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 which often inform decisions related to onward referral, optimal treatment and planning of 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 reports influence patient management. Particular emphasis is given to highlight histologic parameters which are directly linked to a specific management issue. Unravelling the molecular pathogenesis of some of these tumours has paved the way for development of novel molecular targeted therapies in recent years. It is hoped that this article will familiarize the reader with some of these recent 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 responsible for regulating a highly complex series of processes that allow humans to adapt to their environment. It is surfaced by the epidermis which not only provides mechanical protection, but also contains melanocytes which produce melanin. The epidermis is supported by a thick layer of fibroelastic 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 arising on areas exposed to sunlight. The clinical appearance is variable but the most common presentation is that of a slow growing, pale nodule with telangiectasia which frequently ulcerates. Some tumours present as an erythematous 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. Several histological subtypes can be encountered which generally show a close correlation with the clinical picture.[1] In addition to the diagnosis, a pathology report of a BCC provides information which has direct implication on prognosis and management. This includes *histological subtyping* based mainly on the growth pattern into 'low-risk' and 'high-risk' variants and also a comment on *differentiation* concerning whether atypical squamous differentiation is present. Other histologic features of clinical relevance include tumour thickness, perineural and lymphovascular invasion and margin status.

Low-risk BCC variants

Nodular BCC: a nodular BCC presents as a nodule 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 corresponds to the erythematous plaque presentation (Figure 2a). 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 a 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.

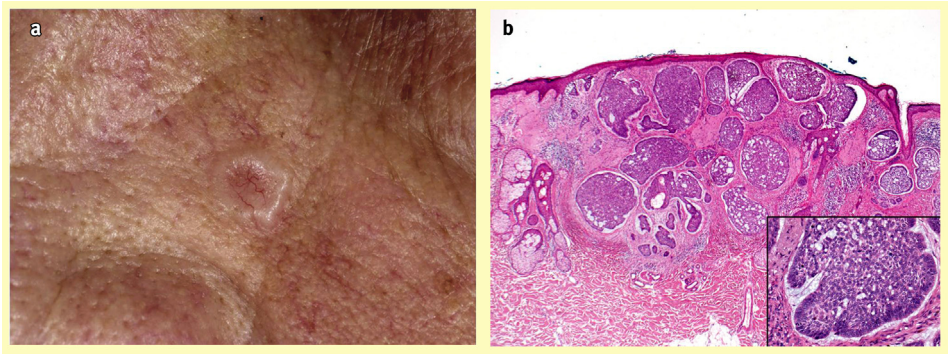

Figure 1 Nodular basal cell carcinoma. (**a**) Pale nodule with raised, rolled borders and telangiectasia. (**b**) Circumscribed tumour composed of multiple nodular aggregates of basaloid cells extending into the dermis. Peripheral palisading of the tumour cells and stromal retraction spaces are seen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

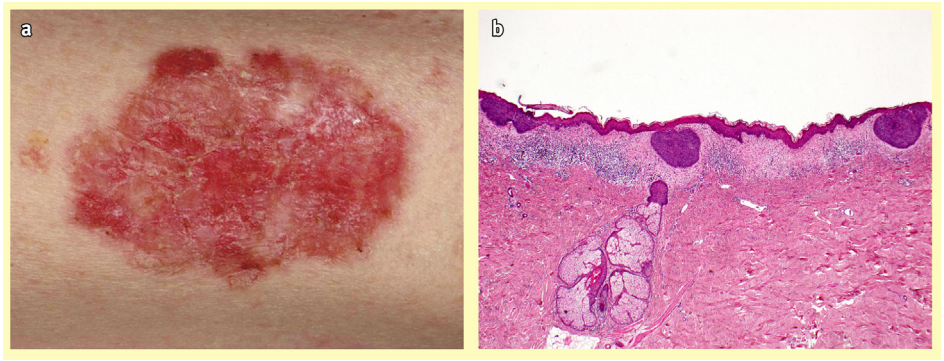

Figure 2 Superficial basal cell carcinoma. (**a**) Well-defined slightly raised erythematous plaque with adherent scale. (**b**) Three discrete nests of basaloid tumour cells adherent to the epidermal undersurface.

Micronodular BCC: although the micronodular variant has some resemblance to nodular BCC, the defining feature is the presence of much smaller tumour nodules (<0.15 mm in diameter) and the lack of circumscription. 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 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.
- *Small superficial BCCs* can be effectively treated non-surgically with topical immunotherapy using *imiquimod* or by *photodynamic therapy*.

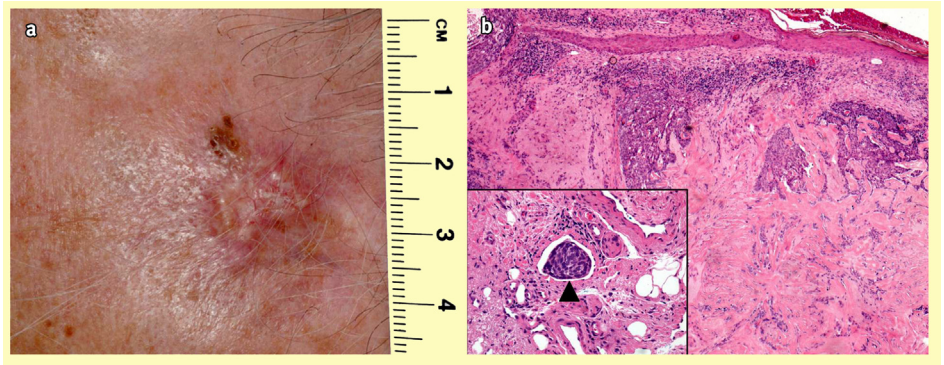

Figure 3 Infiltrative basal cell carcinoma. (**a**) Poorly defined pale indurated plaque with scar-like areas. (**b**) Infiltrative tumour composed of irregular strands of epithelial cells amidst sclerotic stroma. The inset shows a focus of lymphovascular invasion seen towards the periphery.