Case Report

In situ squamous cell carcinoma of male and female external genitalia

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Abstract

In situ squamous cell carcinoma (SCC) of male and female genitalia can present as Bowen's disease (BD), erythroplasia of Queyrat, Bowenoid papulosis, Paget's disease, pseudoepitheliomatous keratotic, and micaceous balanitis. BD is SCC *in situ*. It affects both skin and mucous membranes and has the potential to progress to invasive SCC. BD can be found on any body site, including both sun-exposed and non-sun-exposed regions of the body. However, BD presenting on the genitalia is rare. Here, we present a report of three cases of *in situ* genital malignancies. Two females had BD, and one male had erythroplasia of Queyrat.

Key words: Bowen's disease, erythroplasia of Queyrat, *in situ* squamous cell carcinoma

INTRODUCTION

Squamous cell carcinoma (SCC) of the penis includes both *in situ* and invasive carcinoma. *In situ* SCC of the penis, also known as penile intraepithelial neoplasia, which encompasses three clinical variants: erythroplasia of Queyrat, Bowen's disease (BD), and Bowenoid papulosis. All three share similar histopathologic features and biologic behavior and are associated with similar human papillomavirus (HPV) subtypes. The distinction depends on the anatomic location and morphology of the lesions. BD and erythroplasia of Queyrat are considered to represent clinical variants of a single pathologic process. BD of vulva is considered as vulval intraepithelial neoplasia. Bowenoid papulosis differs from erythroplasia of Queyrat and BD in clinical presentation and exhibits a significantly lower rate of malignant transformation.

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CASE REPORTS

Case 1

A 48-year-old female presented with complaints of an asymptomatic black colored lesion over genitals of 3 months' duration. Initially, it started as a small black colored pea-sized lesion that gradually increased to the present size. The patient attained menopause 2 years prior. Cutaneous examination revealed a single, well-defined, annular hyperpigmented plaque of 3 cm × 2 cm size over inner side of the right labium majus extending onto the clitoris and labium minus with erosions on the surface and whitish discharge [Figure 1a]. There was no evidence of similar lesion elsewhere on the body. There was a single enlarged, firm, nontender, mobile lymph node of 2 cm in diameter on the right side. Enzyme-linked immunosorbent assay for HIV and venereal disease research laboratory test was nonreactive. Gram stain and

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KOH mount from the vaginal discharge did not reveal any significant finding. Histopathology revealed full thickness dysplasia of squamous epithelium and pilosebaceous epithelium showing atypical keratinocytes with disorderly maturation of epidermis, stromal inflammation with higher magnification showing the windblown appearance of keratinocytes which were consistent with the diagnosis of BD [Figure 1b and c]. Scrape cytology revealed the presence of atypical squamous cells in clusters with altered nuclear-cytoplasmic ratio, nuclear hyperchromasia also seen. The patient was treated with partial vulvectomy [Figure 1d]. There has been no recurrence of disease even after 2 years' follow-up [Figure 1d].

Case 2

A 40-year-old female came with complaints of itchy lesion over genitals since 2 months. She was a diagnosed case of systemic sclerosis, being managed on dexamethasone-cyclophosphamide pulse therapy and oral cyclophosphamide 50 mg daily. Cutaneous examination revealed a single well-defined annular plaque with raised violaceous borders and central erosion present on the left side of clitoris extending to the left side of labium minus [Figure 2a]. There was no evidence of regional lymphadenopathy. Histopathology revealed full thickness dysplasia of squamous epithelium with atypical keratinocytes with disorderly maturation of epidermis, stromal inflammation with higher magnification showing windblown appearance of keratinocytes which were consistent with BD [Figure 2b and c]. She was treated with cryotherapy with gradual improvement in the lesion [Figure 2d].

Case 3

A 43-year-old male presented with asymptomatic reddish colored lesion over penis of 3 years' duration with a history of the gradual increase in size over time. There was no history of burning micturition or high-risk sexual behavior. Cutaneous examination revealed erythema over glans with whitish plaque over coronal sulcus [Figure 3a]. Histopathology revealed markedly proliferating epidermis with crowding of basal cell layer, lymphohistiocytic infiltration with multiple dilated blood vessels. On higher magnification, it showed cellular atypia with large hyperchromatic nuclei suggesting the diagnosis of erythroplasia of Queyrat [Figure 3b]. The patient was treated with cryotherapy with the healing of lesion [Figure 3c].

DISCUSSION

The exact prevalence of BD cannot be estimated because of paucity of data in national health databases and regional differences in prevalence. Prevalence varies from 14.9–142 cases per 100,000 whites in different studies.[1,2] BD is most commonly reported in sunexposed sites of whites and rarely occurs in patients with pigmented skin; if it does, it usually affects nonexposed sites.[3] The ratio is approximately equal between males and females. It is more commonly found on the head and neck of men and on the lower limbs and cheeks of women.[4] It occurs in adulthood, with the highest

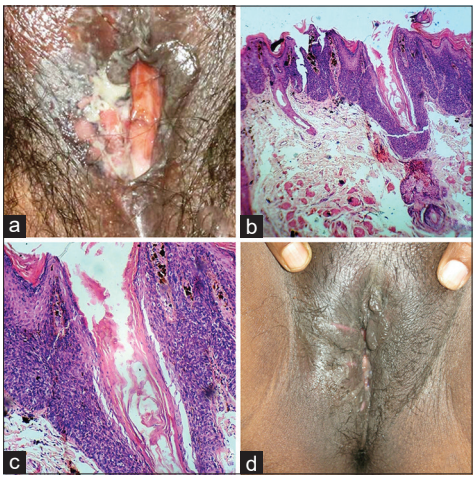

Figure 1: (a) Case 1: A single, well-defined, annular hyperpigmented plaque of 3 cm × 2 cm size over inner side of right labium majus extending onto the clitoris and labium minus with erosions on the surface and whitish discharge. (b) Histopathology revealed full thickness dysplasia of epidermis extending into the pilosebaceous unit with pigmentary incontinence (H and E, ×100). (c) "Wind-blown" appearance of epidermis with multiple atypical keratinocytes and marked pigmentary incontinence in the dermis (H and E, ×400). (d) Postpartial vulvectomy

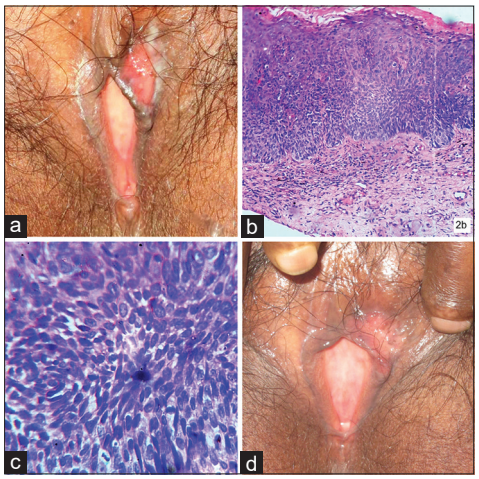

Figure 2: (a) A single well-defined annular plaque with raised violaceous borders and central erosion present on left side of clitoris extending to the left side of labium minus. (b) Histopathology revealed full thickness dysplasia of squamous epithelium with atypical keratinocytes with disorderly maturation of epidermis, stromal inflammation (H and E, ×40). (c) "Windblown appearance" of epidermis with atypical keratinocytes (H and E, ×400) (d) Gradual improvement after three sessions of cryotherapy

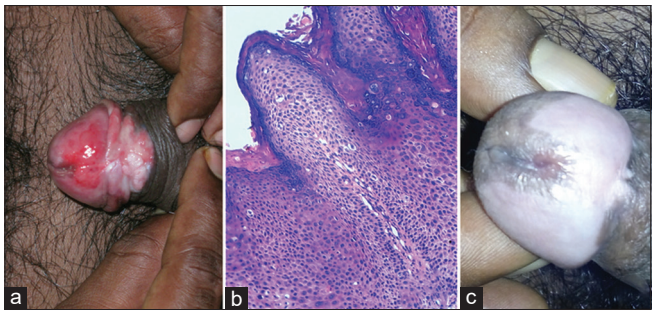

Figure 3: (a) Erythema over glans with whitish plaque over coronal sulcus. (b) Histopathology revealed marked acanthosis with full thickness dysplasia of epidermis, crowding of basal keratinocyte and lymphohistiocytic infiltrate in upper dermis (H and E, ×100). (c) Higher magnification showing full thickness dysplasia with cellular atypia and large hyperchromatic nuclei (H and E, ×400)

incidence in patients older than 60 years. Etiological factors include HPV (type 16 and 18) infection, HIV infection, vulval inflammatory skin diseases, and immunosuppression. It usually presents as an irregular erythematous, white or pigmented plaque on vulva. Colposcopy may be used to see the extent of the condition.[5,6]

Skin biopsy is required to confirm the diagnosis and identify *in situ* and invasive cancer. Various treatment modalities used for the treatment of BD include topical Imiquimod cream, topical 5-fluorouracil cream, cryotherapy, surgical excision, curettage and electrocautery and photodynamic therapy (PDT), lasers and topical diclofenac. PDT has been shown to be an effective treatment option for BD with 80%–95% complete response rates.

Erythroplasia of Queyrat is a rarely reported disorder and accounts for < 1% of malignancies in males.[7] It is a disease of middle-aged to elderly males.[8] It has been described in males ranging from the age of 20–80 years.[9,10] Predisposing factors include lack of circumcision, chronic irritation, inflammation or infection, zoon balanitis, HPV type 8 and 16, immunosuppression, UV light, phimosis, multiple sexual partners, smoking, chronic underlying diseases, social/cultural habits, hygiene, and religious practices.[11,12]

It presents as a bright red-colored, well-demarcated, velvety plaque or plaques commonly involving the glans, coronal sulcus, or prepuce. Ulceration may be a sign of an invasive lesion.

Diagnosis is confirmed by biopsy which shows acanthosis, parakeratosis, partial or full thickness epidermal atypia, dyskeratosis, and lymphohistiocytic dermal infiltrate. It should be differentiated from Zoon's balanitis, erosive lichen planus, genital psoriasis, fixed drug eruption, and sexually transmitted infections (STIs). Medical treatment consists of topical 5-fluorouracil and imiquimod. Surgical options include Mohs micrographic surgery, surgical excision, cryotherapy, electrodissection and curettage, radiation, carbon dioxide laser ablation, and PDT. Approximately 10% of lesions show progression to invasive SCC.

Knowledge about the clinical presentations of *in situ* SCC of external genitalia is very important as they are commonly misdiagnosed as STIs leading to delay in diagnosis and progression to invasive SCC. Hence, timely diagnosis by biopsy and subsequent management improves prognosis.

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Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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