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Improving the detection of cutaneous squamous cell carcinoma

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SPECIAL REPORT

Improving the detection of cutaneous squamous cell carcinoma

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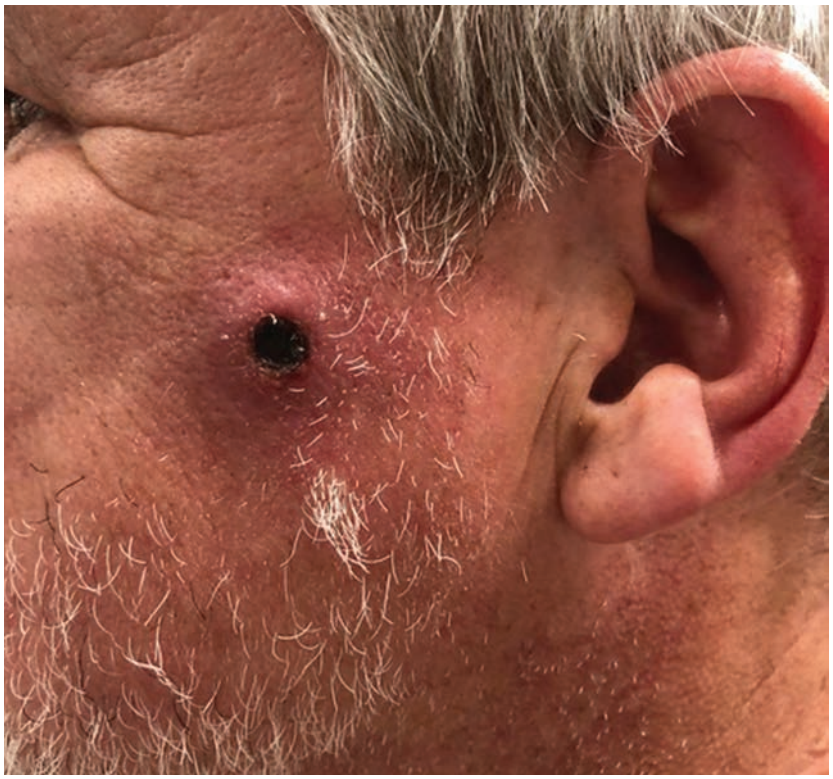

FIGURE 1
A poorly differentiated cSCC on the left cheek

What are the risk factors?

How should patients be assessed?

How should patients be monitored and followed up?

CUTANEOUS SQUAMOUS CELL CARCINOMA (cSCC) IS THE SECOND MOST COMMON NON-MELANOMA skin cancer after basal cell carcinoma.

Since the early 1990s, non-melanoma skin cancer incidence rates have increased by 166% in the UK.[1] A cohort study[2] carried out from 2013 to 2015 estimated the incidence of cSCC as 77 per 100,000 patient-years with a 5% rise per annum.[3]

The presence of abnormal keratinocytes confined to the epidermis is termed actinic keratosis if dysplasia is partial epidermal thickness. In Bowen's disease, also known as cSCC in situ, the dysplasia is of full epidermal thickness. Once the dysplastic keratinocytes breach the epidermal basement membrane and invade into the dermis, it becomes cSCC. The lesions may be well, moderately or poorly differentiated, see figure 1, above. They have the potential to cause local invasion and can metastasise to lymph nodes or other organs.[4]

Mucosal SCC has a different aetiology, and different referral pathways and treatment regimens, and is outside the scope of this article.

RISK FACTORS

The occurrence of cSCC is related to chronic UV exposure, particularly occupational exposure. Risk factors include fairer skin (Fitzpatrick skin types I-II), significant exposure to sunlight or therapeutic UV radiation (PUVA). Given the long latency between exposure and the development of cSCC, increased life expectancy may also be contributing to the rising incidence.

The incidence is also significantly increased in patients who are immunocompromised. Solid organ transplant recipients have a 65 to 250-fold increased risk.[5,6] Long-term exposure to azathioprine,[7] which is photocarcinogenic, is a significant risk factor as is immunosuppression caused by haematological disease, especially chronic lymphocytic leukaemia which confers an 8-10 fold increased risk.[8] cSCC is also associated with oncogenic HPV[9] as well as genetic disorders such as albinism where melanin protection is absent and xeroderma pigmentosum where DNA repair after UV damage is impaired. Risk factors for cSCC are listed in table 1, below.

Table 1

Risk factors for cutaneous squamous cell carcinoma (cSCC)

- Older age
- Male gender (3:1 ratio m:f)
- UV exposure (outdoor occupation, PUVA)
- Fair skin
- Immunosuppression due to disease or medications
- Previous cSCC or another form of skin cancer
- Actinic keratoses or Bowen's disease
- Previous cutaneous injury, thermal burn, ulcer or underlying inflammatory skin disease (e.g. cutaneous lupus)
- Genetic disorders such as xeroderma pigmentosum and albinism
- Exposure to arsenic[13]

As well as developing de novo, cSCC can also develop from pre-existing chronic actinic damage[10] although the probability and speed of transition from actinic keratosis to cSCC is highly variable.

Progression rates range from 0 to 0·075% per lesion-year. Rates of regression of actinic keratoses range between 15 and 63% after one year. After regression, the rate of recurrence is 15-53%.[11] As such giving an accurate risk of an actinic keratosis transforming into cSCC to an individual patient is not straightforward.

The discussion needs to be put into the context of the prevalence rates for non-melanoma skin cancer within the patient's age group, which for patients aged 65 years and over is 2%.

All patients should be given information on the signs to look out for, along with education on the importance of avoiding excessive sun exposure, the use of protective clothing and sun screens (SPF 30+).

ASSESSMENT

When taking the history it is important to check the patient's risk factors and to consider the following:

- Whether there was a pre-existing burn, area of inflammation or area of Bowen's disease or actinic keratosis
- How long the lesion has been present and how quickly it has grown
- Any history of pain or tenderness
- Whether the patient is on anticoagulants or has a clotting disorder. (This information will be particularly relevant to the operating surgeon)

When examining the patient it is important to record:

- The skin type
- Any evidence of surrounding sun damage (actinic keratoses, Bowen's disease, tan)
- The location and diameter of the lesion

The lesion should be palpated to elicit tenderness, and to determine whether it is mobile or fixed to deeper tissues. The draining lymph nodes should also be palpated.

A full skin check for other lesions should also be performed.

All patients with suspected cSCC should be referred via the two-week wait suspected cancer referral pathway to a dermatology department.[12]

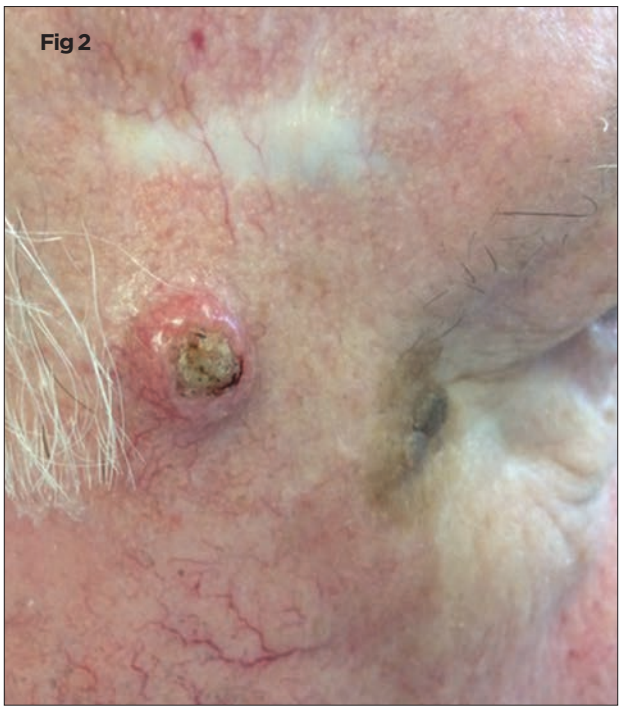

FIGURE 2
A well differentiated cSCC on the temple. Note the keratotic centre and scar from previous excision just above

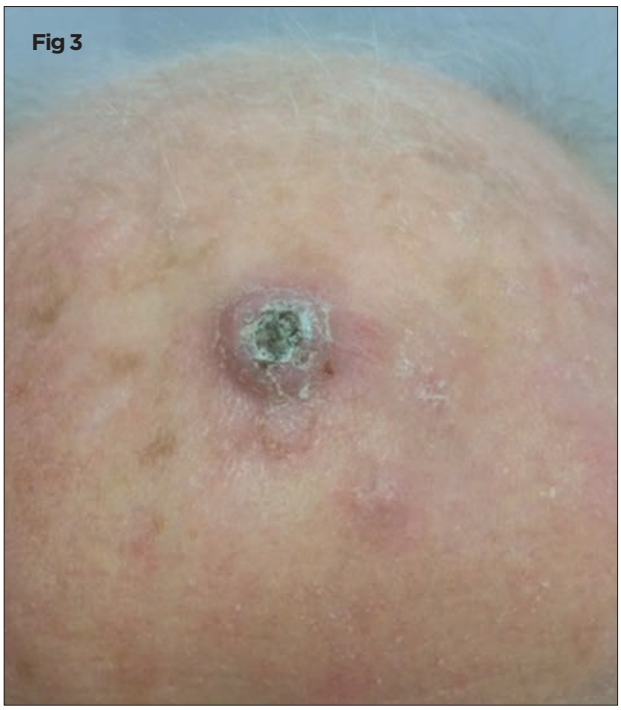

FIGURE 3
A cSCC on an elderly man's scalp

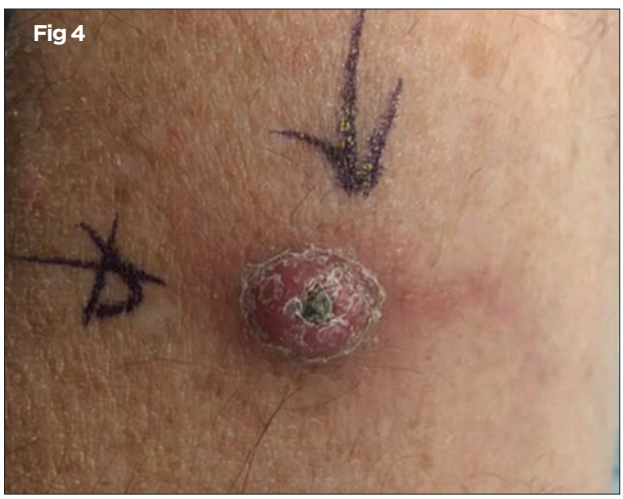

FIGURE 4
A well differentiated cSCC on the arm

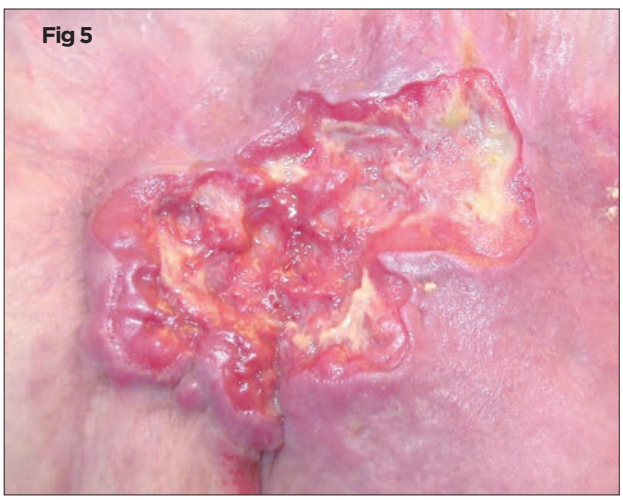

FIGURE 5
A poorly differentiated cSCC in a burn scar

CLINICAL PRESENTATION AND DIAGNOSIS

cSCC usually presents as an enlarging, indurated, scaly, keratotic or crusted lump over a course of weeks to months. The lesions can be dome, crateriform or peaked in shape. They may ulcerate and can often be tender or painful. Common sites are sun exposed areas such as the temple (see figure 2, p24), scalp (see figure 3, p24), face, helical rim, lateral neck, forearms (see figure 4, p24), hands and lower legs. cSCC can also occur in burn scars (see figure 5, p24). Lesions can range in size from a diameter of a few millimetres to several centimetres.

The less aggressive well differentiated lesions grow more slowly and usually have a nodular and exophytic growth with a keratotic surface from early on. The more aggressive, poorly differentiated lesions have less or no keratin. They may be more endophytic in growth and present with an ulcer with no nodular element at all.

DERMOSCOPY

Many features seen on dermoscopy are not specific to cSCC and as such dermoscopy must be used carefully in conjunction with the clinical history and examination with the naked eye. It is important to avoid blanching the blood vessels by pressing too firmly with the dermatoscope. For more nodular lesions, it is advisable to use a more viscous contact medium than alcohol gel such as ultrasound gel for better views.

Features which may be seen on dermoscopy include:

- Vessels:
  - Hairpin with a white halo
  - Glomerular
  - Arborising
  - Polymorphous
- White circles (intrafollicular keratin plugs)
- White structureless areas (cystic cavities of keratin)
- Poorly differentiated, ulcerating cSCCs have very non-specific signs and are predominantly a homogeneous red colour from dense vascularity and bleeding.

The differential diagnosis includes basal cell carcinoma, hypertrophic actinic keratosis and keratoacanthoma. A keratoacanthoma is a well differentiated self-healing cSCC and as it is not possible to differentiate a keratoacanthoma from cSCC clinically with confidence, all lesions should be referred for excision. The differential diagnosis for poorly differentiated cSCC also includes Merkel cell carcinoma and nodular melanoma.

A definitive diagnosis is made histologically following excisional or incisional biopsy. Once diagnosis is made the tumour is then staged using staging criteria such as the Union for International Cancer Control 8th edition (UICC8) criteria to give a tumour node metastasis (TNM) classification. This will determine prognosis and guide subsequent treatment options.

TREATMENT

There is no role for cryotherapy or topical treatments in the management of cSCC.

Surgery

The surgical treatment options are as follows:

Surgical excision: The vast majority of cSCC are treated by surgical excision. This is carried out with a surgical margin of 4-10 mm depending on the size of the tumour.

Mohs micrographic surgery: This approach is advisable if the lesion is in an area where tissue preservation is important such as near the eyelid margin.

Shave curettage and electrocautery: The option of shave curettage and electrocautery should only be considered for low risk, < 1 cm, thin cSCC such as those on the trunk or limbs in immunocompetent patients or for use in palliation.

Radiotherapy

Primary radiotherapy can be considered if the patient declines surgery or for palliation. Radiotherapy is more frequently used as an adjunct following surgery in higher risk cases.

COMPLICATIONS

Untreated, cSCC can cause local tissue destruction and metastasise to lymph nodes or other organs. cSCC usually spreads to local lymph nodes and clinically enlarged nodes should be examined histologically by fine needle aspiration or excision biopsy. Tumour-positive lymph nodes are then managed by regional lymphadenectomy whereby lymph nodes that drain the site of the tumour are removed with therapeutic intent. Imaging is performed to define the extent of regional disease and to identify distant metastases. Adjuvant radiotherapy or chemotherapy can also be considered. With respect to prognosis, several large studies have estimated a mortality rate for metastatic cSCC of more than 70%.[14]

RISK STATUS

The risk of metastasis of cSCC is 1.1-2.6%.[15,16,17] Which lesions are at particular risk of recurrence and metastasis to lymph nodes can be determined by the presence of factors which relate to the tumour itself (size, depth, histology) as well as the host (immune status), see table 2, below.

FOLLOW-UP

The duration and frequency of follow-up varies according to the risk status. A patient classified as low risk has a 40% further chance of cSCC within the next »

Table 2

Cutaneous squamous cell carcinoma tumour characteristics that influence the risk of recurrence

	Low risk	High risk	Very high risk
Tumour size	< 2 cm	2-4 cm	> 4 cm
Tumour site		Lip, ear, area of previous inflammation	
Tumour histology			
Thickness	< 4 mm, dermis only	4-6 mm or into fat	> 6 mm or beyond fat
Lymphovascular invasion	None	Yes	
Perineural invasion	None	Dermis only or < 0.1 mm	Beyond dermis or > 0.1 mm
Differentiation	Good/moderate	Poor	
Subtype			e.g. adenosquamous/ desmoplastic
Immune status	Competent	Compromised	

key points

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Cutaneous squamous cell carcinoma (cSCC) is the second most common non-melanoma skin cancer after basal cell carcinoma, with an estimated incidence of 77 per 100,000 patient-years. cSCC can develop de novo or from pre-existing chronic actinic damage, although the probability and speed of transition from actinic keratosis to cSCC is highly variable.

The occurrence of cSCC is related to chronic UV exposure, particularly occupational exposure. Risk factors include fairer skin, significant exposure to sunlight or therapeutic UV radiation (PUVA). Incidence is also significantly increased in patients who are immunosuppressed, either due to disease or medications. Solid organ transplant recipients have a 65 to 250-fold increased risk. Long-term exposure to azathioprine, which is photocarcinogenic, is a significant risk factor as is immunosuppression caused by haematological disease, especially chronic lymphocytic leukaemia which confers an 8 to 10-fold increased risk.

cSCC usually presents as an enlarging, indurated, scaly, keratotic or crusted lump over a course of weeks to months. The lesions can be domed, crateriform or peaked in shape. They may ulcerate and can often be tender or painful. Common sites are sun exposed areas such as the scalp, temples, face, helical rim, lateral neck, forearms, hands and lower legs. They can range in size from a diameter of a few millimetres to several centimetres. Any evidence of surrounding sun damage should be recorded and the lesion should be palpated to elicit tenderness and determine whether it is mobile or fixed to deeper tissues. The draining lymph nodes should be palpated and a full skin check for other lesions should be performed.

All patients with suspected cSCC should be referred via the two-week wait pathway to a dermatology department. The differential diagnosis includes basal cell carcinoma, hypertrophic actinic keratosis and keratoacanthoma. A keratoacanthoma is a well differentiated self-healing SCC and, as it is not possible to differentiate a keratoacanthoma from a cSCC clinically with confidence, all lesions should be referred for excision.

A definitive diagnosis is made histologically following excisional or incisional biopsy. Once a diagnosis is made the tumour is then staged using the TNM classification. The vast majority of cSCCs are treated by surgical excision with a 4-10 mm margin depending on the size of the tumour.

The risk of metastasis is low (1.1-2.6%), but once metastasis has occurred the prognosis is poor with a mortality rate of more than 70%. Those lesions which are at particular risk of recurrence and metastasis to lymph nodes can be determined from the tumour size, site and histology, and the patient's immune status. Follow-up should include a full skin check, palpation of draining lymph nodes and patient education on skin surveillance. The duration and frequency of follow-up varies according to the risk status.

five years. For high and very high risk patients, this risk increases to 80%.[18]

Follow-up will require a full skin check, palpation of draining lymph nodes and patient education on skin surveillance. Follow-up frequency is recommended as follows:[18]

Low risk cSCC
- Single post treatment appointment

High risk cSCC
- **Year 1:** Every 4 months
- **Year 2:** Every 6 months

Very high risk cSCC
- **Year 1 and 2:** Every 4 months
- **Year 3:** Every 6 months

Follow-up can be organised as a shared care arrangement with appointments alternating between the GP and secondary care. Encouraging patients to carry out self-examination and use sun protection strategies is vitally important.

CONCLUSION

The incidence of cSCC is increasing. Educating all patients, particularly those with risk factors, on skin self-examination and sun protection should be a routine part of GP consultations that relate to the skin. Early recognition of a suspicious lesion by the patient and subsequently the clinician will lead to earlier treatment which is associated with better outcomes for the patient.

Competing interests: None

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Useful information

British Association of Dermatologists Patient information leaflets
Skin cancer - how to reduce getting another one
www.bad.org.uk/patient-information-leaflets

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