

## TUMORS OF THE PENIS

Carcinoma of the penis accounts for <1% of cancers among males in the United States, with approximately one to two new cases being reported per 100,000 men. In contrast, in some other parts of the world such as South America, South East Asia and parts of Africa the incidence is much higher and can account for 1-2% of malignant diseases in men.

Squamous cell carcinoma ( SCC ) accounts for over 95% of penile malignancies. It is not known how often SCC is preceded by premalignant lesions. Penile cancer is common in regions with a high prevalence of HPV and this may account for the worldwide variation in incidence. About one third of cases are attributed to human papilloma virus ( HPV ) - related carcinogenesis. HPV is a cofactor in the carcinogenesis of some variants of penile squamous cell carcinoma ( SCC ), while others are not related to HPV.

The commonest HPV subtypes in penile cancer are types 16 and 18. There is no association between the incidence of penile and cervical cancer, although both are linked to HPV. Female sexual partners of patients with penile cancer do not have an increased incidence of cervical cancer. Other malignant lesions of the penis, all much less common than penile SCC, are melanocytic lesions, mesenchymal tumours, lymphomas and metastases. Penile metastases are frequently of prostatic or colorectal origin.

## PATHOLOGY

### A. Precancerous Dermatologic Lesions

1. Leukoplakia is a rare condition that most commonly occurs in diabetic patients. A white plaque typically involving the meatus is seen. This lesion may precede or occur simultaneously with penile cancer.

2. Balanitis xerotica obliterans is a white patch originating on the prepuce or glans and usually involving the meatus. This condition is most commonly observed in middle-aged diabetic patients.

3. Giant condyloma acuminata are cauliflower-like lesions arising from the prepuce or glans. The cause is believed to be viral ( HPV ). These lesions may be difficult to distinguish from well-differentiated squamous cell carcinoma.

#### B. Carcinoma in situ ( Bowen disease, Erythroplasia of Queyrat )

1. Bowen disease is a squamous cell carcinoma in situ typically involving the penile shaft. The lesions appears as a red plaque with encrustations.

2. Erythroplasia of Queyrat is a velvety, red lesion with ulceration that usually involve the glans.

#### C. Invasive carcinoma of the penis

Squamous cell carcinoma ( SCC ) accounts for over 95% of penile malignancies. Risk factors for penile cancer are: phimosis, chronic penile inflammation ( balanoposthitis related to phimosis ), lichen sclerosus, sporadic and ultraviolet A phototherapy for various dermatological conditions such as psoriasis, smoking, HPV infection, condylomata acuminata, low socio-economic status, unmarried, rural areas, multiple sexual partners and early age of first intercourse.

Penile SCC usually arises from the epithelium of the inner prepuce or the glans. Fourteen different histological subtypes of penile SCC have been identified. They are different in clinical growth, clinical aggressiveness and HPV associations. Pathological subtype, perineural invasion, lymphocytic invasion, depth of invasion and grade in the primary tumor are strong predictor of poor prognosis and high cancer-specific mortality. Basaloid, sarcomatoid and adenosquamous subtype SCC have the worst prognosis. Invasive carcinoma of the penis begins as an ulcerative or papillary lesion, which may gradually grow to involve the entire glans or shaft of the penis. Buck's fascia represents a barrier to corporal invasion and hematogenous spread.

Primary dissemination is via lymphatic channels to the femoral and iliac lymph nodes. The prepuce and shaft skin drain into the superficial inguinal nodes ( superficial to fascia lata), while the glans and corporal bodies drain to both superficial and deep inguinal nodes ( deep to fascia lata ). There are many cross-communications so that penile lymphatic drainage is bilateral to both inguinal areas. Drainage from the inguinal nodes is to the pelvic nodes.

Distant metastases are clinically apparent in <10% of cases and may involve lung, liver, bone or brain.

## TNM clinical and pathological classification of penile cancer

### Clinical classification

T – Primary tumor

Tx Primary tumor cannot be assessed

T0 No evidence of primary tumor

Tis Carcinoma in situ

Ta Non-invasive verrucous carcinoma\*

T1 Tumor invades subepithelial connective tissue

T1a Tumor invades subepithelial connective tissue without lymphovascular invasion and is not poorly differentiated

T1b Tumour invades subepithelial connective tissue with lymphovascular invasion or is poorly differentiated

T2 Tumour invades corpus spongiosum with or without invasion of the uretra

T3 Tumour invades corpus cavernosum with or without invasion of the uretra

T4 Tumour invades other adjacent structures

N-regional Lymph Nodes

Nx Regional lymph nodes cannot be assessed

N0 No palpable or visibly enlarged inguinal lymph nodes

N1 Palpable mobile unilateral lymph node

N2 Palpable mobile multiple or bilateral inguinal lymph nodes

N3 Fixed inguinal nodal mass or pelvic lymphadenopathy, unilateral or bilateral

M – Distant Metastasis

M0 No distant metastasis

M1 Distant metastasis

Pathological classification

The pT categories correspond to the clinical T categories

The pN categories are based upon biopsy or surgical excision

pN – Regional Lymph Nodes

pNX Regional lymph nodes cannot be assessed

pN0 No regional lymph node metastasis

pN1 Metastasis in one or two inguinal lymph nodes

pN2 Metastasis in more than two unilateral inguinal nodes or bilateral inguinal lymph nodes

pN3 Metastasis in pelvic lymph node(s), unilateral or bilateral extranodal or extension of regional lymph node metastasis

pM – Distant Metastasis

pM1 Distant metastasis microscopically confirmed

G – Histopathological Grading

Gx Gradus of differentiation cannot be assessed

G1 Well differentiated

G2 Moderately differentiated

G3 Poorly differentiated

## G4 Undifferentiated

- \*Verrucous carcinoma not associated with destructive invasion

## CLINICAL FINDINGS

### A. Symptoms

The most common complaint at presentation is the lesion itself. It may appear as an area of induration or erythema, an ulceration, a small nodule or an exophytic growth. Phimosis may obscure the lesion and result in a delay in seeking medical attention. Other symptoms include pain, discharge, irritative voiding symptoms and bleeding.

### B. Signs

Lesions are typically confined to the penis at presentation. The primary lesion should be characterized with respect to size, location and potential corporal body involvement. Careful palpation of the inguinal area is mandatory because >50% of patients present with enlarged inguinal nodes. This enlargement may be secondary to inflammation or metastatic spread.

### C. Laboratory findings

Laboratory evaluation is typically normal. Anemia and leukocytosis may be present in patients with long-standing disease or extensive local infection.

### D. Imaging

Ultrasound (US), magnetic resonance imaging (MRI) and penile doppler US are used to estimate the infiltration of the penis body. Metastasis estimates imply use MSCT scan of the abdomen and pelvis, MSCT or X – rays of chest and bone scan. PET/CT is an option.

## Differential diagnosis

We need to think about syphilitic chancre and condyloma accuminata in differential diagnosis.

## TREATMENT

### Primary lesion

Biopsy of the primary lesion is mandatory to establish the diagnosis of malignancy. Treatment varies depending on the pathology as well as the location of the lesion. CIS ( Tis ) may be treated with fluorouracil cream application or with laser therapy.

The aims of the treatment of the primary tumour are complete tumour removal with as much organ preservation as possible, without compromising oncological control. For lesions involving the prepuce, this may be accomplished by simple circumcision.

For lesions involving the glans or distal shaft, partial penectomy with a 2-cm margin to decrease local recurrence has traditionally been suggested. Mohr's micrographic surgery and local excisions which histological margins are taken in a geometrical fashion around a cone of excision is less aggressive surgical treatment.

For the lesions involving the proximal shaft or when partial penectomy results in a penile stump of insufficient length for sexual function or directing the urinary stream, total penectomy with perineal urethrostomy has been recommended.

### Regional lymph nodes

Enlargement of inguinal lymph nodes at presentation does not necessarily imply metastatic disease. In fact, up to 50% of the time this enlargement is caused by inflammation. Thus patients who present with enlarged inguinal lymph node should undergo treatment of the primary lesion followed by a 4 to 6- week course of oral broad spectrum antibiotics. Persistent lymphadenopathy following antibiotic treatment should be considered to be metastatic disease, and sequential bilateral inguinal node dissection should be performed.

However, if lymphadenopathy resolves in higher stage tumors, therefore not Tis and T1, sentinel node biopsy are recommended. If positive nodes are encountered, bilateral

ilioinguinal node dissection should be performed. Patients who have inoperable disease and bulky inguinal metastases or systemic disease are treated with chemotherapy ( cisplatina, bleomycin, methotrexate and 5-fluorouracil ).

Literature:

1. Smith and Tanagho's general urology ( 16 th Edition )
2. EAU Guidelines on Penile Cancer – 2019.

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