Pure Verrucous Carcinoma of the Penis: Two Cases
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Abstract
Verrucous carcinoma is a rare subtype of penile verruciform squamous cell carcinoma. However, in past literature, the diagnosis of verrucous carcinoma has been confused with giant condylomas, and papillary and warty carcinomas due to the absence of critical criteria in pathological diagnosis. We experienced two cases of penile verruciform tumor occurring in a 48-year-old Japanese male and an 88-year-old Japanese male. We performed partial penectomy without lymph node dissection after biopsy. Although we initially detected small palpable lymph node swelling in the latter case, unnecessary lymph node dissection could be avoided by pathological diagnosis using preoperative biopsy. The resected specimens were diagnosed in accordance with the World Health Organization (WHO) classification and current pathological reviews. Histopathological findings and immunohistochemical appearance were compatible with a diagnosis of verrucous carcinoma.

Keywords: Verrucous carcinoma; Human papilloma virus (HPV) infection; Verruciform lesion; Lymph node dissection

Introduction
Verrucous carcinoma is a rare, extremely well differentiated squamous carcinoma with low clinical malignant potential first described in 1948 in the oral cavity [1]. Since then, it has been described in other sites, such as the anus, penis, and the female genitalia [1]. Based on the literature, verrucous carcinoma accounts for approximately 3-8% of all penile cancers and 20% of verruciform lesions of the penis, which also include giant condyloma (Buschke-Löwenstein), warty carcinoma and papillary Squamous Cell Carcinoma (SCC) [1-4]. In the World Health Organization (WHO) classification, each verruciform lesion is clearly defined with histological criteria and verrucous carcinoma is considered a distinct pathological entity separate from the other verruciform tumors. However, the term “verrucous carcinoma” has been used for giant condyloma (Buschke-Löwenstein) and warty carcinoma in past literature, and thus, the true frequency of verrucous carcinoma may be lower than generally assumed [3,4]. In Japan, there have been 83 reported cases of penile verrucous carcinoma [5]. Here, we report two cases of pure penile verrucous carcinoma and discuss the pathological findings.

Case report
Case 1
A 48-year-old Japanese male was admitted to our hospital with a chief complaint of painless swelling of the penile glans. The patient had true phimosis by nature, and the swelling had occurred about 6 months prior to his visit. Physical examination revealed a palpable hard mass under the foreskin. Apparent swelling of the inguinal lymph node was not detectable. We performed dorsal incision of the foreskin to obtain a biopsy specimen. A warty tumor appeared under the foreskin and the pathological analysis of the tumor yielded a diagnosis of verrucous carcinoma (Figure 1a). Neither lymph node swelling nor distant metastasis could be detected by abdominal Computerizing Tomography (CT) and chest X-ray. Then, partial penectomy was performed for radical excision of the lesion. Histological examination of the resected tumor revealed a papillomatous tumor with marked hyperkeratosis and parakeratosis. The papillae lacked central fibrovascular cores and the tumor base showed broad, pushing and regular borders (Figure 1b). The tumor cells were very well differentiated and negative for p16INK4a staining in immunohistochemistry. Koilocytic changes were hardly observed. The final diagnosis was pure verrucous carcinoma, T1N0M0. The resected edge of the penis was free from the cancer cells. The patient recovered well and remained free of recurrence and metastasis for 5 year after surgery without postoperative therapy.

Case 2
An 88-year-old Japanese male, who had received circumcision of the foreskin three years prior to his visit due to balanitisxeroticaobliterans (lichen sclerosus), was admitted to our hospital with a wart-like tumor of the glans associated with bacterial infection on the tumor surface (Figure 2a). Slight inguinal lymph node swelling was detected by CT and we performed a biopsy of the penile tumor, which led to the strong suspicion of verrucous carcinoma. Considering the pathological diagnosis, the patient underwent partial penectomy without lymph node dissection. No other apparent metastatic lesions were be detected by CT and X-ray analyses. Histologically, papillary projections of a stratified squamous epithelium without fibrovascular core accompanying hyperkeratosis were observed. The tumor base had broad, pushing and regular borders (Figure 2b). The nuclei of the tumor cells were bland and round, and apparent koilocyticatypia could not be detected. Immunohistochemically, the tumor cells were negative for p16INK4a. Pathological findings were compatible with pure verrucous carcinoma and the surgical margin was negative. A postoperative CT revealed no apparent lymph node swelling (T1N0M0). The patient recovered and remained well for 4 years following the surgery with no evidence of recurrence or distant metastasis.

Discussion
Verrucous carcinoma is a very well differentiated papillomatous neoplasm with acanthus and hyperkeratosis. The papillae usually lack a fibro vascular core. Koilocytic changes are not evident, suggesting unrelated disease with Human Papilloma Virus (HPV) infection. The

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Other low-grade keratinizing SCCs. In the current case (case 2), the patient had a past history of lichen sclerosus, suggesting a relationship to the verrucous carcinoma.

Clinically, verrucous carcinoma is a slow growing tumor that may recur locally; however, regional node or distant metastasis does not occur in typical cases [2-4]. In spite of its low-malignant potential, treatment for penile verrucous carcinoma is partial or total penectomy. This has a significant psychosexual impact and greatly affects the quality of life. However, metastasis and high recurrent rate have been reported in cases of hybrid-type verrucous carcinoma, in which carcinoma of another histological type is coexisting with verrucous carcinoma. It would be difficult to conclude that the lesion is a typical verrucous carcinoma by preoperative biopsy only. Indeed, at least 20% of verrucous carcinoma is of the hybrid-type [10]. In the current cases, whole specimens were embedded in paraffin for pathological analysis. As a result, pure verrucous carcinoma was considered.

The presence and extent of metastasis to the inguinal lymph nodes are the most significant prognostic factors for survival in patients with penile SCC [11]. In the literature, the presence of palpable lymphadenopathy is associated with proven nodal metastasis in about 43% of cases on average (range 8% to 64%) [11]. In addition, the cure rate with inguinal lymphadenectomy when nodes are positive for malignancy may be as high as 80%; therefore, a constructive inguinal lymph node dissection for palpable inguinal adenopathy may be of considerable benefit [11]. However, on the basis of the histological features of primary tumor, a lymphadenectomy should be carefully assessed because, for example, pure verrucous carcinoma has no risk of metastasis. In case 2, the diagnosis based on analysis of biopsy specimen included an approximately 20% possibility of occult hybrid-type verrucous carcinoma. However, considering patient’s age and risk of postoperative complication following lymph node dissection, we

Figure 1: Histological findings of case 1. a. The tumor show papillae with acanthosis without fibrovascular cores and tumor base is regular, broad, and pushing (magnification: ×4). b. Tumor cells are extremely well differentiated and no koilocytosis are identified (magnification: ×10).

Figure 2: Histological findings of case 2. a. Papillae are straight with surface hyperkeratosis. Interface between tumor and stroma is broad and pushing (magnification: ×4). b. The tumor is composed of well differentiated tumor cells and koilocytic changes are absent (magnification: ×10).
planned close follow-up and delayed lymphadenectomy. As a result, the patient could avoid unnecessary lymphadenectomy [12].

In summary, we have experienced two cases of pure penile verrucous carcinoma with successful treatment, and the patients have remained well without local recurrence and metastasis. Pathological diagnosis in each case was pure verrucous carcinoma. Preoperative biopsy may be useful in making decisions regarding treatment strategy for inguinal lymph node swelling.

References


