HPV-related verrucous carcinoma of the vulva. A case report and literature review

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Summary

Verrucous carcinoma of the vulva is a rare type of squamous cell neoplasm with distinct morphology, pathogenesis and special therapeutic management. A case of a 72-year-old patient who developed verrucus carcinoma of the vulva is reported. Data regarding the diagnosis, management and treatment of this neoplasm are presented, and a review of the literature is performed.

Key words: Vulva; Verrucous carcinoma.

Introduction

Verrucous cancer of the external genitalia is a rare form of genital neoplasm in elderly women, with an incidence of 1-2% of all forms of malignant neoplasms of the vulva [1, 2]. It represents a rare subtype of squamous cell carcinoma which is observed in about 95% of cases of cancer of the external genitalia and is classified among other rare histological types of vulvar cancer such as the warty and basal and basaloid cell carcinomas [2-4]. Verrucous carcinoma of the vulva progresses as a locally invasive tumor [5] with little or no metastatic potential. It is characterized by the development of well differentiated squamous cells with rare mitoses and a hyper keratinized undulating warty surface, a pushing border and minimal basal or suprabasal atypia [5]. There is evidence that about 27% of the verrucous carcinoma cases are related to HPV infection (mainly type 6) [6-8].

Verrucous carcinoma was first described by Ackerman in 1948 [3] as a well differentiated squamous cell carcinoma arising from normally squamous epithelialized tissues such as the larynx, esophagus, vulva and vagina and the perianal and anorectal regions [9].

A case of a 72-year-old patient is presented with a HPV-related verrucous carcinoma of the vulva, together with a review of the current literature in the field.

Case Report

A 72-year-old patient presented at the Outpatient Department of the 2nd Clinic of Obstetrics and Gynecology of Aretaieion Hospital because of vulvar pain and pruritus of some months duration. The gynecological examination revealed a large warty tumor of the left labius majus that extended near the urethra and clitoris. A biopsy was performed which revealed squamous cell carcinoma, probably of verrucous type.

From the patient's medical history, diabetes mellitus, type 2 was reported. No alcohol or cigarette use was acknowledged.

A computed tomography (CT) scan was performed which revealed no metastases. No further findings were found from cystoscopy. The patient underwent radical wide excision of the tumor with free surgical margins. Macroscopic examination showed an exophytic verruciform tumor measuring 2 x 1.6 cm and extending 0.7 cm in depth. Microscopic examination revealed a warty tumor resembling a "giant condyloma" (Figure 1). The tumor had a "pushing border" with minimal stroma and vascular core between the acanthotic epithelium. Hyperkeratosis and parakeratois were also found. Mitoses were rare and no vessel invasion by the tumor cells was observed. The specimen margins were free of invasion. Immunohistochemical study by in situ hybridization showed positivity for HPV types 31-33 (Figure 2). Investigation of the expression of p53 protein (SKYTEK D07, SKYTEK USA), c-neu (CB11-NOVOCASTRA) and EGFR (NOVOCASTRA) by a streptavidin-biotin-Ventana Benchmark method was negative. Because of the nature of this tumor and absence of metastatic potential no adjuvant therapy was recommended and the patient has been free of disease or recurrence for three years.

Discussion

The typical presentation of vulvar verrucous carcinoma is an exophytic mass that could be locally destructive. The first diagnosis is usually made by vulvar biopsy even in a clinical outpatient basis. Local invasion and penetration of deep structures occur, but the tumor does not present lymph node metastases [5].

The histologic criteria for verrucous carcinoma diagnosis include [5]: a) verruciform growth pattern, b) a blunt interface between the neoplastic epithelium and the underlying submucosal stroma, and c) minimal nuclear atypia. The differential diagnosis includes condyloma acuminatum, epithelioid sarcoma, rhabdoid tumor and keratoacanthoma [5]. It should be mentioned that squamous carcinoma with verrucous characteristics should not be characterized as verrucous carcinoma as the prognosis is different. The pathogenetic role of HPV and its interaction with p53 suppressor gene and loss of c-neu expression as observed in our study are in accordance with reported findings and merits further investigation.

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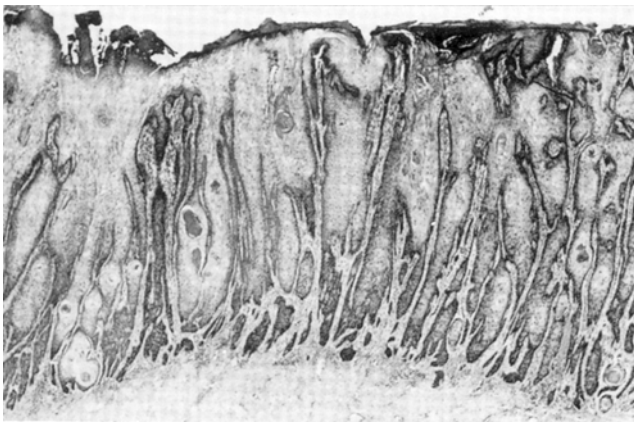
Fig. 1



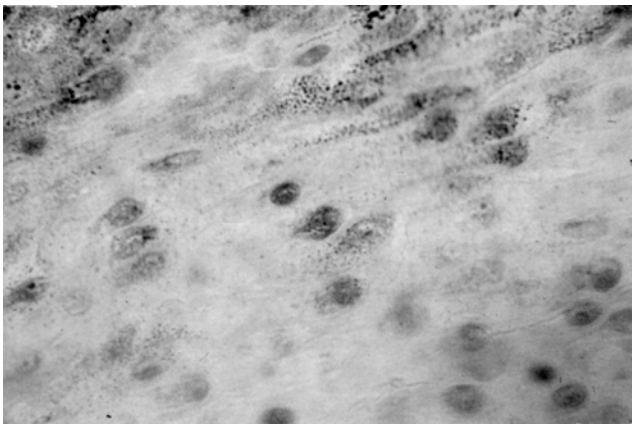


Fig. 2

Figure 1. — Histological section of a verrucous carcinoma of the vulva showing pushing but not infiltrating neoplasmatic borders (hematoxylin-eosin, x25).

Figure 2. — Histological section of the tumor showing positive nuclear HPV/31-33 immunoreaction (in situ hybridization x250).

A radical wide excision of the tumor with free surgical margins is the proposed treatment, however even radical vulvectomy has been performed in some cases [10] as local recurrences are common findings in cases of inadequate resection [9]. The role of radiotherapy and chemotherapy is questionable [11]. In a large retrospective study including 105 cases of verrucous carcinoma, 9/88 surgically treated and 17/17 treated with radiotherapy alone developed local recurrences [12]. Chemotherapy [11] (bleomycin, cisplatin, methotrexate and leucovorin) and other conservative treatments have also been used such as acitretin [1], interferon-α2a [1], podophyllin [13], and 5-fluorouracil [13]. The major prognostic factors are the stage (tumor diameter, node involvement), grade of differentiation, depth of invasion and tumor-free surgical margins. The tumor has an excellent prognosis in most cases. However, it is characterized by frequent local recurrences ranging between 30% and 50% of cases [14].

Conclusion

Verrucous carcinoma is a subtype of common squamous cell carcinoma of the vulva with specific morphology and excellent prognosis without metastatic disease but with local recurrence in cases with inadequate excision.

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