A hybrid penile carcinoma with presence of anterior urethral dysplasia

Georgios Tsamboukas¹, Eleni Vlotinou², Joanna Kotsikogianni², Gerasimos Vandoros², Kristiana Gkeka³, Kartsaklis Panagiotis¹, Athanasios Papatsoris⁴, Aristomenis Gkekas¹

¹Department of Urology, General Hospital of Patras, Greece
²Department of Pathology, General Hospital of Patras, Greece
³Department of Medicine, University of Patras, Greece
⁴Department of Urology, University Hospital of Athens (Sismanoglio), Greece

Abstract

Verrucous carcinoma of the penis is a rare histopathologic variant of squamous cell carcinoma, accounting for less than 10% of the cases of penile cancer. Histopathologically, the tumor is a well differentiated squamous cell carcinoma showing aggressive local growth but never metastasizes, except of cases of mixed type with usual squamous cell carcinoma (hybrid carcinoma). In this paper, we present a case of hybrid penile carcinoma in a 78-year old man, who was treated with partial penectomy. The condition was accompanied with dysplasia of the anterior urethra.

Key words
Penile carcinoma; verrucous; hybrid; anterior urethra; dysplasia

Introduction

Penile verrucous carcinoma (VC) is a well-differentiated variant of squamous cell carcinoma (SCC) of the penis, accounting for 3-8% of cases of penile cancer, therefore uncommonly reported and not well characterized.¹ The pure type of the tumor exhibits invasive local growth but lacks of metastatic potential and distant spread is considered unlikely.² However, in a significant proportion of cases the verrucous lesions contain areas of invasive squamous cell carcinoma; these cases are defined as hybrid carcinoma and tend to behave in a biological manner accordingly to the more aggressive variant.³ In this paper, we present the management of a hybrid penile carcinoma which was accompanied with epithelial dysplasia of the anterior of the urethra. The significance of the verrucous variant and the possible role of urethral lesions are discussed.

Case presentation
A 78-year old man presented to our Department with...
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a painful and gradually swollen penile shaft during the past few weeks. The patient denied comorbidities but he did not exclude possibility of sexually transmitted diseases in the past. Clinical examination revealed phimosis, while the penile shaft was palpated solid, raising high suspicion of underlying pathology. A dorsal slit was performed for the exposure of the glans and an exophytic, cauliflower lesion was revealed, originated from the prepuce. The glans was found also affected (Figure 1). Physical examination did not reveal palpable inguinal lymph node disease. Diagnostic, superficial biopsies were taken, which demonstrated an exophytic neoplastic lesion with histopathologic features of a well differentiated squamous cell carcinoma of the infrequent subtype of verrucous carcinoma (Figure 2). The lamina propria and corpus cavernosa were infiltrated by the lesion, but corpus spongiosum and urethra were unaffected by the tumor. However, multifocal areas of squamous metaplasia (Figure 5a) were found in the epithelium of distal urethra; in some areas, dysplasia of the metaplastic epithelium was present (Figure 5b). The condition was staged T2NxM0, as physical examination and imaging modalities were negative for inguinal lymph node disease but modified inguinal lymph node dissection for definitive staging purpose was denied by the patient. Considering the level of differentiation of the tumor and the absence of apparent lymph node disease we chose to keep the patient in close follow-up. One year after the procedure, the medical course is uneventful with no sings of recurrence or disease progression.
Discussion

Verrucous carcinoma belongs to the family of verruciform squamous cell carcinomas having a distinctive exophytic, papillary, cauliflower-like appearance. Other verruciform lesions include warty carcinomas, Buschke-Lowenstein tumor or giant condyloma accuminatum and papillary squamous cell carcinoma. It most commonly affects the glans and may be presented as a painless penile mass or may be infected, ulcerated and purulent. Phimosis, poor hygiene and redundant prepuce are most commonly implicated as risk factors, although the condition has been reported in a 37-year-old previously circumcised man. Histologically, the tumor exhibits well differentiation and locally aggressive growth isolated in the basement membrane of the tumor with rather “pushing” than infiltrating borders; acanthosis and hyperkeratosis are usually present. Thus, in cases of pure VC, the tumor is staged as Ta. Albeit a variant of SCC, verrucous carcinoma does not demonstrate the same immunochemical characteristics and is not considered as an HPV-related tumor. In the minority of cases that HPV infection is found, the high-risk HPV 16 type is absent and therefore, the typical nuclear p16 marker found in usual SCC is not detected. In addition, the expression of a proliferation marker, named Ki67, is characteristically lower in cases of VCC as opposed to SCC, representing the slow growth rate of the tumor.

The diagnosis and treatment of penile cancer is based on initial confirmative biopsies and surgical resection of the primary tumor with as optimal organ preservation as possible. In cases of pure VC, circumcision, local excision or partial penectomy is considered an adequate approach as far as the tumor lacks of spreading potential and never metastasizes. The intra-Aortic infusion chemotherapy based on methotrexate has been reported as an alternative non-surgical approach for younger men with attractive effectiveness regarding oncologic, cosmetic and functional outcomes; however, several cycles of chemotherapy may be needed for complete response and the initial diagnosis of VC has to be certain. In cases of small lesions, cryosurgery with liquid nitrogen can offer organ preservation without significant risk of recurrence. On the other hand, if an hybrid carcinoma is the definitive diagnosis, the tumor should be regarded as a mixed SCC and must be managed accordingly;inguinal lymph node metastasis should be considered in up to 25% of patients with clinically negative lymph nodes and all patients in the high risk group (T2-T4) should undergo diagnostic procedures for final staging and if indicated, further treatment.

The presence of urethral lesions concurrently with penile cancer is not uncommon according to observation of penectomy specimens. In their study, Velasquez et al. have observed specific abnormalities in the epithelium of anterior urethra in men with penile cancer, consisting mainly of squamous metaplasia. These lesions were in their majority primary, most likely related to chronic obstruction and inflammation due to the presence of phimosis or cancer and not due to direct extension of the tumor. The authors concluded that further keratinization or atypia in these lesions, found in higher frequency with VC, may rep-
resent a mechanical pathway for cancer progression or an independent field susceptible to contemporary cancer transformation. Indeed, primary urethral cancer in distal urethral is of squamous cell carcinoma origin and therefore, attentive tracking of these lesions is mandatory.

In our case, initial diagnostic biopsies demonstrated the presence only of VC, reflecting the superficial penetrating strength of the subtype. The decision for partial amputation was guided by clinical examination and deemed justified since the pathologic examination of deeper layers revealed invasive foci of usual type SCC, a finding that can dramatically change the natural history of the disease and definitely alter the management of the condition. Therefore, we believe that even if VC is found isolated in initial biopsies, the urologist should keep in mind the possibility of a mixed, more aggressive underlying pathology. Finally, the urethral epithelial lesions, albeit of undocumented significance, could not but alert the surgical team to track the patient in close follow-up, especially in cases where distal urethra is utilized as part of the reconstruction procedure.

**Conflicts of interest**

The author declared no conflict of interest.

**Abbreviations**

VC: Verrucous Carcinoma
SCC: Squamous cell carcinoma
HPV: Human papillomatous virus

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**References**