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# Difficult to diagnose skin cancer

## The 'aggressive' BCC

### Background

Basal cell carcinomas (BCCs) are common, and are regularly diagnosed and managed by Australian general practitioners.

### Objective

This article summarises the types, clinical features, treatment and follow up of BCCs. Two cases histories are also presented that highlight the difficulties with diagnosing and treating aggressive BCC.

### Discussion

Aggressive BCCs can invade widely before exhibiting obvious clinical signs. Suspicious skin lesions should have an adequate biopsy taken to guide management options. Complete BCC excision is usually the best treatment, but particular care should be taken when treating lesions on cosmetically or functionally sensitive areas. Recurrent disease can also be difficult and disfiguring to treat. Specialist involvement will be needed for the management of some BCCs. Basal cell carcinomas can recur years after treatment. Regular skin checks are important for high risk patients.

■ **Australia has the highest incidence of skin cancer in the world,<sup>1</sup> with basal cell carcinoma (BCC) being the most common form.<sup>2</sup> As a result, Australian general practitioners regularly encounter BCC during clinical practice. Most BCCs are relatively straightforward to diagnose and treat, with the majority of care provided by GPs.<sup>2</sup>**

Basal cell carcinoma is rarely fatal (metastasising in 0.0028–0.1% of tumours),<sup>2</sup> although it can be locally destructive. Significant morbidity can be associated with the treatment required to eradicate deeply and/or widely infiltrating tumours. A small group of BCCs have few visible signs and can infiltrate large distances into tissue and invade sensitive facial structures before diagnosis. The delay in diagnosis can result in the need for radical and locally destructive treatment, and complicated surgical reconstruction.

### Basal cell carcinoma subtypes

Basal cell carcinoma has various subtypes, which can present with different clinical pictures, have different degrees of 'aggression' in terms of invasion, and require different methods of treatment. The most common types of BCC are 'superficial' and 'nodular' with the latter accounting for approximately 60% of all types in total.<sup>2</sup> *Table 1* lists the more common types of BCC.

### Superficial BCC

Superficial BCC usually presents as a well defined erythematous macule with little, if any, surface scale. Telangiectasia may be visible within the lesion (*Figure 1*).

### Histology

Histologically BCC consist of buds of basaloid cells invading into the upper dermis from the epidermis. Basaloid cells are



Table 1. BCC subtypes according to histopathological growth pattern and potential for aggression<sup>2,3</sup>

**Less aggressive**

- Superficial
- Nodular

**More aggressive**

- Infiltrative
- Micronodular
- Morphoeic

**Other types (uncommon)**

- Basosquamous (metatypical) – BCC with squamous differentiation. Probably more aggressive with a greater chance of metastasis than other forms of BCC
- Adenoid
- Cystic
- Pigmented
- Cornifying/keratotic
- Fibroepithelioma
- Follicular/infundibulocystic

Note: With the exception of basosquamous BCCs, the 'other types' probably have little clinical significance over the 'less aggressive' types

basophilic cells (similar to the basal cells of the lowest layer of epidermis) that are round and have a large nucleus. The buds are surrounded by fibrotic stroma and may appear as separate deposits on microscopy leading to the commonly used term, 'multifocal' superficial BCC. The buds are considered to be part of a single contiguous cancer. The multifocal nature may contribute to local recurrence if there are inadequate treatment margins. However, as the lesion is superficial (usually <1 mm in thickness), there are many treatment options, which are less destructive than surgery.

**Nodular BCC**

Nodular BCC usually present as a firm, well circumscribed, pale, translucent (pearly) nodule (Figure 2). Stretching the surrounding skin will accentuate the lesion and assist with clinical diagnosis. Close inspection will often reveal telangiectasia.

**Histology**

Histologically, the tumour is composed of large clusters of basaloid cells infiltrating into the dermis. Peripherally the cells are classically arranged in a palisading pattern (ie. a single layer of cells arranged side-by-side to form a 'fence'). The cells are surrounded by fibrotic stroma.

Nodular BCC can become locally destructive (Figure 3). Untreated, the tumour will destroy skin, muscle, cartilage and bone. This has been labelled a 'rodent' ulcer due to the area appearing like it has been eaten away by a rat.

Figure 1. Superficial BCC



Figure 2. Nodular BCC with telangiectasia



**BCC with 'aggressive' growth patterns**

Some types of BCCs have an aggressive growth pattern. That is, they can infiltrate widely and deeply with relatively little change in the overlying skin surface. The most common types of BCC that exhibit this behaviour are 'infiltrative' (a potentially confusing name given this word is used frequently to describe cancer growth in general), 'micronodular' and 'morphoeic'. Many BCCs will have features of more than one subtype coexisting, eg. a nodular BCC with micronodular areas.

Clinically these lesions can appear as flat, ill defined areas of skin where the texture and colour changes can be subtle (Figure 4).

Histologically, infiltrative BCCs are characterised by thin cords of basaloid cells with large amounts of surrounding fibrotic stroma. Morphoeic BCC is similar, except that the cords of BCC cells tend to be smaller, more angulated and more widely spread within the surrounding stroma. Micronodular BCC is composed of small round clusters of basaloid cells.

These BCC subtypes can have ill defined borders clinically, meaning incomplete excision and recurrence rates are higher than for less aggressive BCC forms.<sup>1</sup> The tendency for these tumours to be composed of thin cords or small clusters of cells, spread out over



a large distance, makes entire removal more difficult. The 'spread out' nature of the malignant cells with intervening normal appearing tissue increases the chance of the histopathologist reporting the excision lesion margins as clear, when residual disease may be left behind. Furthermore, recurrent or residual disease is more difficult to treat, and itself has higher recurrence and incomplete removal rates.<sup>1</sup>

These tumours require carefully planned, aggressive treatment to cure.

### Treatment and follow up

Generally, BCCs should be biopsied before treatment, allowing both doctor and patient to make an informed decision regarding

treatment option(s). When biopsying a lesion, adequate tissue should be taken. One full thickness 3 mm punch biopsy of the lesion is desirable, however, more and/or larger biopsies are preferable. Small, fragmented tissue samples may make diagnosis difficult; potentially compromising the ability to accurately assess BCC subtype and thickness, which affect the treatment choice.

However, where a confident clinical diagnosis can be made, small and straightforward lesions can be excised without a preceding biopsy.

There are few indications for treating BCC nonsurgically without a preceding biopsy, and these cases are best left to those doctors highly experienced in skin cancer treatment.

A wide range of treatments are available for BCC (*Table 2*).

### Surgery

The gold standard of treatment for BCC remains surgery. Surgery allows the entire tumour to be histologically examined, establishes if there is a healthy tissue margin around the lesion, and assesses other prognostic features such as perineural invasion. Perineural invasion allows the BCC to extend long distances resulting in recurrences, which are notoriously difficult to treat.

Staged surgery involves performing the excision, dressing the open wound, reviewing the histopathology results (usually some days later) and then re-excising (if necessary) and repairing the wound. This is useful where the tumour margins are ill defined or the lesion involves or is adjacent to sensitive structures such as the nose or eyelids.

Mohs surgery involves excising the skin cancer under long acting local anaesthesia and then examining the tissue using frozen section (see *Case study 1*). Repeated excision can be performed during the one visit. The Mohs technique involves horizontal sectioning of the specimen and microscopic scrutiny of all of the lateral and deep margins as opposed to standard vertical 'bread loaf' tissue slicing where about 1% of the entire specimen is examined. Mohs surgery is expensive, time consuming, requires a highly trained professional team and is not available in smaller rural centres. It has a better cure rate than standard surgery (up to 98–99%)<sup>2</sup> and allows for greater tissue conservation. It is the ideal modality for recurrent skin tumours and for those in cosmetically or functionally sensitive areas such as the face.

### Nonsurgical treatment

Radiotherapy, once used more commonly, has lost some favour due to the scarring, skin thinning, alopecia and telangiectasia that often occur years after treatment. It tends to be reserved for patients over 50 years of age where surgery is either not able to adequately remove the tumour or is thought to be too disfiguring (see *Case study 2*). Radiotherapy is also used in patients unfit for surgery and where surgery has incompletely removed the tumour (and further surgery is inappropriate).

Radiotherapy is only available in urban or large rural centres and requires up to 20 daily fractions spread over about 1 month. Other treatment modalities (*Table 2*) tend to be used for thinner and

Figure 3. Locally destructive nodular BCC



Figure 4. BCC with aggressive growth pattern



Table 2. Treatment methods for BCC

- Excision
  - standard
  - staged
  - Mohs
- Cautery and curettage
- Cryotherapy
- Photodynamic therapy
- Imiquimod cream (5%)
- 5-fluorouracil cream (5%)
- Radiotherapy



### Case study 1

Mr VR, 70 years of age, presented for a routine skin check. He had a history of multiple solar keratoses and NMSCs. During the examination a small, irritated, eroded area was noted on the left nasal tip at the edge of previous BCC surgery.

Two 3 mm punch biopsies were taken (*Figure 5*). The biopsy revealed infiltrative BCC. The patient was offered Mohs surgery and radiotherapy. The patient elected for surgery and underwent resection of most of the nasal tip followed by repair using a forehead flap (*Figure 6*). After the flap pedicle was transected and the flap was surgically revised, the patient was happy with the final cosmetic result (*Figure 7*).

Figure 5. Punch biopsies



Figure 7. Final result



Figure 6. Resection



less aggressive lesions. The recurrence rates of these treatments are higher than that of surgery and so careful long term follow up is required to detect early signs of recurrence. Recurrence may occur many years after the initial treatment. Furthermore, nonsurgical treatment of BCC on cosmetically sensitive areas such as the face (particularly the nose, ears and around the eyes) needs to be used with extreme caution, as the treatment of recurrent disease may be difficult and disfiguring.

### Red flags

Diagnosing BCCs such as those presented in *Case study 1* and *2* requires a high degree of vigilance. 'Red flags' which can alert to potential problems include:

- High risk patients:
  - older patients with fair skin, visible sun damage and a history of large amounts of occupational and/or recreational sun exposure
  - organ transplant recipients
  - those with a past history of multiple solar keratoses and/or nonmelanoma skin cancers (NMSCs)
- A history of a nonhealing or recurring skin ulcer or erosion, particularly if adjacent to an area of previous skin cancer treatment
- A lesion developing in an area of previous skin cancer treatment, especially if the original lesion was incompletely excised or treated nonsurgically
- A history of new or changing skin lesions.



**Case study 2**

Mr PA was an ex-dairy farmer, 65 years of age, presenting for a routine skin cancer check. He had a previous history of multiple solar keratoses and NMSCs. Examination revealed two irritated, eroded areas on the forehead. Adjacent to these were areas of hypopigmentation due to previous cryotherapy (*Figure 8*). Careful naked eye examination failed to reveal any other abnormalities of the adjacent skin.

The dermoscopic appearance of BCC has been described.<sup>4,5</sup> Basal cell carcinoma have a white-pink amorphous background with very well defined arborising (tree-like) vessels (*Figure 9*). Using the dermoscope to diagnose and demarcate BCC is in its infancy and currently lacks adequate evidence based support. Dermoscopic examination of Mr PA's forehead skin revealed large areas of tissue consistent with BCC. After receiving informed patient consent, the dermoscope was used to identify the lateral tumour margins. These were marked and seven separate locations were biopsied with a 3 mm punch biopsy (*Figure 10*). All seven biopsies revealed infiltrative BCC with invasion into fat and muscle tissue.

Following discussion with a Mohs surgeon and radio-oncologist, the patient elected treatment with radiotherapy (*Figure 11*). Both the patient and surgeon felt that surgery would be excessively disfiguring.

The patient had good cosmetic results after the radiation dermatitis settled (*Figure 12*) and is clinically disease free 15 months post-treatment.

Figure 8. BCC with areas of hyperpigmentation



Figure 9. Dermoscopic view of BCC

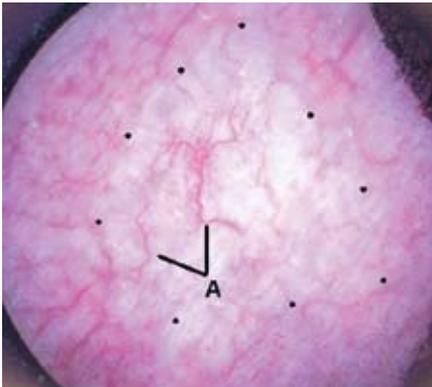


Figure 10. Locations for biopsy



Figure 11. Radiation dermatitis



Figure 12. Patient 15 months post-treatment





## Summary of important points

- Basal cell carcinoma are very common.
- Aggressive BCCs can invade widely before exhibiting obvious clinical signs.
- All suspicious skin lesions should be biopsied or the patient referred to a specialist.
- Adequate tissue should be taken when biopsying a lesion.
- Complete excision of a BCC is usually the best treatment.
- Beware of treating lesions on the face and of using nonsurgical treatments.
- Regular thorough skin checks are advisable for high risk patients.
- BCCs can recur many years after treatment.
- Treatment of a recurrent BCC can be difficult and disfiguring.

Conflict of interest: none declared.

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