Original Article
Penis keratoacanthoma transforming into squamous cell carcinoma: a rare case

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Abstract: Keratoacanthoma is variously regarded as a benign epithelial tumor, characterized by a rapid-growing and solitary flesh-colored nodule with a central keratin plug on the sun-exposed skin. Under certain circumstances, it can transform into squamous cell carcinoma. In this paper, we present a case of a 50-year-old man with a 2.5 × 3 × 2.2 cm mass on his penis stub-end. The patient was treated with a partial penectomy after further expert discussions and histopathology demonstrated penis keratoacanthoma. He received a partial penectomy again and the pathological result revealed squamous cell carcinoma this time. This case indicates that undergoing a partial penectomy on initial diagnosis of a penile tumor secondary to penile keratoacanthoma should be considered because of its high malignant potency. To our best knowledge, this is the first study to describe the malignant conversion of penis keratoacanthoma.

Keywords: Keratoacanthoma, partial penectomy, penis, squamous cell carcinoma

Introduction
Keratoacanthoma (KA), a common benign epithelial tumor of unknown etiology and origin, can be treated in different ways in accordance with the different conditions [1]. KA is usually presented with a fast-growing and solitary flesh-colored nodule with a central keratin plug on the sun-exposed skin of old people such as the neck and face [2]. It is estimated that KA maintains the least rate of 25% in malignant transformation, and the rate is even higher in older patients and in photo-exposed areas [3]. Penis KA is rarely seen in the world, to our best knowledge, only a few cases of penis KAs have been reported up till now [4], and this is the first case that penis KA transformed into squamous cell carcinoma (SCC).

Penis is a SCC-vulnerable organ, especially in the third world. It is reported that more than half of SCCs occurred in penis in China in 1986 [5]. Penile cancer accounts for 10% to 20% of all cancers in some African, Asian, and South American countries, including Uganda, China, and India [6].

Case presentation
A 50-year-old man was admitted to the Department of Urology, The Third Xiangya Hospital of Central South University (Changsha, China) with an 18-month history of a progressing lesion on his penis stub-end. Physical examination demonstrated a cauliflower, 2.5 × 3 × 2.2 cm mass, without obvious secretion or foul smell. On palpation, the lesion was not tender and two inguinal lymph nodes, each about 0.5 × 1.0 × 0.8 cm in size, were noted in the right groin. On pelvic magnetic resonance imaging (MRI), a lesion (2.5×0.7 cm) with high signal on TIW1 and T2W1 was observed on penis stub-end.

In his history, he presented a tumor on the dorsal side of glans penis 8 years ago. The tumor grew drastically, progressing from a small initial size into a cord-like mass stretching from the glans penis to the base of the penis in just 6 months. Physical examination revealed a tough tumor absent of foul smell or tenderness. There existed several ulcer dots on the dorsal side of his penis, and the patient had phimosis. He was
diagnosed with inflammatory mass of penis at first and treated with anti-inflammatory agent. There were no signs of recovery and leakage of urine was noted on the surface of the lesion after 3 months of medication, the mass prevented the patient from engaging in sexual life. The patient was eager to remove the lesion and further expert discussions indicated the possibility of penis cancer. The patient received a partial penectomy and histopathology the lesion demonstrated hyperkeratosis, crateriform hyperplasia, which is a representative feature of KA (Figure 1). The margin of the excised mass was tumor-free (data not show). After the surgery, the patient was in good condition, he was checked in the local hospital's clinic twice a year in following two years and there was no sign of recurrence. No other penis cancer-inducing factors, such as HPV infection and smoking, were noted in his history.

Findings and treatment options were discussed with the patient, and the decision was made to perform a partial penectomy with an additional 5 mm clinical margin under lumbar anesthesia and the post-operative recovery was uneventful. The final histopathology revealed a moderately differentiated SCC (Figure 2). After 4 weeks of oral medication with cefdinir, the enlarged lymph nodes continued. The patient received bilateral inguinal lymph node dissection and no signs of metastasis was noted. He was scheduled for regular follow-up and the following 6 months of follow-up visit indicated no sign of relapse.

Discussion

The etiology remains undefined ever since the first report of KA in 1950 [3]. Exposure of excessive sunlight is generally considered as a key role in pathophysiology of KA, which is based on the fact that KA usually occurs on sun-exposed areas such as the neck and face [2]. Other risk factors include smoking, immunosuppression, burns, oncogenic chemicals and certain dermatoses [7]. Keratin expression analysis claimed that KA arises from the pilosebaceous units [8]. In contrast, this case is a strong evidence against that view, because there exist no pilosebaceous units in glans penis. We are also supported by Patrick Oellers, who recently reported a unique case of KA in the right eye [9]. In conclusion, the origin of KA still remains uncertain.

Medical intervention, radiotherapy and surgical excision can be applied in combination or independently to KA according to the different conditions [1]. We recommend that penis tumor secondary to penis KA can be treat with partial penectomy because of its high malignant potency.

KA is a benign tumor with aggressive behavior. Most KAs behave as a benign tumor, however, 20% can be aggressive, with perineural, perivascular invasion and metastasis to the regional lymph nodes [8-10]. Tschandl P et al. reported a unique case of KA with intravenous spread, a feature normally indicative of malignant behavior and guarded prognosis [11]. Some
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dermatologists even regarded KA as a well differentiated, low grade SCC [12]. In contrast, other dermatologists vehemently opposed that opinion since KA differ SCC in morphology, biological behavior and treatment. Takeda H and Kondo S recently used the immunohistochemical study of angiotensin type-1 receptor to distinguish SCC from KA [13]. KA maintains the least rate of 25% in malignant transformation. Though KA is now generally considered a benign growth, evidence indicates that it may progress to low grade SCC. It is reported that at least a quarter of KAs undergo malignant transformation, this occurs more frequently in older patients and in photo exposed areas [3]. Weedon et al. reviewed 3465 cases of KAs in their patients over a 14-month time period in a retrospective study. Two hundred cases had a distinct development of SCC within the lesion [14]. With a co-carcinogen of ultraviolet irradiation, it is rational to deduce that extra mutations in KAs can lead to the development of SCCs within the lesion. There are numerous examples of skin neoplasms including spiradenomas, mixed tumors and piloatrichomas, in which malignant counterparts evolved by mutation from within the benign tumor [1]. Zhou Y et al. recently reported a case that penile cutaneous horn progressed into penis SCC [15].

In summary, penis KA is unusual, a partial penectomy on initial diagnosis of a penile tumor secondary to penile KA should be considered because of its high malignant potency.

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Disclosure of conflict of interest

None.

Authors’ contributions

FD, YZ, YT and YD conceived and designed the study. FD, JL, JT, KY, BX and XL were involved in revision and preparation of the final version of the manuscript. All authors read and approved the final manuscript.

Abbreviations

KA, Keratoacanthoma; SCC, squamous cell carcinoma.

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