Case report

Penile intraepithelial neoplasia—a veiled lesion in genitourinary medicine

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Penile intraepithelial neoplasia (PIN) is a clinically well known condition. However, its diagnosis is often difficult. We present four cases of PIN, seen in our department. Various histological patterns ranging from PIN I to PIN III were noted in these cases.
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Introduction

Penile intraepithelial neoplasia (PIN) is an HPV associated precancerous lesion of the penis. The course of the disease is usually chronic with an average duration of 2–3 years.¹ The natural history is age dependent. In younger men the disease is generally benign and self limiting. However, in men over 40 years old, the risk of progression to cancer is high.

Case 1

A 44 years old male patient presented to the genitourinary medicine clinic with a small grey spot on the penis which had been present for 1 year.

On examination a white plaque was seen on the foreskin (fig 1). The lesion was biopsied and the histopathology showed mild epidermal dysplasia, amounting to PIN I.

In view of the premalignant condition the patient was referred to the urology department. He was treated with 5% fluorouracil cream topically.

Case 2

A 75 years old male patient presented to the genitourinary medicine clinic complaining of soreness of penis for the past 18 months. On examination a non-tender area of shiny and flaky skin was seen at the glans. Biopsy was done and the histopathology report showed the evidence of intraepithelial squamous carcinoma (Bowen's disease). He was then referred to the urologist, where the lesion again responded to the topical application of 5-fluorouracil cream.

Case 3

A 30 year old HIV positive homosexual man who was on antiretroviral therapy was regularly attending the genitourinary medicine clinic for the treatment of recurrent warts which were resistant to podophyllin and cryotherapy treatment. The patient was offered penile biopsy and hyfrecation for warts. The histopathology report showed the evidence of PIN II; he was treated with cryosurgery.

Case 4

A 41 year old man was seen in the genitourinary medicine clinic complaining of dry skin

Figure 1 PIN lesion (note the biopsy site).

on his penis. Clinical examination showed a pale pink irregular thickened area on the foreskin. A 6 mm punch biopsy showed the evidence of Bowenoid intraepithelial neoplasia PIN III. He was referred to the urologist, where he underwent complete circumcision.

Discussion

The diagnosis of PIN in patients presenting to genitourinary medicine clinics highlights the fact that any suspicious lesion of chronic onset should be biopsied, to determine the nature of the lesion. This is especially important in men more than 40 years old, as in these the risk of progression to cancer is high.

Macroscopically, the lesions are often flat, between 0.2 and 3.5 cm in diameter. They are red or slightly brown with a smooth, glistening, sometimes verrucous surface. There could be a single lesion or multiple lesions (about 30), which may coalesce to form plaques.

The histology of PIN in young adults² shows epithelial proliferation, hyperkeratosis, and

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perakeratosis. The cell nuclei are hyperchromatic, clumped and show lack of organisation, maturation, and cohesion. Mitotic figures are generally numerous and abnormal forms are often present.

PIN has been found to be related to HPV viruses; the most frequently identified type is HPV 16.³ As HPV can be sexually transmitted,^{4,5} the identification of "high risk males" (HRM) has been documented. Studies have shown that HRMs who are the male partners of women with cervical cancer have a higher incidence of penile carcinoma.⁶ Further, some of the HPV induced changes, particularly flat condylomas (FC) and some PIN lesions, are difficult to detect with the naked eye. Some workers⁷ have suggested the routine use of peoscopy (colposcopy to examine penis in magnification) and/or the application of acetic acid to male genital skin as the more sensitive method to detect PIN and FC in partners of women with cervical intraepithelial neoplasia, condyloma acuminata, and flat condyloma. Any suspicious lesion found should be biopsied. Further studies are needed to determine the exact role of peoscopy in diagnosing PIN.

Though it is well known that HPV has an aetiological role in vulval and vaginal intraepithelial neoplasia, as far as we are aware no studies have yet been done to correlate the existence of PIN with VIN (vulval intraepithelial neoplasia) and VAIN (vaginal intraepithelial neoplasia).

Another issue is the co-existence of HPV virus, HIV virus, and the incidence of PIN in those patients who have genital warts resistant to treatment. As the natural history of the virus is not well known, it is difficult to define the exact relation. However, as the natural immunity might be suppressed in HIV positive patients, the HPV virus might play a more active part.

The differential diagnosis of PIN includes pigmented warts, lentigo, naevi and melanoma, seborrhoeic warts, angiokeratoma, lichen planus, and localised psoriatic lesions. It should

also be differentiated from inflammation, allergic responses, and *Candida* infection.

The existence of well defined lesions, vascular punctation, absence of symptoms, persistence of lesions after anti-inflammatory treatment, and ultimately a biopsy establish the correct diagnosis of PIN.

Management of PIN in young patients should be conservative (that is, superficial surgery, electrocautery, therapy with carbon dioxide laser, and cryotherapy). In addition, topical 5-fluorouracil or preparations containing vitamin A acid have been proposed. However, if microinvasion is suspected, wide local excision should be performed.⁸

One of the disadvantages following conservative treatment is a certain degree of anxiety in regular follow up and peoscopic assessment. It is suggested that patient should be seen 3 weeks after the end of the treatment and then every 3 months for a year in the absence of recurrent disease.⁹ Appropriate advice concerning the use of condoms by these patients is controversial. Some clinicians believe that they should be used during the treatment period and at least several months of disease free follow up. This is particularly important if the patient has sexual intercourse with new partners.

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