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REVIEW

Non-melanoma skin cancer of the head and neck

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Abstract

Skin cancer is the most common malignancy in the world, and the majority of cases affect the skin of the head and neck. The face is a particularly emotive area for patients who often present with a lesion that is causing them concern. This article reviews the identification, diagnosis and principles of management of non-melanoma skin cancer of the head and neck. There are many lesions of the skin which are benign and mimic skin cancer. The differential of head and neck skin lesions and how to determine their nature is discussed. The vast majority of non-melanoma skin cancer are basal cell carcinoma, followed by squamous cell carcinoma. These and the other types of non-melanoma skin cancer are described and illustrated. Current methods of clinical identification, diagnosis and evaluation of skin cancers are clarified, and contemporary treatment paradigms are presented.

Key words: Basal cell carcinoma; Cutaneous squamous cell carcinoma; Keratoacanthoma; Merkel cell carcinoma; Non-melanoma skin cancer; Skin cancer

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Introduction

Skin cancer is the most common malignancy in the world, and its incidence is increasing (de Berker et al, 2017; Ferlay et al, 2018; Venables et al, 2019). It can be classified into melanoma and non-melanoma skin cancer. There are several types of non-melanoma skin cancer (Table 1), but by far the most common are basal cell carcinoma and squamous cell carcinoma. In 2003, the World Health Organization estimated that between two and three million skin cancers occur globally each year, 80% of which are basal cell carcinoma, 16% cutaneous squamous cell carcinoma and 4% melanoma (World Health Organization, 2003). Over 80% of these occur on the skin of the head and neck (Alam and Ratner, 2001). Non-melanoma skin cancer is more common in men and with increasing age. The age shift in the population has resulted in an overall increase in the total number of skin cancers. Non-melanoma skin cancers are locally invasive and have better outcomes if treated at an early stage. Early identification of a suspicious lesion, knowledge of the differential diagnosis and an understanding of modern management concepts are of pivotal importance.

The main aetiological risk factor is sun exposure, so the head and neck, hands and forearms are the sites most commonly affected. Risk factors can be related to the individual (Table 2) or the environment (Table 3).

Basal cell carcinoma

This is the most common malignancy in humans. There are five histological subtypes which are important to identify because of their distinct clinical behaviour (Table 4). The Royal College of Pathologists' dataset adopts the term 'infiltrative basal cell carcinoma'

Table 1. Types of non-melanoma skin cancer
Basal cell carcinoma
Squamous cell carcinoma
Merkel cell carcinoma
Skin appendage carcinoma (eg sebaceous carcinoma, microadenexal carcinoma)
Sarcoma (eg dermatofibrosarcoma, angiosarcoma, Kaposi's sarcoma)

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Table 2. Individual risk factors	
Inherent factors	Male gender, pale complexion, fair hair, skin freckles, blue eyes and increasing age (Memon et al, 2000)
Genetic syndromes	Xeroderma pigmentosa increases the risk of developing squamous cell carcinoma, basal cell carcinoma and malignant melanoma. Gorlin's syndrome is characterised by multiple basal cell carcinomas. Patients with albinism, epidermolysis bullosa and prokeratosis are predisposed to skin cancer
Immunosuppression	Organ transplant patients are at high risk of developing skin cancers because of their long-term immune suppression. AIDS predisposes patients to a squamous cell carcinoma at a younger age
Chronic inflammatory disorders	Chronic scarring and inflammation are the most important risk factors in black skin. Squamous cell carcinoma may arise in the scars of skin burns or chronic ulcers (Marjolin's ulcer). Actinic keratosis can also be a precursor of cutaneous squamous cell carcinoma and this tends to be less aggressive

Table 3. Environmental risk factors	
Ultraviolet radiation	Ultraviolet exposure is the main risk factor, eg individuals working outside for extended periods of time or recreational sun exposure. Ultraviolet B is more carcinogenic than ultraviolet A
Ionising radiation	Individuals in mining, airline pilots and radiotherapy are at increased risk
Chemical carcinogens	Occupational exposure (eg arsenic, polycyclic hydrocarbons), tobacco and psoralens have been implicated

Table 4. Subtypes of basal cell carcinoma	
Nodular	This is the most common and has the distinctive features of a raised rolled edge nodule, with a pearly appearance and local telangiectasia. They can be locally invasive. Central ulceration may occur, and this has led to the term 'rodent ulcer' (Figure 1)
Superficial	The least aggressive type and characterised by dry, scaly, erythematous plaques (Figure 2)
Basosquamous	A more aggressive lesion, having histological features of basal cell carcinoma and squamous cell carcinoma. It also has some metastatic potential (Figure 3)
Pigmented	Tend to occur in darker skinned individuals and may be confused with melanoma
Morphoeic	These are pale, indurated lesions, which have indistinct borders. As such there is a propensity to incomplete excision as they may be more extensive than they initially appear (Figure 4)

for all high-risk histological variants (morphoeic, micronodular and basosquamous) and notes that many basal cell carcinomas contain both high- and low-risk subtypes (Slater and Walsh, 2014).

Although most basal cell carcinomas are small and readily amenable to surgery, it should be noted that many patients are often elderly, confused, have dementia and may

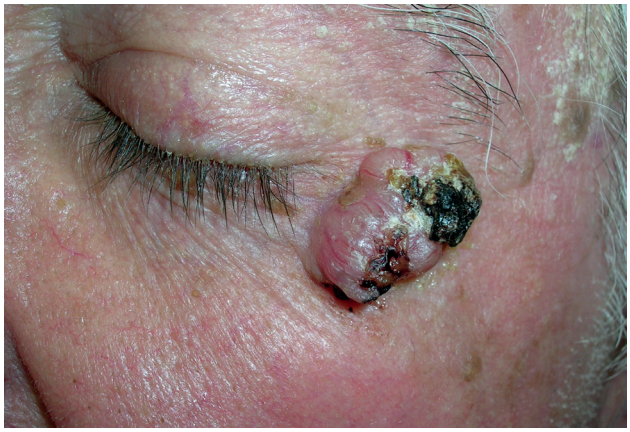

Figure 1. Nodular basal cell carcinoma with typical rolled edge appearance.

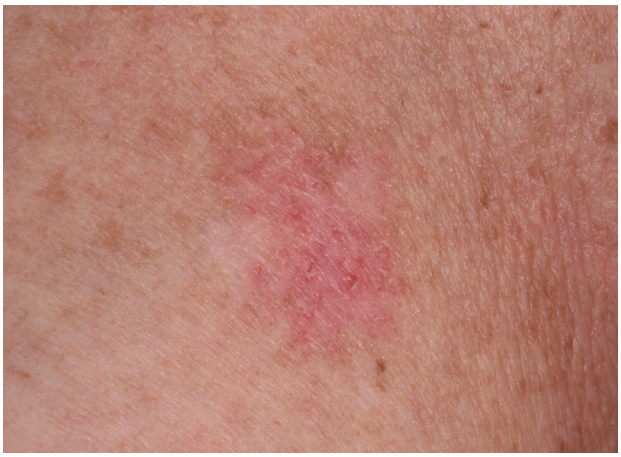

Figure 2. Superficial basal cell carcinoma.

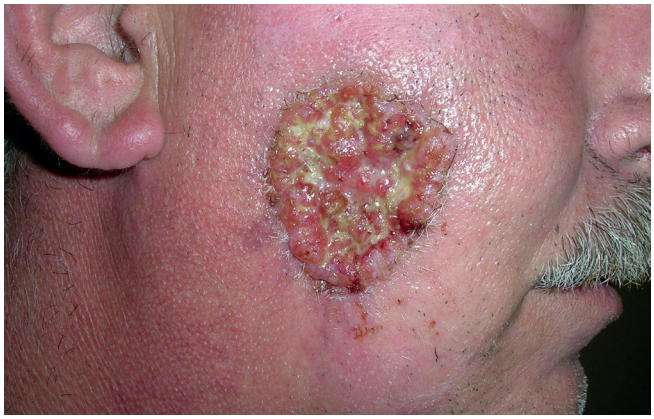

Figure 3. Basosquamous carcinoma.

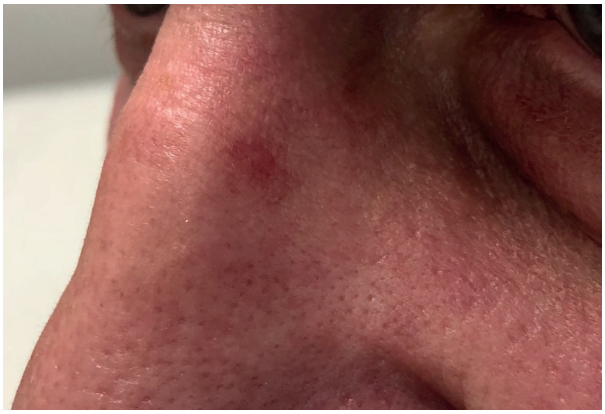

Figure 4. Morphoeic basal cell carcinoma.

present late with extensive lesions. They pose difficult clinical decisions in terms of the excision and reconstruction, particularly as many of them will have significant intercurrent illness, which may preclude general anaesthesia. The British Association of Dermatologists have provided excellent guidelines on the management of adults with basal cell carcinoma (Nasr et al, 2021).

Squamous cell carcinoma

Squamous cell carcinoma usually affects elderly men, with the highest incidence in those aged 85 years or older. One of the strongest predictors of development in previously unaffected individuals is the presence of actinic keratoses. These lesions are a marker of risk, rather than precursor lesions, as the rate of transformation of individual solar keratosis is very low. It typically presents as an enlarging firm papule or plaque that may be rough or smooth. As the tumour enlarges it often ulcerates (Figure 5). It is often asymptomatic, but it can cause tenderness, itching or bleeding. European interdisciplinary guidelines for the epidemiology, diagnosis and prevention of cutaneous squamous cell carcinoma have been published (Stratigos et al, 2020a).

Squamous cell carcinoma of the nasal vestibule is frequently misdiagnosed, mimicking vestibulitis or local trauma. Squamous cell carcinoma of the ear canal is often diagnosed late, as it can look like many other more common conditions of the ear canal. Cancers of the lip, ear and nose are more prone to metastasise than those of other sun-exposed sites. Regional metastases are uncommon, occurring in about 5% of cases but increasing to 20–25% in larger and poorly differentiated tumours, recurrent tumours and those which are incompletely excised. The nodes within the parotid gland, superficial jugular nodes and upper deep cervical nodes are the usual sites.

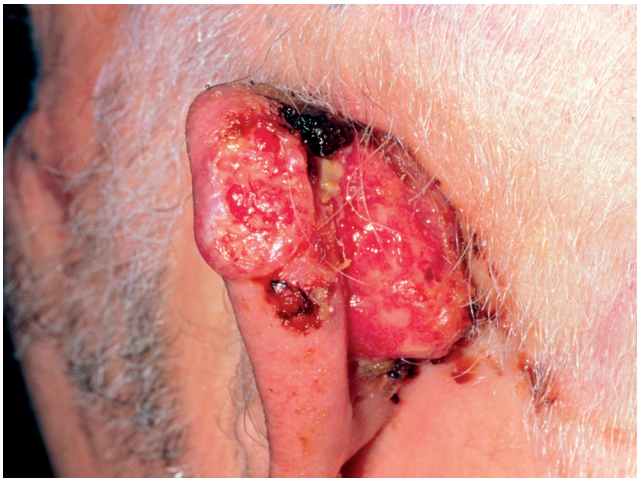

Figure 5. Squamous cell carcinoma of the ear.

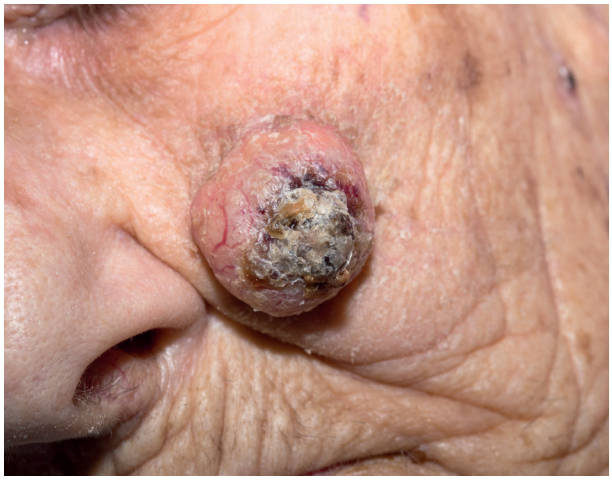

Figure 6. Keratoacanthoma of the face.

Keratoacanthoma

Keratoacanthoma usually presents as a symmetrical, rapidly-growing skin tumour, with a shoulder of stretched normal skin and a central keratin plug (Figure 6). Keratoacanthoma reaches maximum size in 3 months and then begins to resolve spontaneously, so is considered to be a self-limiting benign epithelial neoplasm. It occurs predominantly on sun-exposed areas of the body and is believed to arise from hair follicles. It shows a unique behaviour in being clinically benign and microscopically malignant. Early diagnosis is needed to differentiate a keratoacanthoma from squamous cell carcinoma.

Merkel cell carcinoma

This is a rare neuroendocrine tumour of the skin, so called because it is thought to arise from mechanoreceptor (Merkel) cells. It occurs most commonly in the elderly Caucasian population. Its aetiology is unknown but ultraviolet radiation is thought to be an important factor. Merkel cell polyomavirus has been linked to Merkel cell carcinoma, although there is no developed clinical use for this at present.

Merkel cell carcinoma is difficult to identify clinically and is often misdiagnosed as a benign lesion. It usually presents as a papule or subcutaneous nodule and is highly aggressive, with a propensity to local recurrence and metastatic spread. Its nature is more often likened to malignant melanoma than squamous cell carcinoma.

A biopsy and histological confirmation should be performed in all clinically suspicious lesions. The diagnosis of Merkel cell carcinoma should prompt a complete examination of the entire skin and palpation of the regional lymph nodes for nodal involvement. Initial work up consists of ultrasound of the loco-regional nodes, as well as computed tomography or positron emission tomography–computed tomography. Sentinel lymph node biopsy is recommended (Lebbe et al, 2015).

Patients have a poor prognosis and management should be in a specialist centre and with a multidisciplinary team. Smaller lesions are treated by surgical excision with 1–2 cm margins, taking into account functional considerations in the head and neck region. They are also radiosensitive and adjuvant radiotherapy, and chemoradiotherapy may be used for more extensive disease.

Atypical fibroxanthoma

Atypical fibroxanthoma is a tumour that occurs primarily in older individuals. It often appears in areas that have received excessive sun exposure, usually around the scalp, ears, nose, cheeks and back of the neck, or in areas where individuals may have previously received radiotherapy treatment. It should be considered a type of skin cancer, although it may behave in a benign fashion. Malignant variants usually arise rapidly (over just a few weeks or months), often in skin in which other skin cancers have been found and treated. A solitary tumour or multiple tumours may occur. Typically, atypical fibroxanthoma is a red, juicy, dome-shaped nodule that may be bleeding, ulcerated or crusted (Figure 7). It starts off as a small nodule that grows quickly over 6 months to a size of about 2–3 cm. Four times as many tumours are diagnosed on the head and neck as are diagnosed in other body sites. Although rare, cutaneous metastases from atypical fibroxanthoma have been reported.

Differential diagnosis of non-melanoma skin cancer

A diagnosis of skin cancer should consider alternative diagnoses, including:

- Actinic keratoses
- Seborrhoeic keratoses
- Bowen's disease.

Actinic keratoses

These are areas of sun-damaged skin found mostly on exposed parts of the body. These lesions are small scaly areas, sometimes pink in colour, and can look like dry skin (Figure 8).

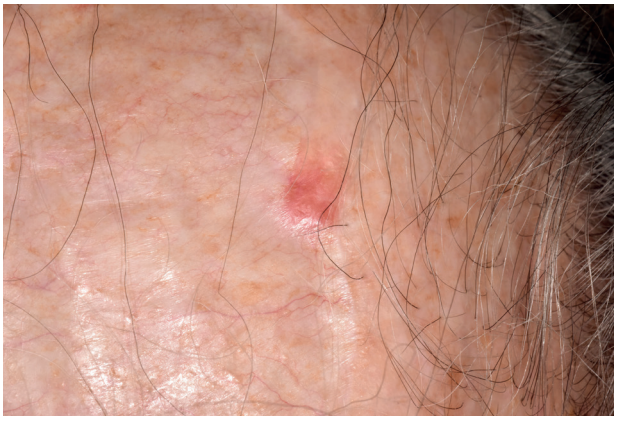

Figure 7. Atypical fibroxanthoma of the scalp.

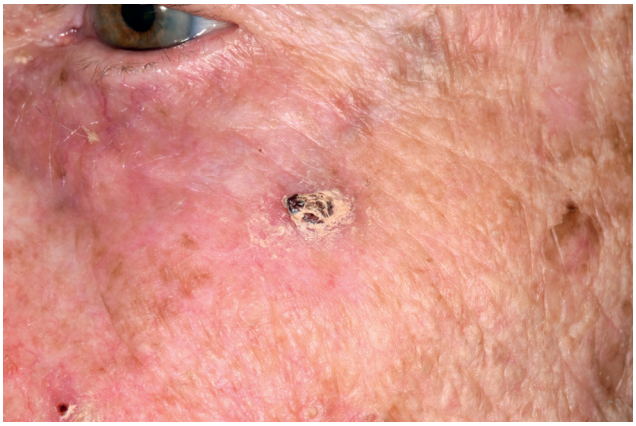

Figure 8. Actinic keratosis with solar-damaged skin.

These can be hard to see but the skin feels quite rough. They are usually small but can grow up to 1–2 cm in diameter. These lesions are benign but carry a small risk of turning into squamous cell carcinoma.

Seborrhoeic keratoses

These are very common benign lesions. The incidence increases with age and almost 75% of the population are affected by the age of 70 years. They are usually raised, light brown warty lesions with a waxy surface, and typically have a stuck-on appearance (Figure 9).

Bowen's disease

Bowen's disease or squamous cell carcinoma in situ is, as the name suggests, a benign lesion with cancerous cells confined to the outer layer of the skin. It usually starts as a small red scaly area and can grow gradually but slowly. It is often 1–2 cm in diameter and looks like a red scaly plaque (Figure 10). It carries a small risk of turning into squamous cell carcinoma if not treated.

Diagnosis

The diagnosis is usually obvious from the history and appearance of the lesion and a whole-body examination (Smith et al, 2020), without the need for biopsy. Diagnostic accuracy is enhanced by good lighting, the skin stretch test and dermoscopy. If a patient is diagnosed with a skin cancer, they are usually offered monitoring (depending on the nature and severity of cancer) and whole body examination by the dermatologists. The patient is examined for any suspicious pigmented and non-pigmented lesion.

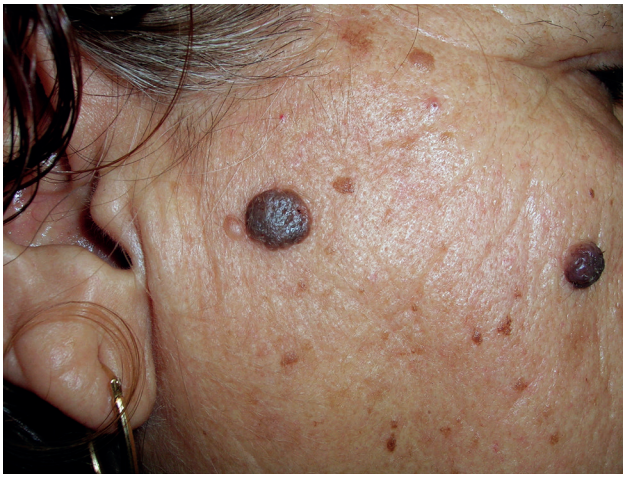

Figure 9. Seborrhoeic keratosis of the cheek.

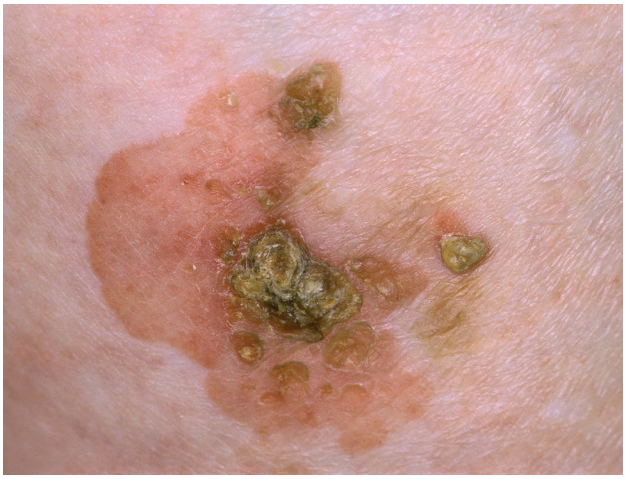

Figure 10. Bowen's disease.

Telemedicine is a rapidly evolving method of care, especially during the COVID-19 pandemic. The ability to diagnose a skin cancer via a digital image is dependent on the quality of the image and adequate history. However, some skin cancers can only be diagnosed by face-to-face consultation. Telemedicine is now established as a sub-speciality of dermatology and is likely to be a good way to of helping GPs to decide which skin lesions need to be seen by a skin specialist. However, evidence is lacking (Chuchu et al, 2018) and work is in progress to standardise the technology so that it could be used more effectively. Phone apps have shown some promise, but further work is needed to refine these techniques (Freeman et al, 2020).

Investigations

The vast majority of non-melanoma skin cancers are suitable for immediate excision biopsy and repair without any other investigation. However, an incisional, shave or a punch biopsy for histology can be very useful before embarking on potentially disfiguring surgery of the face, if the lesion is large and there is diagnostic doubt. Exfoliative cytology can be useful, particularly where the tumour is ulcerated and can guide management where surgical biopsy is difficult, such as in very old patients.

If there is clinical suspicion that the tumour is attached to or extends deep into the underlying deep tissue or bone, then cross-sectional imaging of the area using either computed tomography scanning or magnetic resonance imaging should be considered, and the case should be discussed at a specialist skin cancer multidisciplinary team meeting before treatment.

Clinically palpable lymph nodes should undergo fine needle aspiration, ideally under ultrasound control, for cytological diagnosis. In non-melanoma skin cancer cases, magnetic resonance imaging and computed tomography can help stage the disease, particularly if there is concern that it may involve underlying structures (eg scalp lesions invading the skull or the maxillary spine in squamous cell carcinoma of the columella). Scans are not needed in the N0 neck (a neck without palpable nodal spread), but can help define the presence of metastatic nodal disease in high risk cases and palpable disease. A computed tomography scan of the chest is important in high-risk cases to exclude lung metastases.

Staging systems

The TNM staging system for non-melanoma skin cancer has been problematic, but continues to evolve with available data. The current TNM staging for non-melanoma skin cancer is shown in Table 5. N staging follows that of mucosal head and neck cancers for non-melanoma skin cancer (Union for International Cancer Control, 2017).

Table 5. TNM staging system eighth edition for non-melanoma skin cancer

TX	Primary tumour cannot be assessed
T0	No evidence of primary tumour
Tis	Carcinoma in situ
T1	Tumour 2 cm or less in greatest dimension
T2	Tumour is more than 2 cm, but less than 4 cm
T3	Tumour >4 cm in greatest dimension or minor bone erosion or perineural invasion or deep invasion (invasion beyond the subcutaneous fat or >6 mm)
T4a	Tumour with gross cortical bone or marrow invasion
T4b	Tumour with skull base or axial skeleton invasion (ie foramen of skull base or vertebral invasion)

From Union for International Cancer Control (2017)

Treatment

Surgical excision of head and neck skin cancer is the mainstay of treatment. Many patients with pre-cancerous, small and low risk lesions will have their procedures performed in the community and non-specialist units. Patients with squamous cell carcinoma, high-risk basal cell carcinoma and melanoma must have their care managed by a hospital-based multidisciplinary team meeting with specialist skills. The following patients should all be discussed in a skin cancer multidisciplinary team meeting (Newlands et al, 2016):

- All patients with squamous cell carcinoma
- Those with high-risk basal cell carcinomas (larger tumours, involved margins, recurrent lesions)
- Patients with suspected melanoma
- Patients with an unusual or rare skin cancer
- Patients considered for Mohs' surgery
- High risk patients (immunocompromised, genetically predisposed conditions)
- Metastatic disease
- Patients considered for radiotherapy
- Patients in clinical trials.

Surgical excision

Local, complete, primary excision with a predetermined margin is the aim. The recommended margins for non-melanoma skin cancer differ in the available guidelines, but acceptable ranges for the minimum margin are in Table 6 (Newlands et al, 2016; Stratigos et al, 2020b). The deep margin should include fat. Histological confirmation of clearance can be confirmed by using Mohs' micrographic surgery, frozen section or by waiting for results from paraffin section. It is always good practice to mark resected specimens with an orientation suture, so that further excision can target the close or involved margin if necessary.

Ideally, the surgical defect after excision should be closed primarily. If primary closure is not possible, reconstruction by local flaps or skin grafts will be required. Local flaps are the preferred option when the surgical defect is on the face, because there is a better skin match and a superior aesthetic outcome. Rarely, distant flaps will be required for complex or very large surgical defects. If there is any doubt as to the adequacy of surgical clearance, definitive reconstruction should be delayed pending histological confirmation. Incompletely excised lesions should be discussed at the multidisciplinary team meeting. Re-excision would be recommended for all incompletely excised squamous cell carcinomas and high risk basal cell carcinomas, or where there is deep margin involvement. Lesions with high risk of recurrence should be treated with delayed reconstruction or Mohs' micrographic surgery (Marrazzo et al, 2019).

Elective neck dissection is not done routinely for non-melanoma skin cancer, as there is no evidence that it improves mortality, and it adds to the patient's morbidity. If parotid lymphadenopathy is present then a neck dissection (levels I–III) should be performed, as a high proportion of patients with parotid lymph node involvement will have occult cervical metastases. Patients with parotid and neck nodes need a parotidectomy and level I–V selective neck dissection.

Mohs' micrographic surgery

Mohs' micrographic surgery is a precise technique in which excision of the skin is carried out in stages and each stage checked histologically. It is advocated for use in cases where it is critical to obtain a clear margin, while preserving the maximum amount of normal

Table 6. Recommended excision margins for non-melanoma skin cancer

Basal cell carcinoma less than 2 cm should be excised with a 4–5 mm margin
Low risk squamous cell carcinoma should be excised with a margin of 4–5 mm
High risk squamous cell carcinoma should be excised with a margin of >6 mm
Squamous cell carcinoma that are larger than 2 cm should have at least a 6–10 mm margin

surrounding tissue. Its use is encouraged for recurrent and high-risk aggressive growth pattern basal cell carcinomas, such as morphoeic type basal cell carcinomas and squamous cell carcinomas. The main problems with this technique include the length of the procedure, the need for special equipment and training, and the relatively high cost. However, there is good evidence that both local recurrence and metastases are lower after Mohs' micrographic surgery and because tissue removal is minimised, there are better cosmetic outcomes (Marrazzo et al, 2019; van Lee et al, 2019).

Radiotherapy

The cure rates for radiotherapy are over 90% for most non-melanoma skin cancer lesions, but the long-term cosmesis, particularly for young patients, is often inferior to that following other treatments and there is an increased risk of secondary malignancies. However, radiotherapy is a useful treatment for a subset of patients with non-melanoma skin cancer who cannot, or prefer not to, be treated by surgery. Radiotherapy still has an important role in the treatment of elderly patients, and as an alternative to mutilating surgery in the treatment of advanced disease. It has a role in the palliative treatment of patients with large, inoperable and recurrent squamous cell carcinoma, or if there are inoperable metastases in lymph nodes or elsewhere. Postoperative radiotherapy can be used in cases when the margins of excision appear to be incomplete on histopathological examination, although this is not desirable. It also has a role in adjuvant treatment of extracapsular nodal disease following neck dissection (Veness et al, 2019).

Destructive techniques

Curettage and cautery

This technique is performed using a curette to remove the tumour and the base of the tumour destroyed using either hyfrecation or cautery. It should only be used by experienced practitioners, and may be used to treat small well-defined basal cell carcinomas (<4 mm) and in situ squamous cell carcinomas (<1 cm). It is safe and well tolerated, and usually produces a good cosmetic outcome. However, the histology may be difficult to interpret as the lesion may be incompletely removed and margins of excision cannot be assessed.

Cryotherapy or cryosurgery

Cryotherapy is the destruction of skin lesions using liquid nitrogen. It is a cost-effective treatment and may be used in specialised centres for low risk superficial basal cell carcinoma and in situ squamous cell carcinoma. However, it is inadvisable to use cryotherapy if squamous cell carcinoma is suspected, unless an incisional biopsy is taken first to confirm the diagnosis of an in-situ squamous cell carcinoma.

Photodynamic therapy

Photodynamic therapy involves the use of light therapy in combination with a topical photosensitising agent to destroy cancer cells. Its use has been well described in the treatment of keratoacanthoma, in situ squamous cell carcinoma and superficial basal cell carcinoma. The advantages of photodynamic therapy include a low rate of adverse effects and good cosmesis. The disadvantages are that the patient must be available for a period of at least 3–4 hours for treatment, and that the photosensitiser and equipment are relatively expensive. It is not recommended for invasive squamous cell carcinoma.

Topical drug therapies

A number of topical drug therapies are available including the immune response modifier imiquimod and 5-fluorouracil cream. These are an effective treatment for small primary superficial basal cell carcinomas and in situ squamous cell carcinoma.

Conclusions

The diagnosis of head and neck skin cancer is usually obvious from the history and clinical examination. Confirmatory biopsy is needed in equivocal cases or when major surgery has significant cosmetic or functional implications. Squamous cell carcinoma

and high-risk basal carcinoma should be discussed in a multidisciplinary team meeting. All patients should be given information and written instruction about self-surveillance. Patients who have a confirmed diagnosis of squamous cell carcinoma should have a whole-body examination undertaken by a dermatologist. Patients with completely excised basal cell carcinoma or low risk squamous cell carcinomas do not need long-term surveillance and should be discharged from formal follow-up when they have fully recovered from the treatment. Patients with recurrent or multiple basal cell carcinomas and those with a high-risk squamous cell carcinoma should be reviewed for 2–5 years (3-monthly for the first year, then every 4 months and then biannually).

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Conflicts of interest

The authors declare that they have no conflicts of interest.

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Key points

- The vast majority of non-melanoma skin cancers are basal cell carcinomas.
- Patients with squamous cell carcinoma and high-risk basal cell carcinoma should be discussed at a multidisciplinary team meeting.
- The diagnosis is usually evident from the history and clinical examination.
- Punch biopsy or incisional biopsy are used when there is doubt in diagnosis or when excision has cosmetic or functional implications.
- Other therapies (such as radiotherapy, curettage or topical drugs) can be considered in selected cases.
- Patients with non-melanoma skin cancer should be treated in a multidisciplinary setting.

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