Modern management of penile cancer

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In this article, the authors outline a contemporary management algorithm for penile cancer, with emphasis on developments in organ-sparing surgical techniques and inguinal lymph node detection and management.

Penile cancer is a rare disease, with an incidence of less than 1 per 100,000 men each year in Europe and North America (Figure 1).1 The most important risk factors for the development of penile cancer are listed in Box 1.2

Traditionally, the management of penile cancer has involved radical penile and lymph node surgery, both mutilating and morbid procedures associated with a significant impact on patients’ physical and psychological wellbeing. Improved understanding of the disease has shifted the emphasis of treatment towards minimising treatment-related morbidity while maintaining high oncological standards.

PRESENTATION AND INITIAL INVESTIGATIONS

Penile cancer often presents late3 as a result of patient embarrassment, a fear of the implications of diagnosis and treatment, and the stigma that it may be related to a sexually transmitted condition.

The most commonly affected areas are the glans (48 per cent) and prepuce (21 per cent), or a combination of the two in 80–90 per cent of patients.4 Lesions may present as a nodule, an ulcer, a red patch, or may be an incidental finding at circumcision.5 The history should include enquires about the length of time the lesion has been present, whether it has changed, and whether the patient has noticed any symptoms such as pain, pruritus or bleeding.

Physical examination is directed towards the location, size, morphology and surface appearance of the lesion, with a higher index of suspicion for malignancy in moist-looking lesions, rather than dry and scaly ones. A thorough examination requires full retraction of the foreskin to examine the entire glans as well as the shaft. It should also involve an examination of the groins for any palpable inguinal lymphadenopathy.

Any suspicious penile lesions should be referred for biopsy unless frankly malignant. Patients with palpable groin lymphadenopathy should also be referred for ultrasound-guided fine-needle aspiration of the lymph node.

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Box 1. Risk factors for penile cancer

- Intact foreskin (after infancy)
- Phimosis
- Smoking
- Immunosuppression
- Human papillomavirus 16 and 18
MANAGEMENT OF THE PRIMARY TUMOUR

One of the most pivotal developments in the management of penile cancer in the past decade has been the reduction in the size of the surgical margin thought sufficient for oncological control. Previously, lesions were treated with radical surgery as a rule, as it was thought that a 2cm margin was necessary. This belief has been increasingly challenged, as recent studies have shown that patients treated with a surgical margin of only a few millimetres had equally good outcomes as those treated with total or partial penile amputations. This shift in mindset has subsequently led to the development of a range of conservative surgical techniques that aim to preserve as much penile tissue as possible without compromising oncological clearance.

Box 2 shows the possible treatment options of the primary tumour, classified according to tumour stage.

Topical chemotherapy for carcinoma in situ
Penile squamous cell carcinoma (SCC) in situ accounts for about 10 per cent of penile malignancy at initial diagnosis. The first-line treatment for penile SCC in situ is the use of topical chemotherapy creams, such as 5-fluorouracil or imiquimod. This method of treatment yields reasonable complete response rates of over 50 per cent, but is associated with a significant rate of recurrence of 20 per cent. This method is therefore most appropriate in patients who can be committed to regular self-examinations and intensive outpatient follow-up.

Penile-preserving surgical techniques
Glans resurfacing
Glans resurfacing was first used to treat penile SCC in situ in 2006, and has proven effective in disease resistant to topical chemotherapy. The technique involves dissection of the epithelial layer of the glans in quadrants from the meatus to the coronal sulcus. A partial-thickness graft is then harvested from the thigh and used to cover the denuded glans, and secured with absorbable sutures placed at the coronal sulcus and at the meatus. Good functional and cosmetic results have been reported, and the first series of 10 total-glans-resurfacing operations done for SCC in situ at our unit had no recurrences after 45 months’ follow-up.

Partial-glans-resurfacing techniques have also been used for small lesions. These operations were associated with a higher risk of positive surgical margins necessitating further surgery to clear the disease completely, but were not associated with any increased risk of recurrence or progression compared to total glans resurfacing.

Glansectomy
Patients with disease invading but limited to the glans can be offered a glansectomy, where the glans is completely excised off the distal ends of the corpora. This procedure has excellent oncological outcomes, which are comparable to more radical surgery, but does not sacrifice cosmetic appearance, and the majority of patients retain their sexual function.

MANAGEMENT OF LYMPH NODE METASTASIS

Spread to regional lymph nodes is the single most important prognostic factor in penile cancer survival. All patients should be carefully examined for palpable lymphadenopathy in the groin, as inguinal lymph nodes are almost always the first site of metastasis in penile cancer. All palpable lymph nodes should be biopsied, and any groin with a positive biopsy should be treated with radical inguinal lymphadenectomy.

BOX 2. Treatment options of the primary tumour according to tumour stage

STAGE: Tis
- Topical chemotherapy:
  - 5-fluorouracil or imiquimod
- Laser therapy (Nd: YAG or carbon dioxide)
- Penile-preserving surgical techniques:
  - circumcision (lesions only involving foreskin)
  - total or partial glans resurfacing

STAGE: Ta/T1/T2
- Penile-preserving surgical techniques:
  - circumcision (lesions only involving foreskin)
  - wide local excision
  - glansectomy (if corpus cavernosum not involved)
  - partial penectomy
- Radiotherapy (brachytherapy or external beam, suitable for small tumours)

STAGE: T3/T4
- Partial penectomy
- Radical penectomy
  ± Neoadjuvant chemotherapy
  ± Reconstruction
The management of clinically node-negative (cN0) patients poses more of a challenge. About 20 per cent of cN0 groins in patients with penile cancer are known to harbour occult inguinal metastasis. Waiting until lymphadenopathy becomes clinically apparent before performing lymphadenectomy results in poorer outcomes compared to performing lymphadenectomy electively. However, lymphadenectomy is an operation associated with significant morbidity, including lower limb oedema, deep-vein thrombosis, wound infection and necrosis, and performing it ‘prophylactically’ on all patients would be massive overtreatment. It is therefore important to be able to identify which cN0 patients in fact have clinically occult inguinal metastasis.

**Dynamic sentinel lymph node biopsy**

The theory behind dynamic sentinel lymph node biopsy (DSLNB) is the knowledge that penile lymphatic drainage follows a predictable pattern, draining first to inguinal lymph nodes before involving pelvic lymph nodes. In the absence of tumour in these areas, distant metastases are very rare.

The technique involves the injection of a radiolabelled tracer around the penile tumour several hours prior to surgery. Lymphoscintigraphic images are obtained in order to identify the first draining, or ‘sentinel’ lymph node in that groin, and the positions of these are physically marked on the groin. In the operating theatre, patent blue dye is injected peri-tumorally to ‘sentinel’ lymph node and all blue-coloured lymph nodes that are picked up by the gamma probe and all blue-coloured lymph nodes are excised and sent for histological analysis. Any groin with a positive finding that a reduced surgical margin remains oncologically sound.
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