Pathology of malignant skin tumours

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Abstract

The incidence of malignant skin tumours has significantly increased in recent years. In addition to establishing a diagnosis, histopathological assessment of these tumours provide vital prognostic information that often inform decisions related to onward referral, optimal treatment and follow-up care. Using the example of the three most common skin (cancers basal cell carcinoma, squamous cell carcinoma and malignant melanoma), this review outlines how the contents of the histopathology report influence patient management. Recently, unravelling the molecular pathogenesis of some of these tumours has paved the way for development of novel molecular targeted therapies. This article will familiarize the reader with these developments and also improve their overall understanding of the role of pathology in a multidisciplinary team setting towards management of cancer patients.

Keywords Diagnosis; histopathology; management; prognosis; skin cancers

Introduction

The skin is the largest organ system and is composed of two broad layers. It is surfaced by the epidermis which not only provides mechanical protection but also contains melanocytes which produce melanin. By absorbing visible and ultraviolet light, melanin reduces radiation-induced DNA damage. The epidermis is supported by a thick layer of fibro-elastic stroma called the dermis containing blood vessels and adnexal structures such as hair follicles, sebaceous and sweat glands.

The incidence of all forms of skin cancer in the UK has increased over the last 30 years. Although a malignant tumour of the skin can arise from any of the constituent cell types, those arising from the cells populating the surface epidermis (i.e. keratinocytes and melanocytes) are most frequent. The most common malignant skin tumours in much of the Western world are basal cell carcinoma (BCC), squamous cell carcinoma (SCC) and malignant melanoma.

In this review we shall outline the pathological characteristics of the three most common malignant skin tumours with particular emphasis on aspects which influence prognosis and management.

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Basal cell carcinoma

Clinical presentation

Basal cell carcinoma is the most common malignant tumour of the skin typically, but not exclusively arising on areas exposed to sunlight. The clinical appearance is variable but the most common presentation is that of a slow growing, red-skin coloured nodule with telangiectasia which frequently ulcerates. Some tumours present as an erythematous macule/patch or an indistinct, indurated, scar-like plaque.

Histopathology

BCC derives its name from the histological similarity to normal basal (basaloid) cells of the epidermis. In addition to the diagnosis, a pathology report of a BCC provides information which has direct implication on prognosis and management. This includes *histological sub-typing* based mainly on the growth pattern into 'low-risk' and 'high-risk' variants. These individual subtypes have distinctive clinical presentations (see below). Other histologic features of clinical relevance include tumour thickness, perineural and lymphovascular invasion, margin status and whether atypical squamous differentiation is present. BCCs rarely metastasize to regional lymph nodes – usually only after many years of growth and attaining considerable size.[1]

Low-risk BCC variants

- **Nodular BCC:** This most common subtype presents as a papulonodule clinically (Figure 1a) and is characterized by variably sized solid or cystic islands of basaloid cells. These tumour nests are bordered by a palisaded row of cells at the periphery ('picket fence' appearance). Tumour islands are often separated from the surrounding myxoid stroma by a cleft like space ('retraction artefact') (Figure 1b). In line with the primitive nature of the basaloid cells, the tumour cells tend to be small, hyperchromatic, contain very scant cytoplasm and show brisk apoptosis and mitotic activity.
- **Superficial BCC:** A superficial BCC presents as an erythematous plaque with a subtle raised edge appreciated by stretching the skin (Figure 2a). Scale-crust is not a prominent feature. Histologically it comprises multiple, superficial, bud-like down growths of basaloid tumour cells arising from the under surface of the epidermis. The dermis between the superficial tumour lobules show increased vascularity and fibrosis (Figure 2b). It is sometimes difficult to pinpoint the peripheral extent of a superficial BCC histologically due to an apparently multifocal growth pattern and this explains the high local recurrence rate associated with this subtype.

High-risk BCC variants

- **Infiltrative/morphoeic BCC:** This subtype typically presents as a scar like area of induration (Figure 3a). Microscopically, infiltrative BCC shows thin, infiltrative, linear strands of basaloid cells which lack the circumscription of the low-risk subtypes (Figure 3b). Some infiltrative BCCs showing prominent sclerotic stroma with fibroblastic proliferation are often referred to as the morphoeic type. Perineural, lymphovascular invasion and local recurrences are common.

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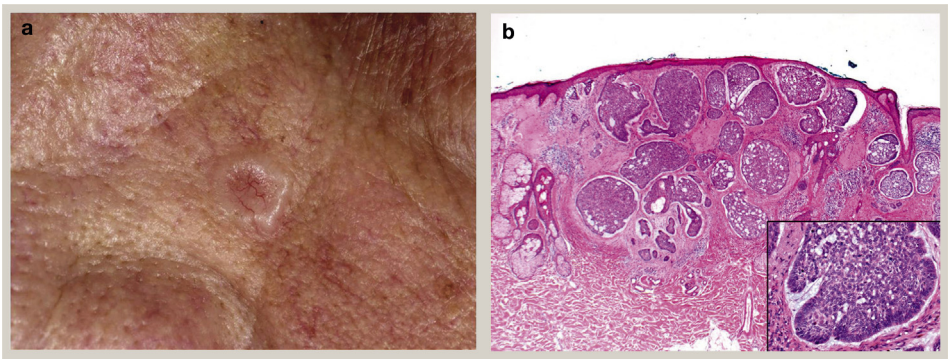

Figure 1 Nodular BCC. (**a**) Pale nodule with raised, rolled borders and telangiectasia. (**b**) Circumscribed tumour composed of multiple nodular aggregates of basaloid cells extending into the dermis. Peripheral palisading of the tumour cells and stromal retraction spaces are seen on higher magnification (inset).

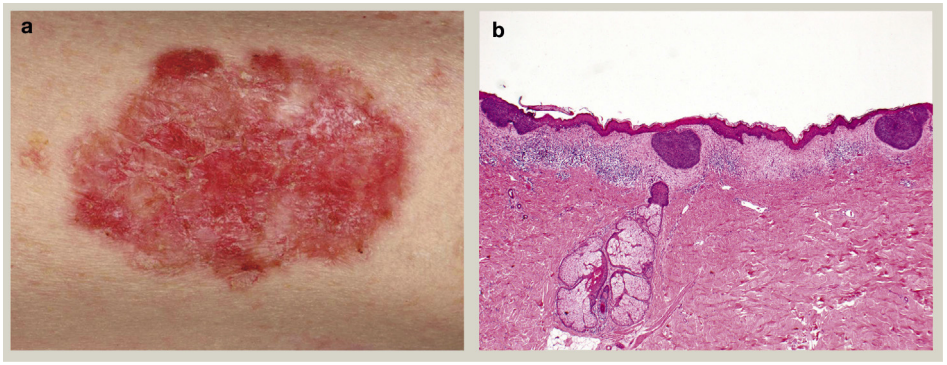

Figure 2 Superficial BCC. (**a**) Well-defined slightly raised erythematous plaque with adherent scale. (**b**) Three discrete nests of basaloid tumour cells adherent to the epidermal undersurface.

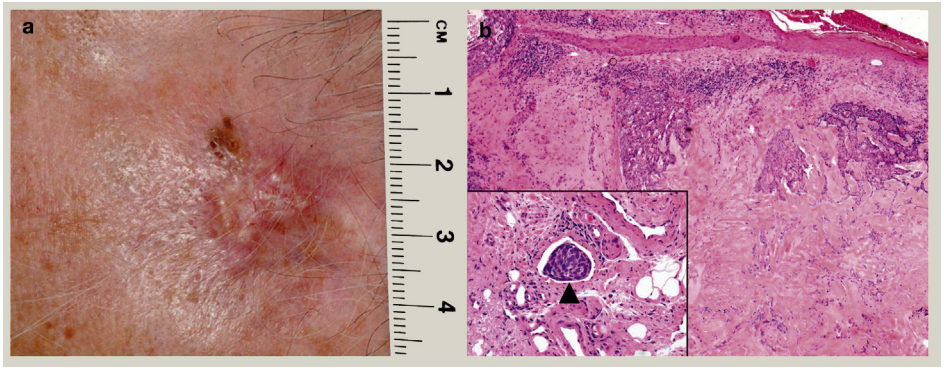

Figure 3 Infiltrative BCC. (**a**) Poorly defined pale indurated plaque with scar-like areas. (**b**) Infiltrative tumour composed of irregular strands of epithelial cells amidst sclerotic stroma. The inset shows a focus of lymphovascular invasion seen towards the periphery.

- **Micronodular BCC:** The micronodular variant resembles nodular BCC, but has much smaller tumour nodules (<0.15 mm in diameter) and is less circumscribed. These micronodules infiltrate widely into the dermis and often extend into the subcutaneous fat.

Summary of pathology related management issues[2]

- *High-risk* histological subtypes (infiltrative/morphoeic, micronodular), histological features of aggression (perineural and/or vascular invasion) and involved/close surgical margins are associated with a higher risk of recurrence and usually require excision with *wider surgical margins*, *Moh's micrographic surgery* and/or *radiotherapy*.
- *Low-risk* histological subtypes without adverse histological features can be treated using *surgical destructive techniques* like curettage and cautery, cryosurgery and carbon dioxide laser ablation.

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