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Short Communication

Images in transplant dermatology

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Abstract

Transplant recipients can develop various skin conditions throughout their lives. Of concern are skin cancers, which are best treated with early detection. We report two cases seen in the transplant dermatology clinic in Singapore General Hospital.

Key words

Transplant, dermatology, keratoacanthoma, Extramammary Paget Disease

Case 1

A 64-year-old Chinese female, with a history of renal transplant over 20 years, presented with a sudden onset of slightly tender nodule (Figure 1) over her right forearm in the past one month. There was no preceding trauma and she never had similar lesions in the past. What was the diagnosis?

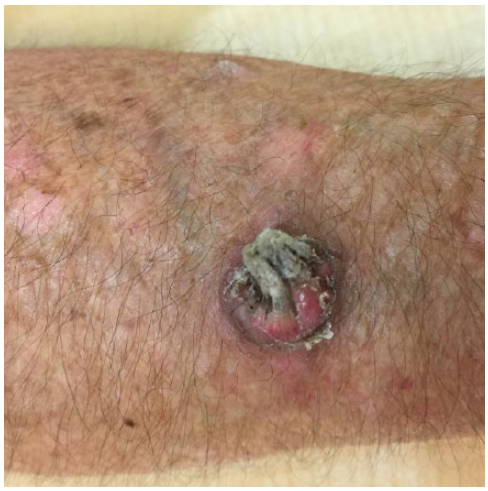

Figure 1. Forearm nodule.

Histology

Sections (Figures 2 and 3) using hematoxylin and eosin stain (H&E) show a well-differentiated squamous proliferation with an endophytic growth pattern, parakeratin plug and peripheral buttressing. A mild lymphocytic infiltrate is seen at the base. Solar elastosis is noted in the dermis. The lesion is completely excised. It is 2 mm from the closest radial margin and less than 1 mm from the deep margin.

Diagnosis

Keratoacanthoma. Keratoacanthomas are common self-limited squamous proliferations. They have been considered a benign neoplasm with involution and complete resolution within few months. It is a low-grade tumour that originates in the pilosebaceous glands and closely resembles squamous cell carcinoma (SCC). While it is clear in some cases, the histological and cytological features of SCC and keratoacanthoma are often difficult to distinguish.[1–3]

Keratoacanthoma is characterized by rapid growth over a few weeks to months, followed by spontaneous resolution over 4–6 months in most cases. In rare cases, keratoacanthoma may progress to invasive or metastatic squamous cell carcinoma.[4]

In transplant patients, the pathogenesis of skin tumour is multifactorial, with extrinsic and intrinsic factors. Ultraviolet radiation generates mutations in the p53 gene, secretion of immunosuppressive factors and inhibition of antigen-presenting cells and Langerhans' cells. Immunosuppressive treatments also inhibit antigen-presenting cells. Local and systemic immunodeficiency favours the proliferation of human papillomavirus, which acts as a co-carcinogen. Genetic factors (such as fair skin and polymorphism in p53), ageing and smoking may also play a role.[5]

Keratoacanthoma typically grows rapidly, attaining 1–2 cm within weeks, followed by a slow involution

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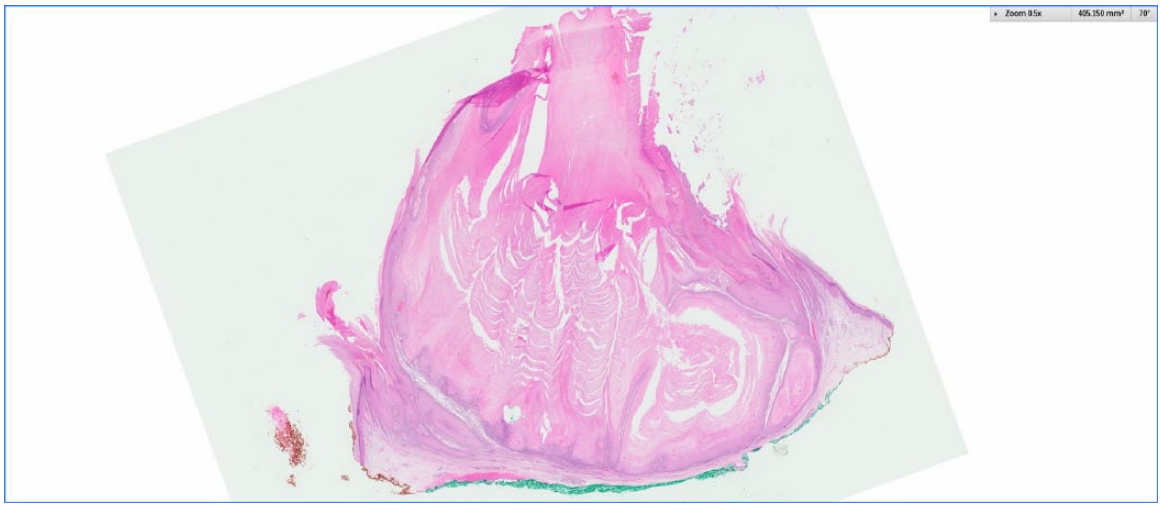

Figure 2. Section of nodule, low power (×40) H&E.

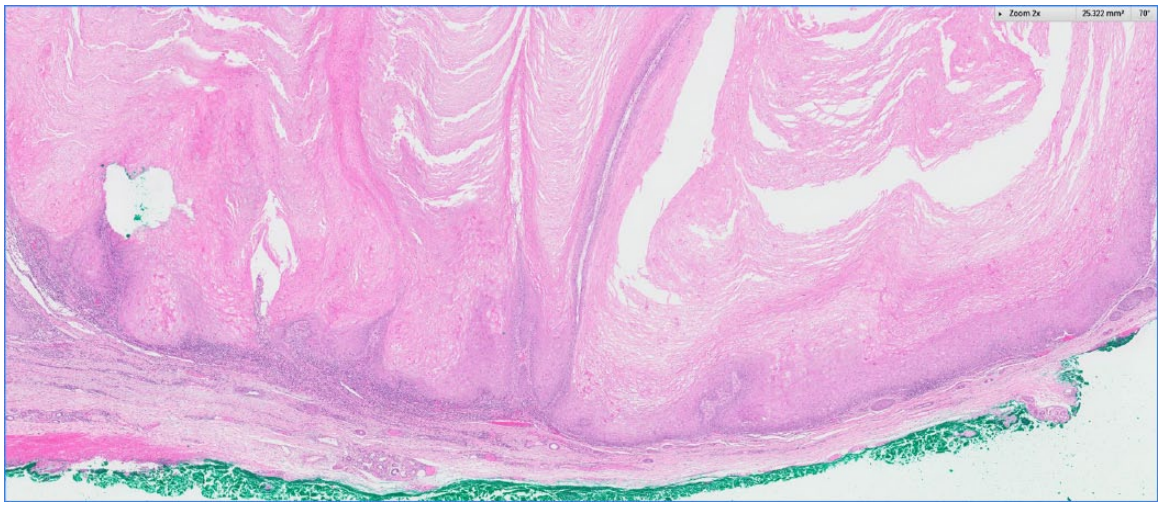

Figure 3. Section of nodule, high power (×200) H&E.

period lasting up to 1 year and leaving a residual scar if not excised preemptively.[2]

Lesions typically are solitary and begin as firm, roundish, skin-coloured or reddish papules that rapidly progress to dome-shaped nodules with a smooth shiny surface and a central crateriform ulceration or keratin plug that may project like a horn. Most keratoacanthomas occur on sun-exposed areas.

The primary therapy for keratoacanthoma is surgical excision. Tumours should be excised with adequate margins (3–5 mm) and histopathologic evaluation to exclude invasive SCC. Partial shave biopsy is not recommended as inadequate tissue may not distinguish between keratoacanthoma and invasive SCC. Mohs micrographic surgery may be considered for large or recurrent keratoacanthomas or keratoacanthomas located in anatomic areas with cosmetic or functional considerations.[2]

Antineoplastic agents like topical and intralesional 5-fluorouracil, intralesional MTX, interferon alfa-2a and bleomycin have been reported as alternative treatment modalities for keratoacanthoma. These are useful in situations where patients have large or multiple tumours or tumours that are inoperable because of anatomic location or the patient's poor medical status.[2]

Patients who develop non-melanoma skin cancer, such as keratoacanthoma, SCC, Bowen disease or basal cell carcinoma, are at high risk for developing subsequent non-melanoma skin cancer. Education, periodic follow-up examinations and early detection and treatment of actinic keratosis and skin cancer are important in these patients. Importantly, patients must be educated about sun-protection technique (including sunscreen) and skin self-examination.[5]

Case 2

A 55-year-old Chinese male, with a history of renal transplant in 2008, presented with an erythematous scrotal growth (Figure 4) for the past 4 months. There was no pain or itch, and he had no similar lesions in the past. What was the diagnosis?

Histology

H&E low power section (Figure 5) illustrated an acanthotic epithelium containing basally situated tumour cells, also involving an underlying hair follicle.

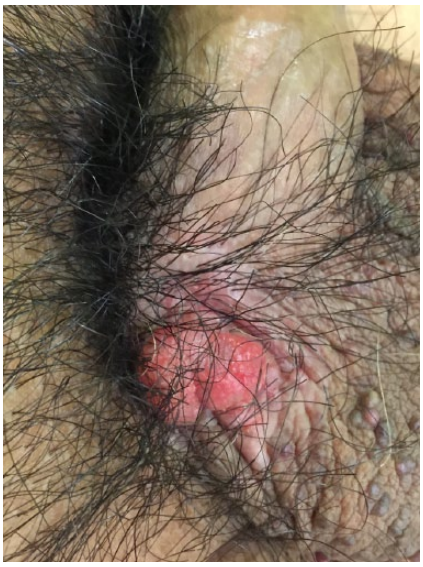

Figure 4. Erythematous scrotal growth.

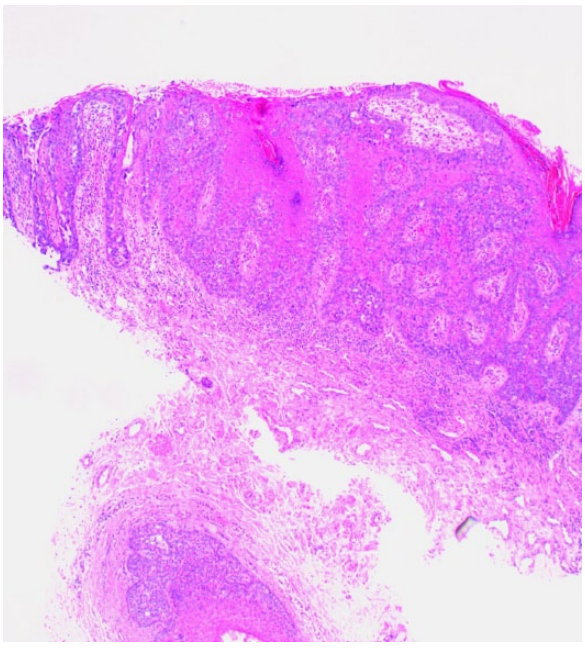

Figure 5. Section of scrotal growth, low power H&E.

The acanthotic epidermis shows a confluent distribution of partly acantholytic epithelioid cells, also involving an underlying follicular adnexal structure. The atypical cells (Figure 6) have enlarged vesicular nuclei containing prominent nucleoli, surrounded by moderate amount of pale cytoplasm. Occasional mitoses and intracytoplasmic mucin droplets (Figure 7) are seen. No invasive behaviour is evident. Positive immunoreactivity of tumour cells with CEA, CAM5.2 (Figure 8) and CK7, and lack of reactivity with Melan A (Figure 9), CK20, PSA and PSAP support the diagnosis of a primary type of Paget's disease.

Diagnosis

Extramammary Paget's disease. Extramammary Paget Disease (EMPD) is an uncommon adenocarcinoma of apocrine gland-bearing skin. It usually occurs in individuals between the ages of 50 and 80 years. In the Asian population, men are more likely to be affected.

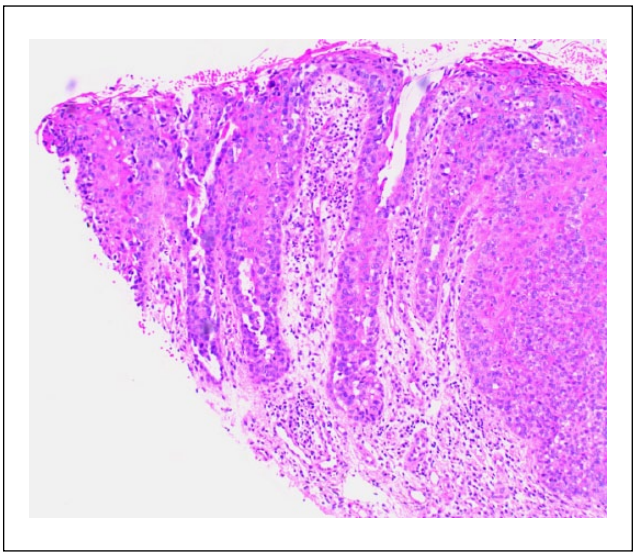

Figure 6. High power H&E section of intra-epidermal pale tumour cells.

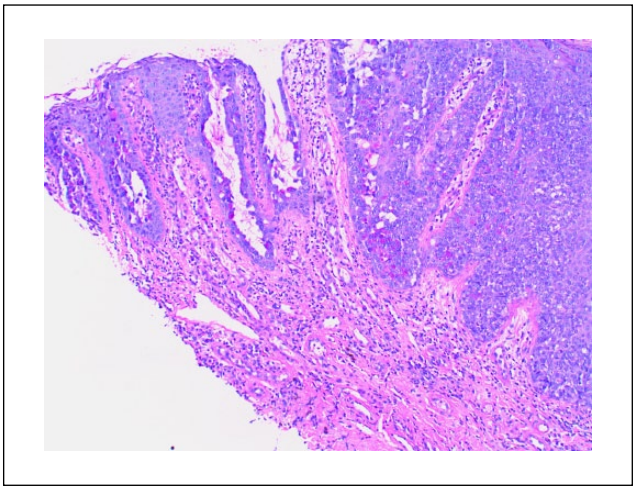

Figure 7. PAS/diastase stain demonstrates intracytoplasmic mucin droplets.

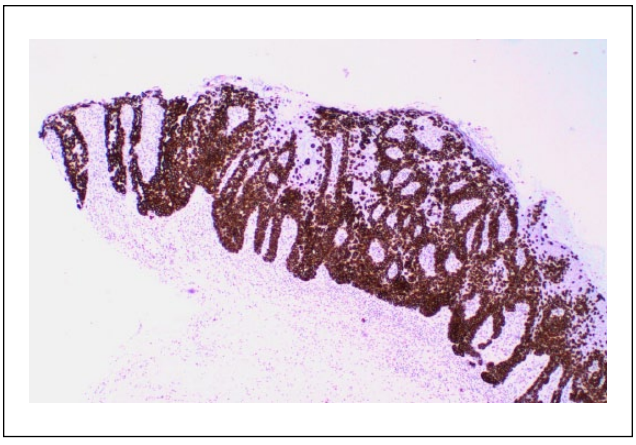

Figure 8. Diffuse strong positive CAM5.2 immunoreactivity is seen within tumour cells.

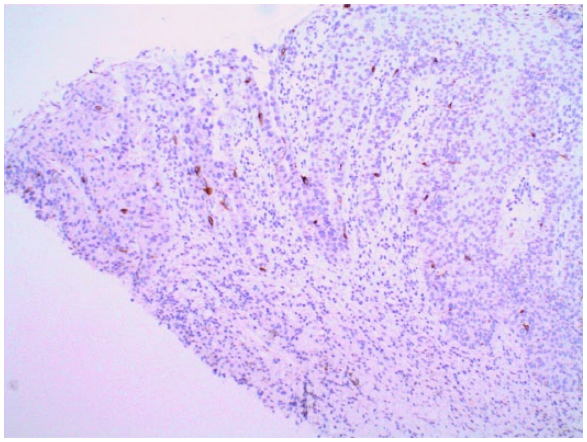

Figure 9. Melan A immunostaining is positive only within residual melanocytes.

Approximately 25% of the cases of EMPD are associated with an underlying in situ or invasive neoplasm. In all patients, the neoplasm most likely to be associated with EMPD is an adnexal apocrine carcinoma. This associated neoplasm probably represents infiltration of the deeper adnexa by epidermal Paget cells. The anatomic location of EMPD plays a role in predicting the risk of associated carcinoma. For instance, genital disease is associated with carcinoma in about 4–7% of patients. Perianal disease is associated with underlying colorectal carcinoma in 25–35% of cases.[6]

There is no strong association of EMPD with transplant patients, till date with only one case report of renal transplant patient with vulva EMPD.[11]

The possibility of EMPD should be carefully considered in any patient with chronic dermatitis of the groin, vulva or perianal area. Patients with EMPD usually present with non-resolving eczematous lesions in the groin, genitalia, perineum or perianal area. Delays in diagnosis are common owing to the non-specific clinical findings that can be difficult to distinguish from psoriasis, dermatophytosis or contact dermatitis. The most common symptom of EMPD is intense pruritus. Most patients have only pruritus in the affected area and no other symptoms.

The diagnosis of EMPD requires a high degree of clinical suspicion followed by skin biopsy with pathologic correlation. A review of systems and physical examination should be performed in all patients. The examination should include full skin examination, palpation of all lymph nodes, rectal examination, sigmoidoscopy and cystoscopy. Women will also require pelvic examination with a Papanicolaou test, breast examination and colposcopy.[6]

Histopathologic examination of EMPD shows intraepidermal Paget cells, which are large, round cells with abundant pale-staining cytoplasm and a large nucleus. Immunohistochemical staining is important to confirm the diagnosis of EMPD. These stains include cytokeratin 7, carcinoembryonic antigen (CEA) and anti-cytokeratin (CAM5.2).[7]

Margin-controlled surgical excision of all the involved epidermis is the most effective treatment. Topical treatments reported include imiquimod and fluroruracil.[8–10]

Treatment should be coordinated with an appropriate surgical subspecialist (e.g. a urologist, a colorectal surgeon or a gynaecologist).

The prognosis for EMPD depends on early diagnosis with definitive surgical treatment. Full recovery is possible in patients with purely epidermal disease and negative margins after micrographic surgery. Perianal disease, dermal invasion and lymph node metastasis are poor prognostic indicators.[9,10]

Our patient had wide local excision of his scrotal EMPD by the urology team, and is scheduled for subsequent gastroenterology consultation.

Conflict of interest

The authors declare that there are no conflicts of interest.

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