Not all penile cancers are created equal

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Warty carcinoma variant of squamous cell carcinoma of the penis is a rare condition, making up 7% to 10% of all penile carcinomas. We present a case of warty carcinoma variant of squamous cell carcinoma of the penis in a 43-year-old Caucasian. The tumor presented in a locally invasive manner, requiring a total penectomy. The primary lesion measured over 15 cm x 16 cm, covering the entire perineum. The clinical features, diagnosis, surgical treatment and pathology are reviewed. In light of the locally invasive nature of warty carcinoma of the penis and high recurrence rate, early diagnosis and aggressive treatment is necessary for this type of unique penile cancer.

Key Words: penectomy, warty carcinoma, penile cancer

Introduction

Here we discuss the clinical presentation, diagnosis and treatment of penile warty carcinoma. In light of the locally invasive nature of warty carcinoma of the penis and its high recurrence rate, we would like to emphasize an early diagnosis and proper treatment for this type of unique penile cancer.

Case report

A 43-year-old otherwise healthy Caucasian male presented with a large, fungating penile mass. He reported having a small, non-healing lesion on his penis for approximately 20 years. However, the mass had grown substantially in the past 18 months. Social history revealed that he is married, with two children, a non-smoker, but occasionally uses chewing tobacco, and reports only one sexual partner in his lifetime. He confirmed being circumcised shortly after birth but reported always having 'excess skin' on his penis. On physical examination he was found to have a large, fungating and grossly infected mass covering his entire perineum as well as bilateral, palpable inguinal lymphadenopathy.

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Diagnostic assessment

Preoperative metastatic work up included a computed tomography (CT) scan with intravenous contrast of the chest/abdomen/pelvis. The CT scan revealed bilateral inguinal adenopathy with no evidence of other areas of metastasis. Grossly, the patient presented with an exophytic, cauliflower-like, white mass replacing a significant portion of the perineum, Figure 1.

Differential diagnosis

Differential diagnosis for a large fungating penile lesion can include warty carcinoma, giant condyloma, papillary carcinoma, verrucous carcinoma, warty-basaloid carcinoma, and squamous cell carcinoma. The definitive diagnosis is made based upon histologic findings, which we will discuss in further detail in the discussion section.

Management and outcome

Shortly after initial presentation, a radical penectomy with perineal urethrostomy and complex wound closure was performed. Cystoscopy at the time of penectomy did not identify tumor involvement of the bladder, urethra or prostate. Palpable nodes were found at initial presentation but considering suspected infection of the mass, nodal biopsy and/or dissection was delayed. He was treated with Keflex 500 mg PO TID for 6 weeks postoperatively. Palpable adenopathy persisted and bilateral superficial and deep inguinal lymph node dissection was completed.

Figure 1. Exophytic, cauliflower-like, white massreplacing perineum.

Initial pathology came back as pT2Nx, "invasive well to moderately differentiated squamous cell carcinoma consistent with warty (condylomatous) carcinoma with negative surgical margins; tumor invaded the corpus spongiosum and corpus cavernosum, along with a focus suspicious for vascular involvement." Due to the rarity of the diagnosis of warty carcinoma, the specimen was sent to a second pathology department for confirmation of the diagnosis.

Warty carcinoma, as presented in our patient, has exophytic, infiltrating tumor characterized by papillary

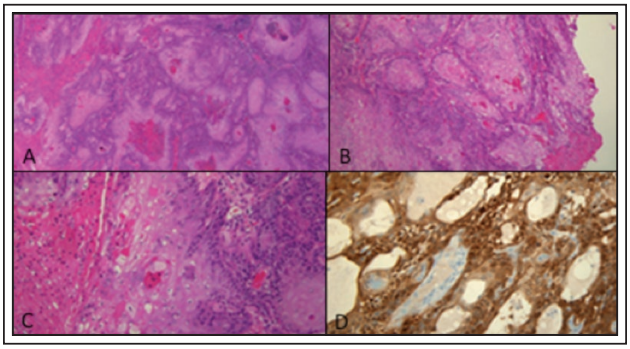

Figure 2. A) 40X H&E: undulating, complex, hyperkeratotic papillae with infiltration at the base; **B)** 100X H&E; **C)** 200X H&E. High power view of papillae with parakeratosis and koilocytotic atypia; **D)** 200X P16 stain.

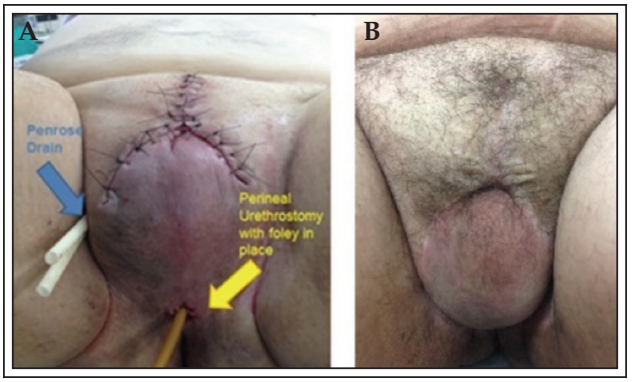

Figure 3. Appearance immediately postoperative and at 24 months. **A)** After the penectomy; **B)** 24 month follow up.

architecture and marked cytological atypia with prominent koilocytic features. The tumor also stained positively with P16 stain, Figure 2. This indicates that carcinoma was secondary to high risk HPV type, unlike other tumors from our differential diagnosis such as Buschke-Lowenstein or low grade verruciform tumors, which are associated with negative P16 stain.[1]

All lymph nodes from the inguinal dissection were negative for disease making the final TNM stage pT2N0M0. Due to the high recurrence rates of warty carcinoma, the patient remained on a close surveillance protocol post operatively. At the 24 month follow up the patient was free of cancer, Figure 3.

Discussion

Penile cancer makes up only 0.5% of all cancers in North America and other developed nations.[2] Penile cancer is subdivided into different variants based on histology: giant condyloma, also known as Buschke-Lowenstein tumor, is a benign tumor that could present similar to warty carcinoma. However, on microscopic exam, human papilloma virus (HPV) changes are only found in superficial layers, and no pleomorphism, nor invasion is found in Buschke-Lowenstein tumors.[2,3]

Papillary carcinoma, unlike warty carcinoma, lacks HPV changes on microscopic exam. Histologically, irregular fibrovascular cores with complex papillae are found, along with invasive jagged borders. Furthermore, it is likely to have inguinal metastases.[2,3]

Verrucous carcinoma also lacks HPV changes microscopically and is found to have inconspicuous fibrovascular cores with a broad based invasive front, unlike warty carcinoma which has obvious HPV changes. This carcinoma typically does not present with regional or distant metastases.[2,3]

Warty-basaloid carcinoma is a variant of warty carcinoma mixed with basaloid squamous cell carcinoma. Microscopically it shows basaloid cells in bottom layers of papillae or in deeply infiltrative nests. This carcinoma is more aggressive than pure warty carcinoma.[2,3]

Histological examination of squamous cell carcinoma, the most common penile cancerous lesion, presents with moderately differentiated keratinized cells. Twenty-five percent of these carcinomas are found to have positive HPV staining.[3]

One of the rarest forms is warty carcinoma, also known as condylomatous carcinoma. It is associated with HPV-related low-grade verruciform tumor, identical to vulvar, cervical or anal counterparts. This unique cancer only makes up 7% to 10% of all penile carcinomas. Warty carcinoma typically presents between the ages of 48 and 66.[4] Risk factors include poor hygiene in uncircumcised men, HPV infection, cigarette smoking, chewing tobacco, chronic balanitis and inflammation, and immunosuppression.[4] Twenty-two percent to 100% of this cancer is associated with HPV, usually HPV 16 and 18.[4]

Most men with warty carcinoma present with a lesion affecting the glans, foreskin or coronal sulcus. Grossly, warty carcinoma typically presents as an exophytic mass arising from the glans. It tends to look verruciform, white-tan in color, cauliflower-like in shape, and can be up to 5 cm in size. This cancer may have a cobblestone surface. Characteristically, warty carcinoma tends to be slow growing and locally invasive. However, warty carcinoma may penetrate deep into the corpus spongiosum or corpora cavernous with broad or irregular contours. Deep invasion can be associated with lymph node metastasis. Lymph node metastases are found in 17%-18% of cases.[2] Histopathologically, warty carcinoma presents as a low grade verruciform tumor with acanthosis, hyperkeratosis, and parakeratosis. It appears identical to warty carcinomas of vulva, uterine cervix or anus. However, unlike verrucous carcinoma, warty carcinoma has many squamous cells with koilocytotic atypia. Furthermore, papillary pattern with long, rounded or spiky papillae with prominent fibrovascular cores are found.[5]

Typically, treatment for this rare cancer requires partial or total penectomy, depending on the degree of invasion.[5] If the lesion only involves the foreskin, circumcision alone is a treatment option. Inguinal lymph node dissection is based on risk group stratification or a preoperative nomogram.[6] Certain lesions without invasion of the corpora cavernosa or the corpus spongiosum with a high degree of cell differentiation can be treated conservatively with cryotherapy, laser therapy, imiquimod 5%, 5-fluoruracil, radiotherapy, brachytherapy, or photodynamic therapy.[7] When distant invasion is appreciated, location of the metastases dictates the treatment plan. If inguinal nodes are palpable, options for management include needle biopsy, excisional biopsy, lymph node dissection or neoadjuvant chemotherapy depending on the size of the nodes and risk category. Although antibiotic treatment prior to treatment decision is no longer recommended, evidence of gross infection of the specimen with purulent drainage and malodorous presentation guided our decision to delay node dissection and treat with antibiotics. In cases involving distant metastases, especially lymphatic involvement, chemotherapy with cisplatin, methotrexate, and bleomycin has been shown to increase survival.[7]

This unique cancer has an intermediate behavior between low grade verrucous or papillary carcinoma and squamous cell carcinomas of the penis clinically, with a low mortality rate of 0%-9%. However, loco-regional relapse is more common, which warrants reliable patient follow up.[7] In conclusion, warty carcinoma is locally invasive with a lower mortality rate, yet higher loco-regional recurrence rate compared to squamous penile cancer. Recognizing warty carcinoma of the penis and understanding its pathology is essential to successfully treating patients with this disease. □

References

1. Cubilla AL, Lloveras B, Alejo M et al. Value of p16(INK)[4](a) in the pathology of invasive penile squamous cell carcinomas: A report of 202 cases. *Am J Surg Pathol* 2011;35(2):253-261.
2. Cubilla AL, Velazques EF, Reuter VE, Oliva E et al. Warty (condylomatous) squamous cell carcinoma of the penis: a report of 11 cases and proposed classification of 'verruciform' penile tumors. *Am J Surg Pathol* 2000;24(4):505-512.
3. Velazquez EF, Cubilla AL. Penile squamous cell carcinoma: Anatomic, pathologic and viral studies in Paraguay (1993-2007). *Anal Quant Cytol Histol* 2007;29(4):185-198.
4. Deem S, Keane T, Bhavsar R et al. Contemporary diagnosis and management of squamous cell carcinoma (SCC) of the penis. *BJU Int* 2011;108(9):1378-1392.
5. Bezerra AL, Lopes A, Landman G et al. Clinicopathologic features and human papillomavirus DNA prevalence of warty and squamous cell carcinoma of the penis. *Am J Surg Pathol* 2001; 25(5):673-678.
6. Arrabal-Polo MA, Arias-Santiago S, Jiménez-Pacheco A et al. Condylomatous cell carcinoma of the penis associated with multimetastatic human papillomavirus. *Actas Urol Esp* 2010;34(4): 392-393.
7. Solsona E, Algaba F, Horenblas S et al. EAU guidelines of penile cancer. *Eur Urol* 2004;46(1):1-8.