Penile Cutaneous Horn Ten Years after Treatment of Verrucous Squamous Cell Carcinoma on Penile Glans: Case Report

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SUMMARY Penile cutaneous horn is a clinical term that describes protruding hyperkeratosis, usually conical in shape, located on penile glans. Penile localization of this lesion, predominantly located on sun-exposed areas, is very rare. The association with malignancy on the penis makes proper identification of these lesions essential. We present a 45-year-old man with a cutaneous horn, 25 mm in size, located on the basis of penile glans. The patient had a history of phimosis, pseudoepitheliomatous balanoposthitis, surgical excision of penile verrucous squamous cell carcinoma (SCC) and postoperative radiotherapy of carcinoma in situ on the same localization, ten years before. Complete surgical removal of the horn with separate excision of the margins and base was done. Pathologic examination revealed squamous hyperplasia with suspicion of carcinoma in situ. Additional negative p16INK4a immunohistochemical analysis confirmed benign proliferative lesion. DNA polymerase chain reaction for human papilloma virus infection was negative. These findings suggested sparing surgical procedure in our patient, without indication for partial penile amputation, but with mandatory follow-up. Our case confirmed the association of pseudoepitheliomatous balanoposthitis with verrucous SCC, as well as the possible influence of radiotherapy on the development of penile cutaneous horn. Additionally, we showed the important role p16INK4a immunohistochemical analysis in the differential diagnosis of alterations adjacent to invasive SCC of the penis.

KEY WORDS: penile horn, penile carcinoma, p16INK4a
**INTRODUCTION**

Penile cutaneous horn (*cornu cutaneum*) is a clinical term that describes protruding hyperkeratosis with an erythematous base on penile glans. The incidence of the lesion is very low, with only 30 cases reported in 25 years (1). The disease may be benign in 42%-56%, premalignant in 22%-37%, or frankly malignant in 20%-22% of patients (2). Herein we present and discuss an additional case of cutaneous penile horn, which originated 10 years after surgical and oncologic treatment of verrucous penile carcinoma and squamous cell carcinoma (SCC) *in situ*.

**CASE REPORT**

A 36-year-old man presented to our Department 10 years before with hyperkeratotic plaque of penile glans. One year before, he had undergone circumcision for severe phimosis, with the pathological finding of pseudoepitheliomatous posthitis. Excision of hyperkeratotic plaque of the penile glans was done and pathology showed verrucous SCC with tumor at one margin. On pathologic examination after re-excision, differentiated carcinoma *in situ* and lichen sclerosus were found. Local radiotherapy was performed and control biopsy three months after irradiation was normal. Four years after completion of surgical and local radiotherapy, all clinical examinations revealed normal findings. During the following six years, the patient did not attend recommended control examinations. Ten years after the treatment, cutaneous horn on the penile glans occurred. It was 25 mm in size, located at the site of previous excision (Fig. 1). Inguinal lymph nodes were not enlarged on clinical examination. The entire lesion was excised with 5 mm margins, along with separate biopsy from the base of the lesion. Histopathologic examination was done by two consultant pathologists from two international pathological institutions. The examination revealed epithelial acanthosis with prominent granular layer and hyperkeratosis of orthokeratotic type. Basal layer was characterized by sporadically elongated rete ridges with the signs of incipient keratinization and few mitotic figures (Figs. 2 and 3). Additional negative p16 INK4a immunohistochemical analysis confirmed benign proliferative lesion.

The margins and deep glans biopsy were tumor-free. DNA polymerase chain reaction for human papilloma virus (HPV) infection was negative. The patient was advised to remain under close follow-up, without indication for partial penile amputation or adjuvant oncologic treatment.

**DISCUSSION**

The European Association of Urology (EAU) guidelines on penile cancer report three categories of pre-
malignant lesions, each with different probability of developing into SCC of the penis: lesions sporadically associated with SCC of the penis (cutaneous horn of the penis and Bowenoid papulosis); lesions at an intermediate risk of progression to SCC (balanitis xerotica obliterans); and lesions at a high risk of developing into SCC of the penis (penile intraepithelial neoplasia occurring as Bowen’s disease or erythroplasia de Queyrat) (3). Unfortunately, none of these seems to correlate with current understanding of the penile cancer pathogenesis. It has been suggested that penile carcinogenesis follows a bimodal pathway, one associated with human papillomavirus infection and the other related to nonviral factors such as phimosis, chronic inflammation, and lichen sclerosus (4). Few pathologic reports of precancerous penile lesions are mostly related to carcinoma in situ and HPV, and information about low-grade lesions is limited (5).

Similar to the first reported case of pseudoepitheliomatous balanoposthitis (6), our patient had pre-existing phimosis, too. Originally, the lesion was thought to be benign or of limited malignant potential (6). However, Beljaards et al. report on two cases of verrucous SCC, which developed subsequently after pseudoepitheliomatous balanitis (7). Similarly, in our patient, pseudoepitheliomatous balanoposthitis progressed to verrucous SCC, clinically evident one year after circumcision. Surgical excision followed by penile irradiation in our patient resulted in the absence of tumor evidence on control biopsy, three months after irradiation.

Cutaneous horn of the penis occurred in our patient at the same localization as previous verrucous carcinoma, after a lag time of ten years upon radiotherapy for carcinoma in situ. To our knowledge, previously only two such cases have been reported in the literature, where cutaneous horn occurred over a long standing chronic radiodermatitis, 5 and 12 years after radiotherapy (8,9). Our study, together with the aforementioned studies, suggests the possible influence of radiotherapy on the development of penile cutaneous horn.

Recently, several studies indicated that immunohistochemical expression of p16INK4a may be used not only as a marker of high-risk HPV infection, but also on differential diagnosis of penile epithelial abnormalities and precancerous lesions. Earlier data showed strong association of HPV with high-grade SCC, whereas well-differentiated SCC subtypes were not HPV-related. Chaux et al. have published a study designed to seek an immunohistochemical profile that can be helpful in the classification and differential diagnosis of penile epithelial abnormalities and precancerous lesions (10). In the cited study, all patients with squamous hyperplasia and differentiated penile intraepithelial neoplasia (PIN) were p16INK4a negative; on the contrary, patients with basaloid and warty PIN were p16INK4a positive. Overexpression of p16INK4a showed sensitivity rate of 67% and specificity of 91% for defining the HPV status (11). The sensitivity of p16INK4a positivity for discriminating types of penile intraepithelial neoplasia was 82%, with specificity of 100% and accuracy of 95% (12). In our patient, negative immunohistochemical finding of p16INK4a, interpreted with regard to histopathologic examination, allowed us to confirm the diagnosis of squamous hyperplasia. Additionally, DNA polymerase chain reaction for HPV infection was negative in our patient.

In conclusion, tumor recurrence can arise in a pre-malignant form even with a lag time of 10 years, as described in our case. Regarding the choice of treatment option and prognosis, proper identification of these lesions is essential. Our study showed that p16INK4a immunostaining can be helpful in the classification and differential diagnosis of penile lesions.

References

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Light, air and sun with Nivea cream; year 1936.
(from the collection of Mr. Zlatko Puntijar)