A challenging diagnosis of penile sarcomatoid squamous cell carcinoma

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Abstract
We report a patient with penile sarcomatoid squamous cell carcinoma (SCC) initially misdiagnosed as condyloma acuminatum. Sarcomatoid SCC is a rare, aggressive, biphasic cancer that often presents a diagnostic challenge and carries a poor prognosis, especially after a delay in diagnosis. Although sarcomatoid SCC may exhibit a broad range of clinical features, the expression of p63 and keratin 34BE12 is a common finding. Our case highlights the importance of accurate clinicopathologic correlation to facilitate a timely diagnosis and management of this rare and highly aggressive malignancy.

Keywords: sarcomatoid squamous cell carcinoma, squamous cell carcinoma

Introduction
Sarcomatoid carcinomas are rare, aggressive biphasic tumors that can occur anywhere on the body, rarely involving the genitourinary system, particularly the penis [1]. Typically, this entity represents one to two percent of all penile carcinomas and is considered a variant of squamous cell carcinoma (SCC). Sarcomatoid SCC is challenging to diagnose histologically and carries a poor prognosis. To our knowledge, only 39 cases of penile sarcomatoid SCC have been reported [2, 3]. We report a 79-year-old man with penile sarcomatoid SCC, initially misdiagnosed as condyloma acuminatum.

Case Synopsis
A 79-year-old man with a history of cirrhosis and hypothyroidism presented with tender, bleeding nodules on his corona and glans penis. Over the previous two years, the patient underwent two biopsies by his urologist and both were diagnosed histologically as condyloma acuminatum. The patient was circumcised and failed to improve after a one-month trial of 5% imiquimod cream before presenting to the dermatology clinic. The patient denied hematuria or dysuria but endorsed difficulty voiding owing to urethral meatal stenosis along with an acutely enlarging, darkening, and bleeding penile tumor. The patient also complained of foul smelling urethral discharge and a burning scrotal sensation. The patient denied constitutional symptoms such as fatigue, fever, chills, or night sweats but endorsed a 30-pound weight loss over the previous year.

As shown in Figure 1, the patient had two (3×3 cm and 2.4×2.1 cm) fungating, friable, bleeding nodules on the glans penis as well as white and pink friable plaques on the coronal sulcus. Both nodules were transected at the base in the office and sent for histology examination. In addition, left inguinal lymphadenopathy was palpable. Histopathologic examination revealed a malignant spindle cell proliferation (Figure 2) with lesional cells positive for...
INI1 and vimentin in addition to being focally positive for pancytokeratin, CK5/6 (Figure 3A), p63 (Figure 3B), 34βE12, Ki-67 (Figure 3C), CD1138, CAM 5.2, and calponin; the lesional cells stained negative for Sox-10, S-100, synaptophysin, NSE, GFAP, actin, myogenin, CD45, CD3, CD20, CD30, CD117, CD123, CD138, kappa, lambda, MUM-1, EBER, HHV8, CD99, SALL-4, ALK, MUC-4, ERG, CD31, CD34, EMA, and p40. The patient was diagnosed with penile sarcomatoid SCC based on clinicopathologic correlation.

In the two-week interim before scheduled penectomy, one penile nodule regrew and the patient developed disabling fatigue and dyspnea. Upon inpatient admission for planned surgery, additional workup revealed leukocytosis of $89 \times 10^9/L$ and elevated lactate of 5.6mmol/L. Computed tomography of the chest revealed innumerable pulmonary metastases with bilateral malignant pleural effusions. The patient died shortly after opting for comfort care.

### Case Discussion

Penile sarcomatoid carcinomas are rare, aggressive variants of SCC that may be difficult to diagnose without a high clinical index of suspicion. The differential diagnosis may include giant condyloma

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**Figure 1.** Clinical presentation of the penile sarcomatoid squamous cell carcinoma. Clinical examination demonstrated two (3×3cm and 2.4×2.1cm) fungating, friable, bleeding nodules on the glans penis as well as white and pink friable plaques on the coronal sulcus.

**Figure 2.** Sarcomatoid squamous cell carcinoma presents as a poorly differentiated spindle cell neoplasm. A) Low power (2×) examination of H&E sections revealed a poorly demarcated, ulcerated, exophytic mass with a condyloma-like epidermis overlying large areas of hemorrhage and necrosis. B) Higher magnification (20×) revealed pleomorphic spindled cells with eosinophilic vacuolated cytoplasm embedded within a somewhat myxoid stroma. Noted were prominent nucleoli and numerous mitoses, including atypical forms, accompanied by an inflammatory infiltrate composed predominately of lymphocytes and neutrophils.
acuminata of Buschke and Löwenstein, leiomyosarcoma, and melanoma [3, 4]. A prompt and comprehensive histological and immunohistochemical evaluation with a broad panel of markers as above is necessary to establish an accurate diagnosis.

Previously reported cases have also presented as friable, pedunculated masses with notable spindle-cell morphology [1]. Two separate cases of elderly men in India and Japan presented with metastases to the lungs and stomach, respectively, and resulted in death within 6 months [5, 6]. Other reported cases of penile sarcomatoid SCC have demonstrated locoregional metastases to bilateral inguinal lymph nodes in 89% of patients, as well as metastases to the lung, pleura, skin, bone, pericardium, and heart [7, 8]. The malignant potential of sarcomatoid SCC may be attributed to the vascular invasion as well as the unrecognized presence of corporal intrapenile metastasis [4]. Furthermore, a review of all cases of penile SCC in the Paraguayan literature identified the sarcomatoid variant in 15 of 400 cases (4%), which manifested a broad range of clinicopathologic features but exhibited a common expression of p63 and keratin 34βE12 [4]. Notably, in situ hybridization studies for HPV were negative in this cohort [4]. Of the few reported cases of sarcomatoid SCC, the majority had poor outcomes, particularly when the diagnosis was delayed. Therefore, a low threshold of clinical suspicion is warranted to initiate a comprehensive histologic workup.

**Conclusion**

We report a rare and aggressive penile sarcomatoid carcinoma variant of SCC that was initially misdiagnosed as condyloma acuminatum. Importantly, previous studies have documented considerable difficulty in differentiating the histological morphology of human papillomavirus-infected epithelia and various penile carcinomas [9]. Therefore, it is essential for dermatologists, urologists, and other healthcare professionals who may encounter this aggressive subtype of SCC to quickly reach an accurate diagnosis through comprehensive clinicopathological correlation.

**Potential conflicts of interest**

The authors declare no conflicts of interests.

**References**


