

Malignant spiradenoma/cylindroma of the vulva

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ABSTRACT

يعد الورم الغدي العرقي الأسطواناني والخبيث من الفرج من الأورام النادرة للغاية في الملحقات الجلدية. نستعرض في هذا المقال الملامح السريرية لحالة امرأة عمرها 58 عاماً تقدمت مع ورم غدي عرقي أسطواناني الخلايا وخبيث نشأت في الفرج وانتشر إلى الغدد الليمفاوية الأربية. ولقد تم إجراء الاستئصال الجراحي مع هوامش كافية وتشريح العقد الليمفاوية. لقد قمنا بالدراسة المناعية النسيجية الكيميائية باستخدام أجسام مضادة للمستضدات، وإيما، وسيتوكيراتين 5/6، وp63، والمضاد السرطاني الجنيني، وسيتوكيراتين 7، وأكتين العضلات الملساء، وإس 100. وقد كانت أجزاء الورم المشابهة للورم الغدي العرقي إيجابية لإيما، والمضاد السرطاني الجنيني من ناحية أخرى. وأظهرت أجزاء الورم المشابهة لفصيصات الورم أسطواناني الخلايا تفاعلية مناعية قوية لب63، وسيتوكيراتين 5/6، في حين أن كلا الورمين كانا سلبين إلى إس 100، وأكتين العضلات الملساء، وسيتوكيراتين 7. وهكذا ينبغي أن يُنظر إلى الورم الغدي العرقي الأسطواناني الخلايا والخبيث في التشخيص التفريقي من الأورام الأولية والثانوية للملحقات الجلدية المنتشرة في الفرج. كما وينبغي تشجيع الدراسات لمثل هذا النوع من الأورام وعلى نطاق أوسع.

Malignant spiradenoma/cylindroma of the vulva is an extremely rare adnexal tumor. We report the clinicopathological features of a 58-year-old woman who presented with malignant spiradenoma/cylindroma originating in the vulva and metastasized to the inguinal lymph nodes. Surgical excision with adequate margins and lymph node dissection was performed. Sections from the case were stained with Periodic Acid Schiff stain before and after diastase. Immunohistochemical study of the case using antibodies to carcinoembryonic antigen (CEA), epithelial membrane antigen (EMA), cytokeratin 5/6 (CK 5/6), p63, cytokeratin 7 (CK 7), smooth muscle actin (SMA), and S100 were performed. Microscopic examination revealed that spiradenoma nodules were positive to EMA and CEA. However, the cylindroma lobules showed strong immunoreactivity to p63 and CK5/6, whereas both tumor components were negative to S100, SMA, and CK7. Malignant spiradenoma/cylindroma is a rare tumor with controversial histogenesis that should be considered

in the differential diagnosis of primary adnexal carcinoma and secondary metastatic tumors in the vulva. Further studies on a wider cohort should be encouraged.

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Malignant cutaneous adnexal neoplasms are one of the most challenging areas of dermatopathology. Carcinomas of the adnexal glands are rare group of tumors with potential for local destruction, metastasis and high recurrence rates following surgical excision.¹ They are believed to arise from transformation of a long-standing benign tumor. The specific classification of eccrine carcinomas is complex because of the paucity of reported cases, heterogeneity of histological features, and dissimilarity of some types to their benign counterparts.² Recent study tried to elucidate the cell of origin of spiradenoma and cylindroma; spiradenomas were believed to be of eccrine origin, cylindromas were believed to be of apocrine origin, while spiradenocylindroma, a tumor occupying an intermediate position, is a hybrid form.¹ An elaborate immunohistochemical study² of spiradeno/cylindroma was conducted and provided compelling evidence that the cell of origin for both of these tumors might be a multipotential cell of abortive adnexal anlagen. On the other hand, other study¹ suggested an origin from folliculo-sebaceous-apocrine unit that would help to explain the occurrence of hybrid forms of these tumors, such as the 2 malignant variants in this report.¹ Precise identification and classification is of

significant importance because therapy and prognosis vary according to microscopic appearance. The aim of the present work is to study the clinicopathological features and immunohistological characteristics of this rare tumor entity.

Case Report. A 58-year-old woman of African descent presented with a complaint of progressively enlarging mass on the right labia majora of one-year duration. She reported no pain or other symptoms. Personal and family medical history was unremarkable except for hypertension for which she had been taking Tenomin. She had no prior history of gynecologic complaints. She was diagnosed as a case of vulval carcinoma following an incisional biopsy that was diagnosed as basal cell carcinoma versus squamous cell carcinoma with basaloid features, and underwent radical vulvectomy with bilateral inguinal lymphadenectomy. Laboratory workup was ordered including complete blood count, liver profile, standard serum chemistry and chest radiograph. All blood tests were within normal limits except for hepatitis B surface antigen that was positive. Chest radiograph showed no evidence of metastasis. Gross examination of the vulvectomy specimen showed an exophytic firm nodular mass measuring 1x1cm, in the right labia majora. The mass was fungating over the skin surface with an area of ulceration (<1cm). On serial sectioning, the mass was invading deeply to the underlying tissue measuring 6x5x4 cm. The cut surface was firm, grayish yellow, and lobulated with area of hemorrhage and necrosis (Figure 1). The mass was located 1-cm away from the deep margin. Four inguinal lymph nodes were submitted for histological evaluation.

The specimens were fixed in 10% buffered formalin, embedded in paraffin, and stained with hematoxylin and eosin and Periodic Acid Schiff (PAS) stain before and after diastase (PAS-D) treatment. Immunohistochemical studies were performed via the avidin–biotin peroxidase complex technique using an automatic immunostainer (Ventana FBMK 750600, Ventana Inc., Tucson, AZ, USA) for the following antibodies; carcinoembryonic antigen (CEA) (Dako Cytomation, Glostrup, Hovedstaden, Denmark; 1:50), epithelial membrane antigen (EMA) (Novocastra, Newcastle, UK; 1:200), cytokeratin 5\6 (CK5\6) (Dako Cytomation, Glostrup; dilution1:100), P63 antigen (Novocastra, Newcastle, UK; 1:50), cytokeratin 7 (CK7) (Novocastra, Newcastle, UK; 1:100), S100 (Dako Cytomation, Glostrup, Hovedstaden, Denmark; 1:200) and smooth muscle actin (SMA) (Dako Cytomation, Glostrup; Hovedstaden, Denmark 1:50). Microscopic

examination revealed a well-circumscribed neoplastic growth occupying the dermis covered by focally ulcerated epidermis. There was no attachment of the tumor mass to the epidermis. At low power examination, the tumor was formed of 2 different components (Figure 2); the first component (spiradenoma pattern) was formed of regular round lobules composed of solid masses and interanastomosing trabecula with scattered glandular lumina and focal cystic dilatation filled with eosinophilic material. Two cell populations were noted; peripheral dark cuboidal cells and central larger cells with paler cytoplasm and distinct cell membrane. Occasional lymphocytic infiltrate was noted. Focal atypical features in the form of hyperchromatism, pleomorphism, and occasional mitosis were evident (Figure 3). The PAS stain showed positive luminal surfaces and intraglandular



Figure 1 - Cut surface of tumor mass covered by ulcerated skin. The tumor is lobulated, firm and grey-white in color, with areas of hemorrhage and necrosis.

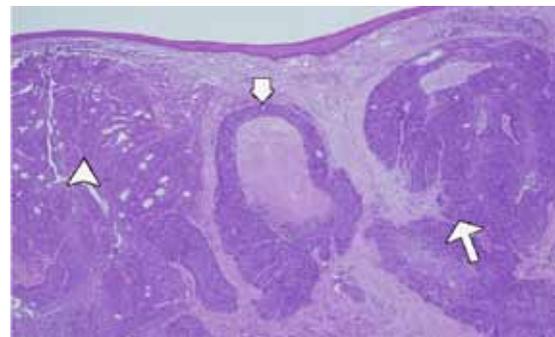


Figure 2 - Low-power view demonstrating a lesion comprised of multiple tumor islands showing solid sheets with intervening glandular lumina (arrow head), solid sheets with peripheral palisading (arrow) and masses with central necrosis simulating comedo pattern and more infiltrative appearance at the periphery (wide arrow). No connection to the overlying skin. (Hematoxylin and Eosin, X100).

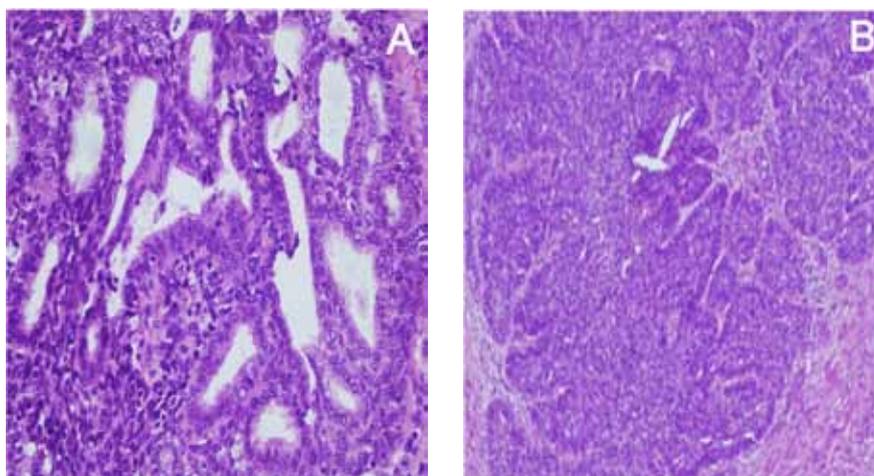


Figure 3 - High power view of the previous case showing: **A)** intertwining cords with glands formation representing spiradenoma zone (Hematoxylin and Eosin X400). **B)** Solid sheets of basaloid cells with peripheral palisading representing cylindrocarcinoma areas. Note irregular infiltrative borders of tumor masses. (Hematoxylin and Eosin X200)

secretion resistant to digestion. Another component (cylindroma pattern) was composed of solid lobules arranged in a mosaic pattern and composed of cuboidal basaloid cells having uniform appearance with round nuclei, high nuclear-cytoplasmic ratio, and frequent mitosis. Peripheral palisading tall columnar cells outlined tumor nodules. **Figures 2 & 3** shows PAS stain focally highlighted thinned-out basement membrane surrounding solid masses. The tumor showed the transition to an invasive component consisted principally of tumor cords, solid lobules with central necrosis giving a comedo-like pattern (**Figure 2**) and individual cells. The intervening stroma is fibrous and shows lymphocytic infiltrate. The tumor was seen reaching near the inked surgical safety margins. Lymph vascular invasion were observed. Two out of 4 inguinal lymph nodes were positive for metastatic carcinoma. The immunohistochemical profile of 2 tumor components is shown in **Table 1**. The spiradenoma lobules showed strong positive staining to CEA, and EMA whereas they were negative to CK5/6, and CK7 (**Figures 4 & 5**). Weak focal positivity to P63 and S100 was seen. On the other hand, the cylindroma lobules showed strong immunoreactivity to p63 and CK5/6 (**Figure 6 & 7**), occasional positivity to EMA and S100 while negative to CEA, CK7, and SMA.

Metastatic workup (bone scan, CT scans of the chest, abdomen, and pelvis) was negative. No adjuvant radiation or chemotherapy was administered. The patient will be followed-up every 3 months with chest radiograph, and there was no evidence of recurrence for the last one and half years.

Table 1 - Comparison between immunohistochemical results in 2 tumor components.

Immunohistochemical stains	Spiradenoma foci	Cylindroma foci
Cytokeratin 5/6	-ve	+ve
Cytokeratin 7	-ve	-ve
P63	Weak, focal	+ve
Carcinoembryonic antigen	+ve	-ve
Epithelial membrane antigen	+ve	occasional
S100	-ve	focal
Smooth muscle actin	-ve	-ve
-ve - negative, +ve - positive		

Discussion. As a result of the rarity of malignant spiradenoma/cylindroma, the correct diagnosis of this tumor entity is a challenge, particularly when it occurs in a rare location such as the vulva; most of these tumors occur in scalp, trunk, and proximal extremities.¹⁻⁶ The disease is usually confused with benign and malignant adnexal tumors, as well as metastatic carcinomas from the cervix, endometrium, kidney or urothelial tract. Imaging techniques are mandatory to exclude a metastasis from any of these origins (as was carried out in our case) before giving such a diagnosis. The histological diagnosis of malignant spiradenoma/cylindrocarcinoma depends mainly on the detection of foci of benign spiradenoma/cylindroma with transition to malignant areas.^{1-4,6-7} Our case showed benign spiradenoma component showing transition to malignant spiradenoma mixed with a malignant cylindromatous

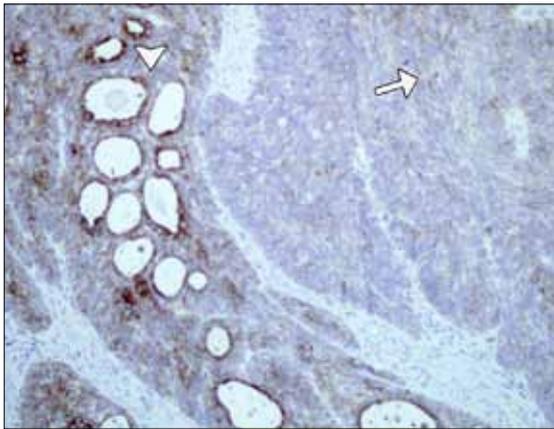


Figure 4 - Immunohistochemical stain for epithelial membrane antigen showing positive luminal staining in spiradenoma areas (arrow head), in contrast to occasional staining in cylindroma foci (arrow). (Immunostaining, original magnification X 400)

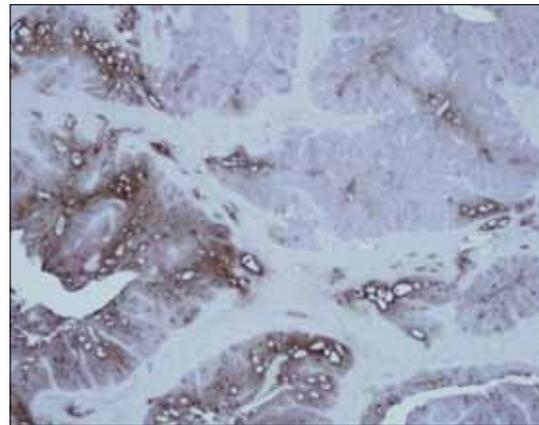


Figure 5 - Carcinoembryonic antigen immunohistochemical stain. Note positive cytoplasmic and luminal stain in spiradenoma areas, in contrast to negative cylindroma foci. (Immunostaining, original magnification X 200)

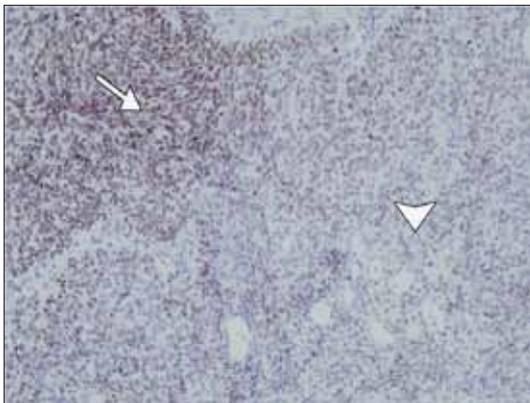


Figure 6 - Immunohistochemical stain for p63 showing positive nuclear staining in cylindroma areas (arrow), in contrast to focal staining in spiradenoma foci (arrow head). (Immunostaining, original magnification X 400)

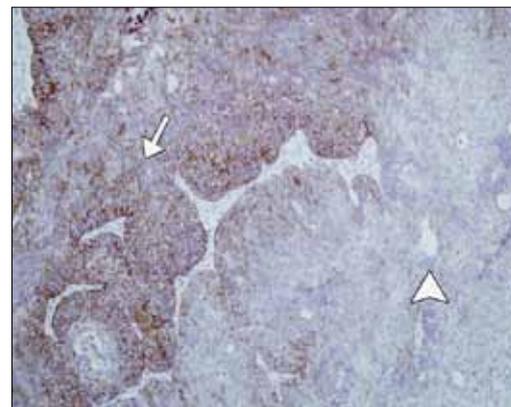


Figure 7 - Immunohistochemical stain for cytokeratin 5/6 showing positive cytoplasmic staining in cylindroma areas (arrow), in contrast to negative spiradenoma foci (arrow head). (Immunostaining, original magnification X 400)

component. The malignant behavior of the tumor was evidenced by loss of nested and trabecular growth patterns, along with increased mitotic rate, nuclear atypia, pleomorphism, and hyperchromasia, presence of wide areas of necrosis, invasive destructive growth pattern, loss of PAS positive basement membrane, as well as associated lymph node metastasis.

Immunohistochemical study of the present case was performed to differentiate the tumor from primary or secondary malignancies such as basaloid carcinoma and basal cell adenocarcinoma. The former is characterized by diffuse positivity to CK7 and CK5/6⁶, while the later is characterized by diffuse positivity to SMA and EMA.⁷ The variable immunoreactivity of tumor components highlighted and documented the presence of 2 variable components of this tumor, which is supported by

the differential expression of CEA, and EMA in the spiradenoma component in contrast to positivity with CK5/6 and p63 in the cylindroma foci. The variability of immunoreactivity of both tumor components is contradictory to the speculations of previous studies of Carlesten,⁸ and Jukic,⁹ who suggested that spiradenoma and cylindrocarcinoma tumor components have a similar immunohistochemical profile.

There are conflicting data in the literature on the expression of SMA, and CK7 in cylindroma and spiradenoma. In our study, both tumor components failed to express both antigens, contrasting the results of Missall,¹⁰ Carlesten⁸ and Jukic⁹ who reported moderate CK7 and SMA staining in around 25% of cylindroma and spiradenoma cells, suggesting similar heterogenous origin, characterized by myoepithelial, ductal, apocrine,

with possible eccrine features. Occasional positive nuclear staining to S100 was identified as a few positive intermingled cells within both tumor nodules that were interpreted as langerhans cells within the neoplasm.

In conclusion, malignant spiradenoma/cylindroma is a rare tumor with controversial histogenesis that should be considered in the differential diagnosis of primary adnexal and secondary metastatic tumors in the vulva. Further studies on a wider cohort should be encouraged.

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