

Focus



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Periocular Basal Cell Carcinoma

Basal cell carcinoma (BCC) is the most common form of skin cancer in Europe, Australia and the US, representing 90% of all eyelid malignancies¹. As a result of inconsistent reporting, the exact incidence in the UK is unknown but estimates suggest that 53,000 new cases are diagnosed in the country each year².

The causal link between sun exposure and all skin cancers is well described³. BCCs are most common in people over 50 years, but an increasing number of younger adults are developing this form of skin cancer because of prolonged sun exposure and the use of sunbeds. BCCs may also develop in scars or sebaceous naevi, and are associated with several genetic syndromes, including basal cell naevus (Gorlin's) syndrome, xeroderma pigmentosa, Bazex syndrome and albinism.

Effective in reducing the incidence of these tumours are sunscreens, particularly those with protection against UVA and UVB⁴. In order to be effective, sunscreens need to contain both a physical blocker (eg zinc oxide) and a chemical blocker (eg avobenzone). However, the difficulties of applying sunscreen to the lids often mean that this part of the face is neglected. The photoprotective power of sunglasses is dependent on the quality of the glasses, their size and the position on the face (displacement of sunglasses a few mm down the nose results in a significant increase in the amount of UV light reaching the eye⁵).

The location of periocular tumours follows a consistent pattern; with the most common site being the lower lid followed by the medial canthus, eyebrow and upper lid and finally lateral canthus. It has been recorded that in men these tumours are more likely to occur on the right side of the face, this is probably related to differential sun exposure⁶.

There is a wide variation in the clinical appearances and morphology of basal cell carcinomas. Clinically the lesions may be nodular, cystic, superficial, morpohic (sclerosing), keratotic and pigmented variants. Common histological subtypes include nodular, superficial and pigmented forms, in addition to morpohic, micronodular, infiltrative and basosquamous variants which are particularly associated with aggressive tissue invasion and destruction⁷.

Whilst these tumours very rarely metastasise (a reported incidence of less than 0.1%), they can be locally destructive. Perivascular or perineural invasion are features associated with the most aggressive tumours⁸. In the recent NICE guidelines,

all BCCs above the clavicle are identified as high risk lesions and need to be managed by specialists as part of a multidisciplinary cancer team⁸.

As clinical presentation can be very variable, biopsy is recommended for all suspicious lesions and, in particular, if the tumour is large and reconstruction is needed. A simple punch biopsy is a reliable technique and can be performed easily in outpatients.

Several treatment modalities are available to the clinician including surgical excision, Mohs' micrographic surgery, topical Imiquimod, 5-fluorouracil, photodynamic therapy and radiotherapy. To date, few high quality studies compare the different treatment modalities for facial BCCs⁹. Of all the treatment techniques available, surgical excision with monitoring of excision margins has the highest cure rate and generally is the treatment of choice; a number of articles discuss treatment options and recommendations^{1,10}.

Medical management: Imiquimod is an immune response modifier that is a Toll-like receptor 7 agonist. It induces interferon and other cytokines, and stimulates cell-mediated immunity through T cells and stimulation of apoptosis in BCC cells. It has been shown to be effective as a topical treatment



for superficial basal cell carcinoma, achieving histological clearance rates of 82-90% using a treatment regime of 5x/week Imiquimod for six weeks¹¹. Detailed patient counselling on the use and side effects of this medication is essential prior to treatment.

It has been reported that 5% 5-fluorouracil is 90% effective in treating BCCs following a 12-week course, although there were lesions on the trunk. Its use is only recommended in low-risk sites so it should not be used to treat periocular BCCs.

Photodynamic therapy (PDT) involves the destruction of sensitised cells by an irradiating light source. A prodrug, either 5-aminolaevulinic acid (ALA) or methyl aminolaevulinic (MAL), is applied to the skin prior to treatment. Superficial BCCs have been shown to achieve 87% clearance. The five-year recurrence rate in nodular BCCs is higher, 14%, if treated with PDT as compared with standard surgical excision, 4%. A multicentre study, of 'difficult-to-treat' facial BCCs suggests that MAL-PDT may be an option for high-risk disease when other more effective treatments are contraindicated. Nevertheless as the clearance rates are lower than for surgical treatments, PDT is not generally recommended for management of nodular BCCs on the head or neck^{1,10}.

Surgical management: The surgical excision of periocular BCCs involves removing the lesion with a predetermined margin of 3-4mm around the macroscopic tumour margin, and is regarded as standard treatment. The use of smaller margins has been reported although the presence of residual tumour tissue requires re-excision. It has been demonstrated that when excision of facial BCCs is undertaken with narrower margins, histological clearance is not reliably achieved. Morphoeic and large BCCs required wider surgical margins in order to maximise the chance of complete excision.

Basal cell carcinoma on the face, and particularly on the eyelid, appears to have a higher degree of subclinical spread than tumours arising elsewhere. Tumour recurrence where complete tumour clearance is reported is recorded as between <2% and 4%¹². It is recognised that incomplete excision leads to a higher recurrence rate; studies with a five-year follow up have reported recurrence rates of 21-41% for patients following previous incomplete excisions¹³.

When incomplete excision occurs on the face there is good evidence to support the need for re-excision. Boulinguez et al report a 24% chance of incompletely excised BCCs becoming more aggressive when they recur¹⁴.

The use of staged tumour resections first pioneered (as chemosurgery) by Frederic Mohs in the 1940s¹⁵, which was later refined as Mohs' micrographic surgery (MMS), is well described. MMS results in extremely high cure rates for both primary and recurrent tumours, together with maximal preservation of normal tissues¹⁶. Modifying standard ways of examining convention histopathological specimens may simulate MMS and improve tumour clearance whilst minimising normal tissue loss.

Whilst it is a more time-consuming technique, requiring a range of specialists, a recent study comparing Mohs' surgery to standard excision for facial and auricular non-melanoma skin cancer found MMS to be more cost effective than standard surgical excision. However, a Cochrane review compared MMS to surgical excision and stated that no reliable conclusions could be reached regarding which method of treatment resulted in a lower recurrence or complication rate for periocular BCC, and no studies were found comparing the cost of either method directly¹⁷.

Radiotherapy: May be considered in those patients not suitable for surgical excision, the cure rates are reported as over 90% for most skin lesions. Tumours of the lower eyelid, inner canthus, lip, nose and ear are amenable to radiotherapy. However, the upper eyelid is not an appropriate site for radiotherapy due to keratinisation of the conjunctiva and damage to the tarsal plate and the eye.

Radiotherapy may be a good option for elderly patients, with very large BCCs of the scalp, but it is not appropriate for recurrent BCCs or patients with Gorlin's syndrome¹⁰. Treatment in fractions over several visits may produce better cosmetic outcomes than a single fraction treatment. A randomised trial recorded a higher recurrence rate in those undergoing radiotherapy for small facial BCC when compared with surgical excision; 7.3% and 0.7%, respectively¹⁸. The cosmetic outcome of radiotherapy is reported to be worse than that achieved by surgical excision.

In addition, radiotherapy tends to be more expensive than any other form of treatment. A recent prospective study by Lear et al in Canada looked at the cost of MMS and radiotherapy for 49 BCCs. The authors found the cost of radiotherapy to be significantly greater at approximately four times the cost of MMS¹⁹.

Conclusion: The indolent nature and lack of metastatic spread has led to irregular reporting, and thus an underestimation of the true incidence of BCCs in the UK. At present the standard surgical excision is the treatment of choice for periocular BCCs, although the advantages of Mohs' excision should not be understated in this area where tissue loss is often difficult to reconstruct.

The recent development of medical treatments, and in particular Imiquimod, offers other treatment options. With increasing experience of this medication, future ophthalmologists may find that time-consuming and unpleasant surgery is replaced, at least in part, by medical treatment for periocular BCCs.

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