infiltrative, ulcerated	T1N1M0	HT+ LGND
Dietel *et al.* 1981	Germany	70	2.5×1.5 cm	T2N1M0	RT
Baker *et al.* 2013	USA	69	-	T?N1M0	Not reported

VT: vulvectomy; HT: hemivulvectomy; BGND: bilateral groin nodal dissection; LGND: left groin nodal dissection; RT: radiotherapy; QT: quimiotherapy; TNM: classification tumor size – lymph nodes - distant metastasis.

Table 3. — *Literature review of 4 case reports of apocrine adenocarcinoma of the vulva with distant metastasis.*

Study	Country	Age	Clinical lesion	TNM	Treatment
Plachta *et al.* 1954	USA	64	Weeping erythema and whitish areas about vulvar surface	T2N2M1	Symptomatic therapy
Kiyohara *et al.* 2003	Japan	72	Bruise-like tumor, 4×7 cm, on left inguinal area	T2N0M1	Inoperable. QT
Bagwan *et al.* 2008	Switzerland	71	Hard, 1.5 cm, left labia majora	T1N2M1	Left VT + BGND + RT+ QT
Goldstein *et al.* 2012	U. Kingdom	72	Relapse; papule within right inguinal region	T1N1M1	Tamoxifen therapy

VT: vulvectomy; HT: hemivulvectomy; BGND: bilateral groin nodal dissection; LGND: left groin nodal dissection; RT: radiotherapy; QT: quimiotherapy; TNM: classification tumor size – lymph nodes - distant metastasis.

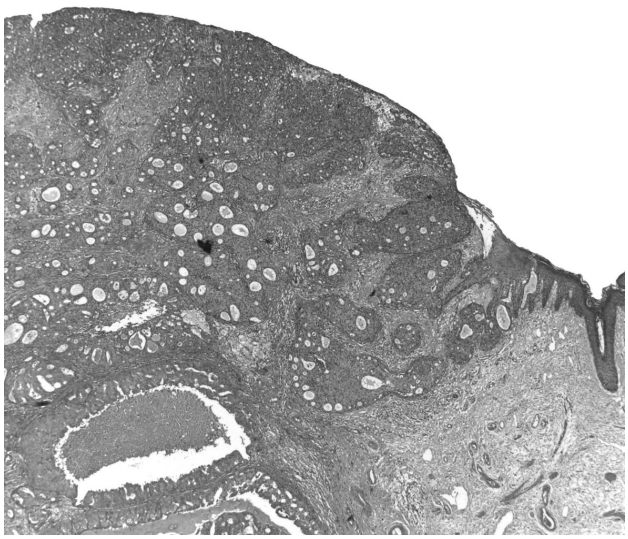

Figure 1. — Intraepidermal spread of tumoral tissue composed of solid and ductal areas ×2.

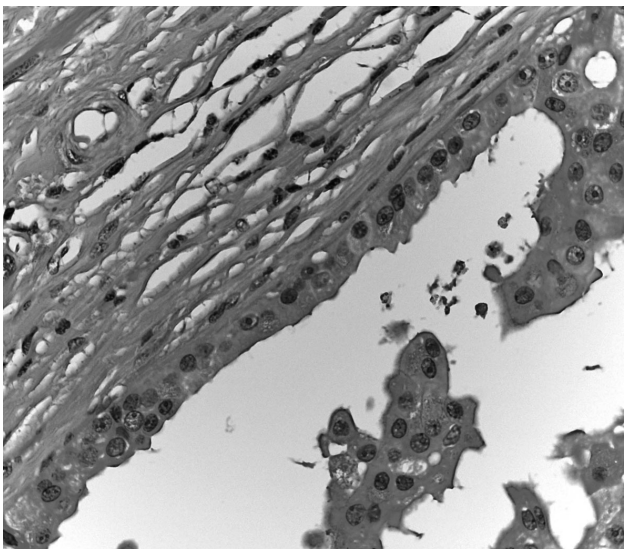

Figure 2. — Apocrine cells with wide cytoplasm and circular nuclei with characteristic features of decapitation ×20.

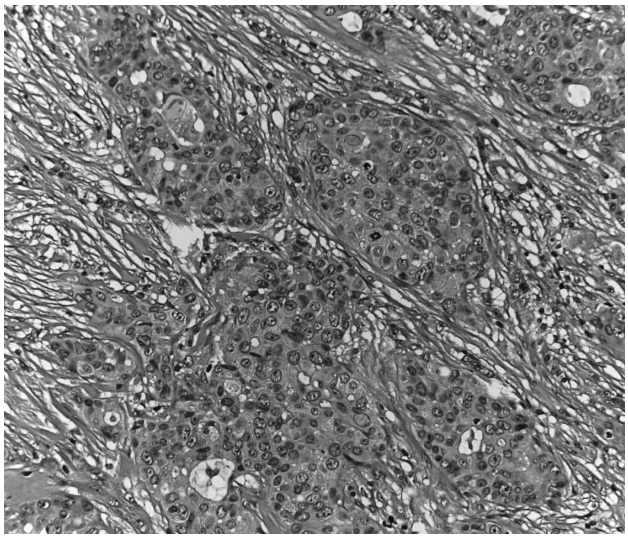

Figure 3. — Solid nest of tumor with characteristic malignant features: focal stromal infiltrating areas composed by mitotic cells with significant nuclear atypia ×10.

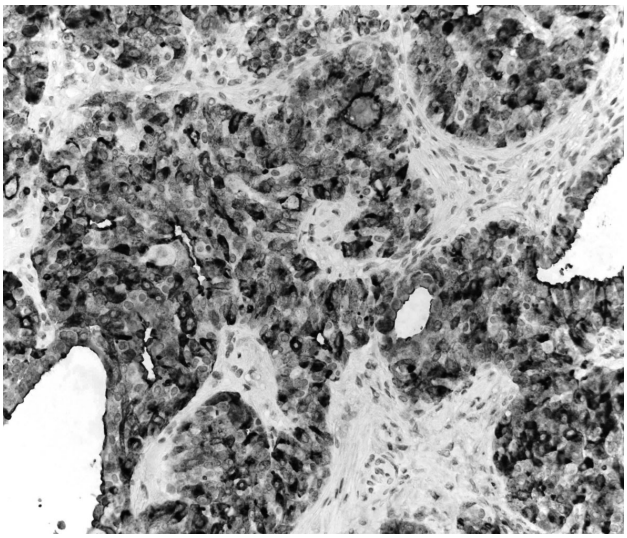

Figure 4. — EMA ×10.

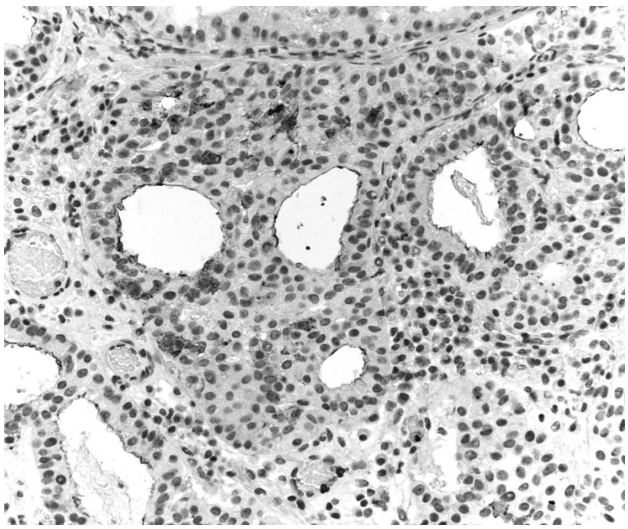

Figure 5. — CEA ×10.

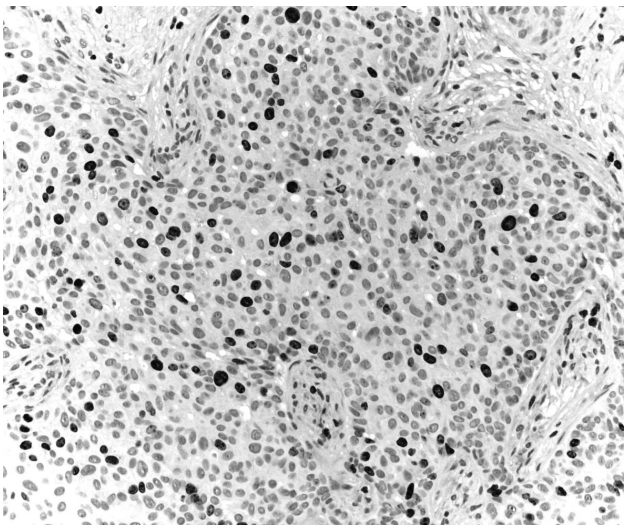

Figure 6. — Ki-67 index, 20% ×10 .

inguinal node dissection depending on the findings of the anatomopathological intraoperative examination. Scintigraphy with Technetium (T99m) was executed and two sentinel inguinal nodes were identified in right chain, one of them accessory. Security wider resection margins and dissection of sentinel nodes were performed and microscopic study revealed absence of tumoral invasion. In the postoperative follow-up three rigid consistences and painless lymphocyst formations appeared, the largest of them of four cm, and ultrasound study confirmed these discoveries. Follow ups and management were recommended. Currently, after two years of routinary clinical checkups the patient is alive, the lymphocyst formations have disappeared, and there has been no evidence of tumor relapse.

Discussion

Primary adenocarcinoma of the vulva is a rare entity that can be classified as sweat gland carcinomas, extramammary Paget's disease, and primary breast carcinoma of the vulva. This neoplasm occasionally may have its origin from Bartholins glands.

The histogenesis of these tumors are unclear. Two theories have been proposed. The first one suggests that their origin could be on sweat glands native to the vulva; the second theory argues that the origin is an ectopic breast tissue [1].

Apocrine carcinoma of the vulva is an extremely rare subtype and may occur in conjunction with extramammary Paget's disease [2, 3]. This tumor can be diagnosed in several tumor stages: from adenocarcinoma in situ to invasive forms. As has been described, potential of lymphatic invasion and metastasis is not negligible [4, 5].

Treatment of vulvar apocrine carcinoma is controversial given its low incidence and the small number of reported cases. Surgery remains the first-line of treatment in these tumors. As a rule of squamous vulvar carcinoma, surgeons make different types of incisions depending on the size and depth of the lesion. In the present case, given the size of the tumor, wide local excision was decided. Treatment with tamoxifen in tumors that present positive estrogen hormone receptors, may also be a therapeutic alternative, especially in cases where the first-line surgical treatment is discarded [4].

Regarding inguinal lymphadenectomy, there is no consensus. Although published data are quoted, it has been shown that these tumors metastasize relatively frequent to inguinal lymph node chains [2, 5, 6]. In early stages without palpable nodes, as in the present case, ipsilateral lymphadenectomy should be indicated as a first-line treatment. In recent times, as is evident from the GROINSS-V study by Van der Zee *et al.* [7], selective sentinel node biopsy reduces the number of surgical complications, such as lymphocyst, lymphedema, neurological or vascular injury or others. In the present case the authors report an apocrine vulvar adenocarcinoma with inguinal sentinel node biopsy and they propose it as an efficient therapeutic option in early stages, given the benefits in terms of reduced morbidity described above. The occurrence of complications is greatly diminished by performing selective sentinel node biopsy instead of inguinofemoral lymphadenectomy. As evidenced by the present case, the appearance of three inguinal lymphocyst in surgical site could be explained because the patient had previously been operated on a liposarcoma in the same region, consequently without adequate peripheral circulation return.

Conclusion

Apocrine adenocarcinoma of the vulva constitutes one of the rarest neoplasm worldwide, with uncertain evolution and prognosis. There is inexistent consensus for therapeutic management of this tumor because of its low incidence and infrequent report cases.

Selective sentinel lymph node biopsy may provide a valid option in selected patients, decreasing complications, risk associated to other more invasive procedures. like inguinofemoral lymphadenectomy. The absence of clinically negative inguinal lymph nodes, tumor size, and no infiltration of adjacent organs makes this technique a valid and recommended alternative because it has a negative predictive value close to 100%.

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