Skin cancer

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Abstract

Skin cancer is the most common cancer in the UK, and incidence rates are continuing to increase. We discuss the common presentations, clinical features, referral guidelines, management and prognosis of both non-melanoma skin cancer (basal cell carcinoma, squamous cell carcinoma) and melanoma.

Keywords Basal cell carcinoma; melanoma; skin cancer; squamous cell carcinoma

Key points

- Basal cell carcinoma and squamous cell carcinoma are types of epidermally derived tumours known as non-melanoma skin cancers
- Melanoma derives from melanocytes
- The main risk factor for the development of skin cancer is prolonged exposure to ultraviolet light
- Immunosuppressed individuals are at high risk, as are those with a low Fitzpatrick phototype I skin
- Early referral and correct treatment from the outset will decrease morbidity and mortality

Introduction

Skin cancer is the most common type of cancer worldwide, and its incidence continues to increase. It is broadly divided into cancers deriving from melanocytes (melanoma) and from the epidermally derived cells (non-melanoma skin cancers). These groups represent the majority of skin cancers (95%), with other skin tumours thus making up only a very small percentage. Their high prevalence and frequent occurrence makes them an important public health problem. The risk of developing skin cancer arises from a combination of genetic and environmental factors, the most common cause being prolonged exposure to ultraviolet (UV) light.

Genetic factors

The skin colour phenotype of the patient is important: individuals with a low Fitzpatrick phototype are at increased risk. Patients with red hair and freckling carry two copies of the R allele variant of the *MC1R* gene and are at increased risk of developing skin cancer.

The rare autosomal recessive condition xeroderma pigmentosa is a disorder of DNA repair in which the ability to repair damage caused by UV light is defective. This predisposes patients to an increase in freckling, sunburn and early childhood skin malignancies.

Basal cell naevus syndrome is autosomal dominant condition caused by a mutation in the tumour suppressor *PTCH1* gene. This allows cells to proliferate uncontrollably, and patients present with multiple basal cell carcinomas (BCCs).

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Although 90% of melanomas are thought to arise sporadically, some inherited mutations have been identified. The most common cause of inherited melanoma is a mutation in the *CDKN2A* gene. Mutations in the *MDM2* gene predispose women to develop melanoma at an earlier age.

Environmental factors

The main risk factor is exposure to UV radiation (sunlight, sunbeds). Additional risk factors include the presence of more than 50 naevi, multiple atypical naevi or dysplastic naevi, exposure to arsenic, immunosuppression (particularly in transplant patients) and viral infections (human papillomavirus).

Basal cell carcinoma

BCCs are the most common neoplasm of the skin and are usually related to chronic and frequent sun exposure. They arise from pluripotent cells within the follicular epithelium that have usually developed mutations within the *p53* gene. Some BCCs arise from aberrant activation of the sonic hedgehog signalling cascade resulting from a mutation in the *PTCH1* gene.[1]

BCCs are slow-growing tumours but can be locally aggressive depending on their subtype. They rarely metastasize, and the main morbidity arises from neglected or inappropriately treated lesions that have recurred. BCCs usually occur in patients over 40 years of age. They are classified by their histological subtype, as follows.

Low-risk subtypes:

- **superficial BCCs** – present clinically as well-defined plaques that slowly expand. They are usually red, pink or brown in colour. They are commonly found on the trunk, and there may be multiple lesions. The edge tends to become thread-like with scale, crust and bleeding
- **nodular BCCs** – the most common subtype. They present clinically as well-defined pearly white nodular lesions with associated telangiectasia.

High-risk subtypes: these tend to follow a more aggressive growth pattern, infiltrating deeply and widely. *Infiltrative* and

morphoeic BCCs can be similar in appearance, both having a sclerotic, scar-like quality. The *micronodular* subtype tends to have a yellow/white waxy surface and is firm in texture.

Diagnostic approach

The patient will probably give a history of chronic and repetitive sun exposure and is likely to have skin damage reflecting this. The cause is rarely related to a known genetic mutation or to X-ray or arsenic exposure.

A BCC can have the following characteristics, which are more obvious on stretching (Figure 1):

- a pearly papule with a rolled edge and telangiectasia (Figure 1)
- a non-healing scab
- an erythematous patch with a slightly rolled edge
- a scar-like thickened white area within the skin.

A biopsy should be taken for routine histopathological examination to identify the subtype of BCC, stratify it as high or low risk (Table 1); based on this the following treatment options are discussed.[2]

Management

Surgical treatment: direct excision with a margin (3 mm–1 cm) is the mainstay for low-risk lesions or high-risk lesions at a non-cosmetically challenging site.

Mohs micrographic surgery is used for high-risk lesions, usually those confined to the head and neck. This technique removes the tumour in a staged way, removing smaller margins of tissue but allowing 100% of the margins to be visualized. The advantage is that the cure rate for the tumour is higher than for conventional excisional surgery, and the approach is tissue sparing, giving smaller more cosmetically acceptable scars. This technique is particularly important at sites where recurrence would cause great morbidity, for example periocularly.

Radiotherapy: this is a very effective treatment for BCC, with reported cure rates of 92% at 5 years. However, the adverse effects can be marked, with tissue atrophy, necrosis, telangiectasia and poor cosmetic scar outcome over time; and new tumour development reported. Therefore radiotherapy is used when surgical treatment is not possible. The application of near-source radiation, brachytherapy, is a developing area in this field as it achieves tumour destruction but minimizes the radiation dose delivered to healthy tissue.

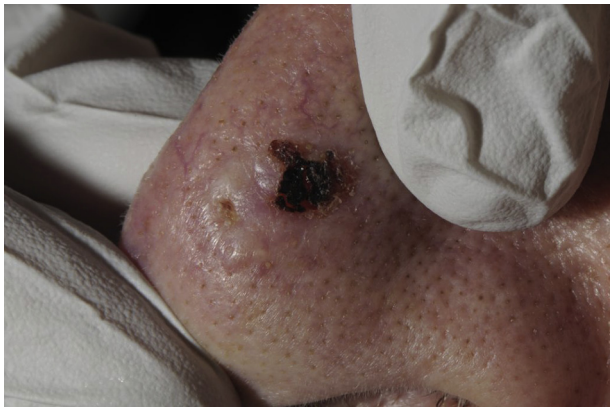

Figure 1 Basal cell carcinoma with a pearly edge that is more obvious on stretching the lesion.

Criteria indicating high risk in basal cell carcinoma (BCC)

- Patient aged <24 years
- Patient who is immunosuppressed or has a genetic syndrome
- Lesion situated on the head or neck
- Lesion >1 cm diameter in size
- Recurrent or incompletely excised BCC
- Aggressive growth pattern on histology

Table 1

Cryotherapy: this is effective for the treatment of superficial BCC.

Topical treatment: topical 5-fluouracil or 5% imiquimod is generally reserved for superficial BCCs, owing to the limited depth of penetration. The treatments are applied daily and take several weeks to complete. A marked inflammatory reaction is associated with the treatment as there is a destruction of tumour cells.

Photodynamic therapy: this modality can be used to treat both nodular and superficial BCC. A topical photosensitizer, such as 5-aminolaevulinic acid or methyl aminolaevulinic acid, is applied to the skin. This is rapidly taken up by the keratinocytes and converted into porphyrin IX. The sensitized tumour is then exposed to specific light wavelengths and undergoes destruction.

Vismodigib: this is the first approved (Food and Drug Administration, National Institute for Health and Care Excellence) oral agent for the treatment of BCC. It acts via the hedgehog pathway, the molecular driver for BCC, and inhibits abnormal signalling. It is intended for use in patients with locally advanced BCC who cannot undergo radiotherapy or surgery, and patients whose cancer has metastasized.

Squamous cell carcinoma

Squamous cell carcinoma (SCC) is a malignant tumour arising from squamous keratinocytes in the epidermis of the skin or mucous membranes. SCCs are most frequently seen in photodamaged skin and with a fair Fitzpatrick skin type. The metastatic potential for all SCCs is 3%; however, in lesions with additional poor prognostic factors, may be up to 30%. Poor prognostic factors associated with SCC include the size of the tumour, diameter over 2 cm and depth over 4 mm; SCC occurring on the lip, ear, UV-protected sites and areas of previous irradiation; patient immunosuppression; and the histological subtype of the tumour and presence of perineural disease.

The main risk factor for developing SCC is UV radiation; this can induce precursor lesions and actinic keratosis, or SCC *in situ* may be noted. Other risk factors include chronic immunosuppression (organ donor recipients), chronic scarring conditions (lupus erythematosus, leg ulcers, burns) smoking, arsenic and infection with human papillomavirus.