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CASE SERIES

Condyloma-like squamous cell carcinoma of the vulva: report of two midline cases

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Abstract: Vulvar cancer is uncommon and may be confused with genital condylomata. We report two cases of middle-aged women presenting with exophytic vulvar tumors of the midline for which diagnosis of a vulvar squamous cell carcinoma was confirmed by histopathology. Risk factors, staging, and treatment options are discussed.

Keywords: condyloma, human papillomavirus (HPV), squamous cell carcinoma, surgery, vulva

Introduction

Vulvar carcinomas are rare malignancies, and squamous cell carcinoma (SCC) of the vulva account for about 80% of such cases.[1] Vulvar intraepithelial neoplasia and vulvar Bowen's disease are considered as possible precursors of vulvar SCC.[2]

There are two major ways vulvar SCC can develop: (a) 8.6%–40% of cases emerge due to infection with carcinogenic subtypes of human papilloma virus (HPV) and (b) 60%–70% of tumors are not related to HPV.[3–5] Among HPV types, HPV-16 seems to be the most commonly isolated in vulvar carcinomas with HPV-11 and HPV-6 being less common.[4] Vulvar SCC with a warty surface has been strongly linked with HPV-33, HPV-45, HPV-52, HPV-18, and HPV-16.[6]

Several conditions of either autoimmune or infectious origin and miscellaneous disorders have been associated with development of vulvar SCC, such as Hailey–Hailey disease,[7] pemphigus vulgaris and systemic lupus erythematosus,[8] lichen sclerosus and Langerhans cell histiocytosis,[9] Crohn's disease,[10] Fanconi's anemia,[11] and infection with human immunodeficiency virus (HIV).[12]

In women aged less than 40 years, vulvar SCC is extremely rare.[13] The availability of HPV vaccination may lead to a reduction in HPV-associated vulvar SCC.[4] SCC is an important clinical and histological differential diagnosis in anogenital condylomata accuminata.[14] However, SCC may be misdiagnosed as condyloma. We report two middle-aged females presenting with condyloma-like vulvar midline SSC.

Case reports

Case 1

A 41-year-old woman was seen in consultation for the combination of an asymptomatic hyperpigmented plaque type vulvar lesion on the right side and a painful exophytic nodule of the contralateral site arising from a larger flat leucoplakic lesion (Figure 1). The lesions were noted for >1 year (plaque) and 3 months (nodule). She was obese and was on treatment for insulin-dependent diabetes mellitus.

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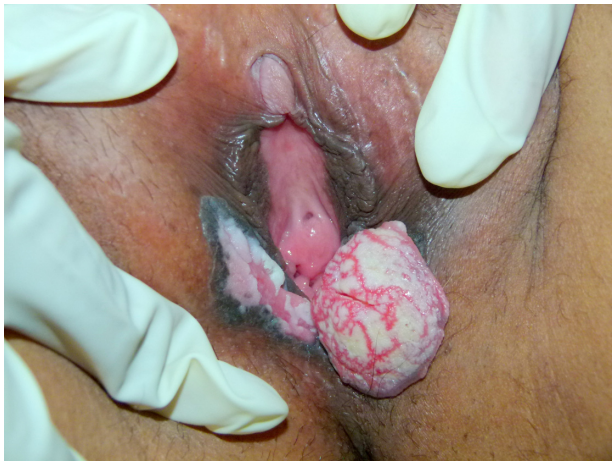

Figure 1 Warty exophytic SCC of the vulva (case 1).
Abbreviation: SCC, squamous cell carcinoma.

The hyperpigmented lesion was flat, macular, and had well-defined borders. The nodule on the left side of the vulva was about 4 cm in diameter, was pedunculated, had a firm consistency, was covered in whitish film-like material and exhibited a verrucous whitish cover. Two diagnostic biopsies were taken from each side. Histopathological examination of the nodule revealed an epithelial proliferation with the formation of horn pearls, keratinocytes with nuclear polymorphism, and increased mitotic activity (Figure 2). The basement membrane was not well-maintained but deeper infiltration was absent. The diagnosis was squamous cell carcinoma, Broder grade II. The other lesion was diagnosed as pigmented Bowen's disease with pagetoid growth of enlarged intraepithelial keratinocytes developing into SCC. The tumor was staged as stage II according to International Federation of Gynecology and Obstetrics staging guidelines and T2N0M0 according to Union for International Cancer Control guidelines (Table 1).[15] The patient was referred to the gynecologist for vulvectomy.

Case 2

A 44-year-old female presented with asymptomatic condyloma-like protrusions affecting labia majora and perineum and she noted > 2 years of slow enlargement (Figure 3). She was a smoker for >20 package-years but her medical history was unremarkable. The tumor presented as firm mass infiltrating the deeper structures. Magnetic resonance imaging revealed a deep subcutaneous neoplasia, extruding vagina and anus, and penetrating urogenital diaphragm including the musculus peroneus profundus measuring $33 \times 43 \times 42$ mm. Lymph node metastasis was observed in the right groin. Histopathology revealed SSC, Broder grade III.

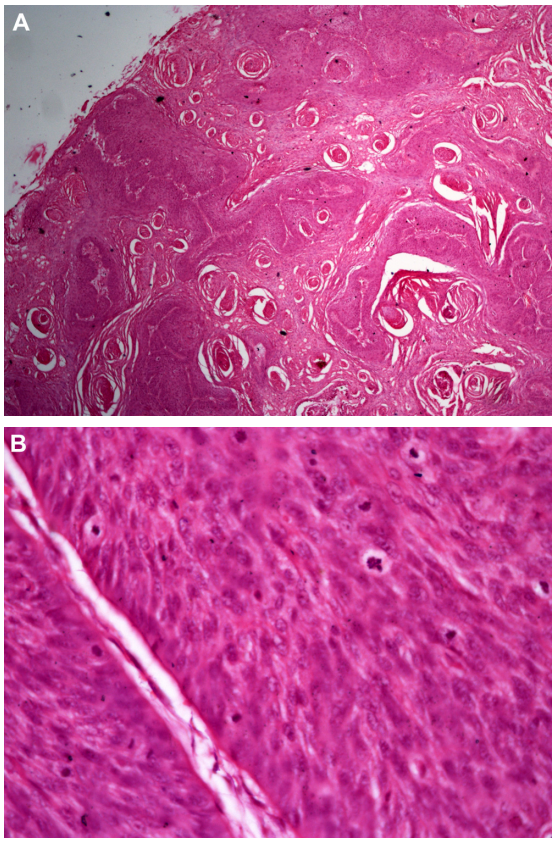

Figure 2 Histopathology of the vulvar squamous cell carcinoma (case 1): (**A**) Overview with epitheloid strands, cellular and nuclear atypias and formation of horn pearls (×4). (**B**) Multiple mitoses (×40). Hematoxylin-eosin stains.

The tumor was staged as stage IIIA according to International Federation of Gynecology and Obstetrics staging guidelines and T3N1M0 according to Union for International Cancer Control guidelines (Table 1).[15] Surgery was performed for

Table 1 Revised FIGO classification of vulvar carcinoma[15]

IA	Tumor confined to the vulva or perineum, ≤2 cm in size with stromal invasion ≤ 1 mm, negative nodes
IB	Tumor confined to the vulva or perineum, >2 cm in size or with stromal invasion > 1 mm, negative nodes
II	Tumor of any size with adjacent spread (1/3 lower urethra, 1/3 lower vagina, anus), negative nodes
IIIA	Tumor of any size with positive inguinofemoral lymph nodes
	(i) 1 lymph node metastasis greater than or equal to 5 mm
	(ii) 1–2 lymph node metastasis(es) of less than 5 mm
IIIB	(i) 2 or more lymph nodes metastases greater than or equal to 5 mm
	(ii) 3 or more lymph nodes metastases less than 5 mm
IIIC	Positive node(s) with extracapsular spread
IVA	(i) Tumor invades other regional structures (2/3 upper urethra, 2/3 upper vagina), bladder mucosa, rectal mucosa, or fixed to pelvic bone
	(ii) Fixed or ulcerated inguinofemoral lymph nodes
IVB	Any distant metastasis including pelvic lymph nodes

Abbreviation: Reproduced, with permission granted by the International Federation of Gynecology and Obstetrics (FIGO), from:Pecorelli, S. Revised FIGO staging for carcinoma of the vulva, cervix, and endometrium. *Int J Gynecol Obstet* 2009;105(2):103–104.

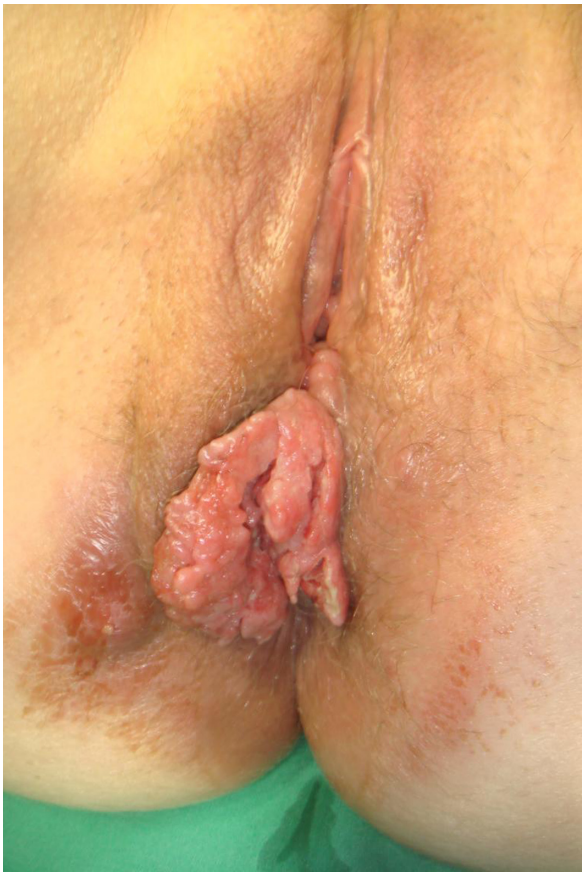

Figure 3 Condyloma-like exophytic growth of vulvar squamous cell carcinoma (case 2).

tumor debulking (Figure 4). The patient was referred to the gynecologist for combined chemoradiotherapy.

Discussion

Vulvar cancer can be differentiated as two types: type 1 is seen in patients younger than 65 years old with frequent detection of HPV DNA and a strong association to pre-existing condyloma, vulvar intraepithelial neoplasia, sexually transmitted diseases, and cigarette smoking. Type 2 affects elderly women. SCC is seen more often in type 2 vulvar cancer.[16] Our patients, however, belonged to the age-group of type 1 and both had SCC Broder grades II and III.

Vulvar SCC may be completely asymptomatic. When symptoms are present, the most common include pruritus vulvae, vulvar bleeding or pain, swelling, or vaginal discharge.[16,17] Often, the patient does not complain due to cultural reasons, the so-called "culture of silence", due to embarrassment, or for economic reasons. Vulvar SCC may be confused with condyloma[14] and therefore may be inadequately treated by various modalities. Important differential diagnoses of vulvar SCC are listed in Table 2.

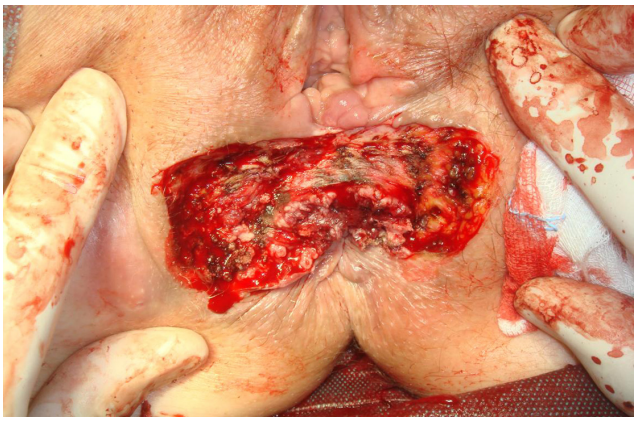

Figure 4 Operation situs after debulking surgery (case 2).

Table 2 Differential diagnoses of vulvar SCC

Nonmalignant
Vestibular papillomatosis
Condylomata accuminata
Condylomata lata
Epidermal nevus
Epidermolytic akanthoma
Lipoma
Lichen sclerosus
Leiomyoma
Lymphangioma
Fibroadenoma
Genital herpes simplex infection
Hidradenoma papilliferum
Angiofibrolipom
Actinomycosis
Rheumatoid nodule
Schistosomiasis
Syringoma
Verruciform xanthoma
Pinworm infestation
Benign phylloides tumor
Lymphedematous pseudotumor
Malignant
Paget's disease
Adenocarcinoma
Angiomyxoma
Basal cell carcinoma
Verrucous carcinoma
Bartholoni's gland carcinoma
Merkel cell carcinoma
Melanoma
Malignant schwannoma
Malignant fibrous histiocytoma
Malignant giant cell tumor
Myoepithelial carcinoma
Ductal carcinoma
Malignant phyllpoides tumor
Sarcomas
Lymphomas (including mycosis fungoides)
Metastases

Abbreviation: SCC, squamous cell carcinoma.

The 5-year survival rates for vulvar SCC have been estimated as 41% for India,[18] 68% for South Korea,[19] and 86% in the United States.[1] The most important negative prognostic factor for vulvar SCC is the inguinofemoral lymph node status at the time of initial diagnosis.[20] Surgery remains the cornerstone of therapy. Individualized vulvectomy should be accompanied by groin lymph node dissection for tumors with a diameter of at least 2 cm and those invading 1 mm or deeper. Medially located tumors may spread bilaterally.[21,22] Surgery, tumor stage, and stromal invasion of less than 9 mm were the most dominant predictors for relapse-free survival in a recent study in Italy.[23] The distance of the surgical margins is critical for the prevention of local relapses. In a study analyzing 93 patients with vulvar carcinoma, a margin of more than 8 mm did not improve recurrence rate.[24] In advanced cases, neoadjuvant chemotherapy is a beneficial option if surgery can be performed thereafter.[25] The combination of chemotherapy and radiation is an option for patients where surgery is impossible.[26,27] In our cases, vulvectomy is planned for case 1 and combined chemoradiotherapy after debulking surgery is planned for case 2.

In conclusion, it is important for dermatologists to be aware of vulvar SCC and consider this malignancy when dealing with large vulvar condylomas. Early recognition with reference to treatment by gynecologists, oncologists, and radiologists helps to improve outcome.

Disclosure

The authors report no conflicts of interest in this work.

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