Basal Cell Carcinoma

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Basal cell carcinoma (BCC) is a common, slow-growing malignant skin tumour that only very rarely metastasizes. The main subtypes of BCC are nodular, superficial, and sclerosing. The most important risk factors for the development of BCC include fair skin, extensive sun exposure as a child, past personal history of skin cancer, and advanced age. Basal cell carcinoma is the most common human malignancy, and its incidence is increasing worldwide. There are a number of different treatment modalities for BCC including topical therapies, cryotherapy, electrodesiccation and curettage, surgical excision, radiotherapy, and Mohs' micrographic surgery. Treatment should be tailored to the individual situation, and advanced age does not typically alter the management choice or reduce the expectation of an excellent outcome, including cure.

Key words: *basal cell carcinoma, nonmelanoma skin cancer, risk factors, epidemiology, treatment*

Introduction

Basal cell carcinoma (BCC) is the world's most common human cancer. Of the three major types of skin cancer, which also include squamous cell carcinoma (SCC) and melanoma, BCC accounts for approximately 70–80% of all skin cancers, while SCC accounts for 10–20% and melanoma 2–7%.[1,2] BCC, SCC, and melanoma are distinct entities that do not transform into each other. Basal cell carcinoma is predominantly seen among fair-skinned individuals in middle to late life. In Canada, there are more than 78,000 cases of BCC and SCC per year, which roughly equals the incidence of lung, breast, and colorectal cancers combined (Figure 1). Incidence rates vary by geographical location, sun exposure, and skin type.

The highest incidence of BCC is observed where fair-skinned people inhabit regions with heavy exposure to ultraviolet (UV) light, such as Australia.[3,4] Comparison data from across Canada, the U.S., and Australia have shown a continuous steady rise in the incidence of BCC—on average, 3–8% per year.[5,6] Basal cell carcinoma most often develops on sun-exposed areas—80% occur on the head and neck[7]—but can occur anywhere on the body. Basal cell carcinomas are locally invasive tumours that are usually slow growing and only rarely metastasize.

A history of an otherwise-asymptomatic skin lesion that bleeds with little trauma (such as washing the face), heals, and then rebleeds is characteristic of BCC. If left untreated, the tumour may extend into cartilage and bone causing disfigurement. Morbidity is more often associated with tumour extension into a vital structure than from metastasis, which is rare (metastasis rates of 0.0028–0.55% have been reported).[7]

In BCC, genetic injury to cells in the lower epidermis and hair follicle is the inciting pathogenic event, followed by dysregulation in immune system controls and local protective mechanisms for stopping the spread. There is evidence that older skin is at particular risk, not only due to a lifetime of genetic injury via UV damage, but also because local and systemic immune responses are less able to react to the threat. Older skin has been shown to have a reduced ability for repair of deoxyribonucleic acid (DNA), lowered cell-mediated immune surveillance, and decreased barriers to tumour spread as aging weakens tissue planes.[8]

Risk Factors

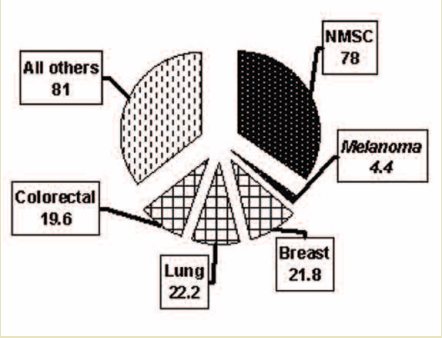
The most notable risk factors for BCC are UV exposure and fair skin (Table 1). Inter-

Table 1: Risk Factors for Development of Basal Cell Carcinoma

White skin: especially in those with photodamage, freckling, light hair and eyes
Ultraviolet light exposure: especially sunburns during childhood
Advanced age: usually seen in those over age 50 years
Male sex
Previous basal cell carcinoma
Family history of skin cancer
Immunosuppression or certain genetic disorders of DNA repair
Ionizing radiation or arsenic exposure
Smoking
High-fat diet

DNA = deoxyribonucleic acid.

Figure 1: Canadian Incidence of Cancers, in Thousands of Cases



NMSC = nonmelanoma skin cancer.
Source: Adapted from Lear W *et al.*, 2007.[1]

mittent intense UV exposure (especially blistering sunburns in childhood and adolescence) has been shown to correlate with an increased risk of BCC development.[9,10] This childhood exposure typically has a very long latency period, which explains the development of BCC in middle to later life. Ultraviolet exposure in adult life may also play a role, although this is less clear.[10,11]

Fair skin and all of its manifestations (white skin that burns in the sun, freckling, red or blonde hair, and light eye colour) are features associated with a much higher risk of developing BCC.[9,12] In fact, over 95% of all BCCs occur in white people.[3] While BCCs can occur in young people, most occur in people over 50 years of age, and the median age of diagnosis is 60–68 years. Basal cell carcinomas are slightly more common in males; the male-to-female ratio for BCC is about 1.5:1.[1,9]

Once a patient has had a BCC, there is a 35–77% chance that this patient will develop another BCC in the next 3 years; thus, skin surveillance after such a diagnosis is important. The highest risk of developing a subsequent BCC is in the first year following diagnosis.[1,13] A person with a diagnosis of BCC is also at increased risk of developing SCC and melanoma compared with the general population.

Other factors that raise the risk of BCC include anything that lowers the immune system (long-term immunosuppressive therapy), associations with skin injury (radiotherapy or occupational ionizing radiation, such as for pilots), and reduced DNA repair (certain genodermatoses such as xeroderma pigmentosum and Gorlin's syndrome).[14–17]

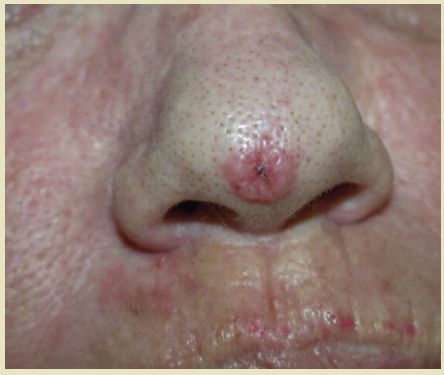
Morphology

Over 42 different variants of BCC have been described; these vary in presentation, histopathology, and aggressiveness (Table 2).[18,19] Below is a description of the main subtypes.

Nodular Basal Cell Carcinoma

Nodular (noduloulcerative/classic) BCC appears as a raised semitranslucent papule or nodule with telangiectasia (Figure 2). It sometimes forms a central depression that may bleed, crust, or ulcerate. The edge of the lesion has a characteristic rolled white pearly border that is more visible when the surrounding skin is held taught. A *rodent ulcer* is a historic term for a nodular BCC that has ulcerated.

Figure 2: Nodular Basal Cell Carcinoma



Source: Courtesy of Dr. Christian Murray.

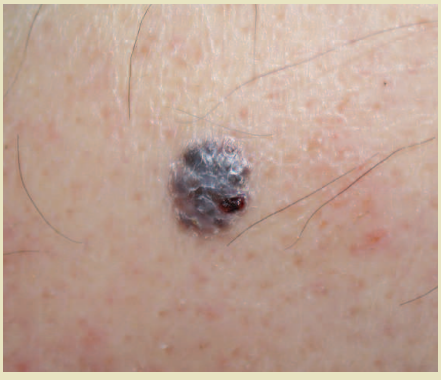
Pigmented Basal Cell Carcinoma

Pigmented BCC is a variant of nodular BCC that contains brown, black, or blue pigment (Figure 3). These pigmented growths are often confused clinically with angiomas, seborrheic keratosis, nevi, or melanoma. Asian and Hispanic people predominantly develop the pigmented variant of BCC.

Superficial Basal Cell Carcinoma

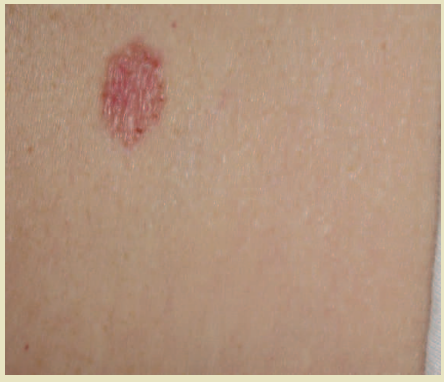
Superficial BCC looks like a dry, scaly, flat erythematous plaque with telangiectasia and a thread-like raised border (Figure 4).

Figure 3: Pigmented Basal Cell Carcinoma



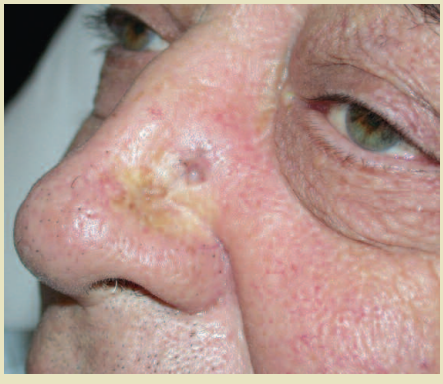
Source: Courtesy of Dr. Christian Murray.

Figure 4: Superficial Basal Cell Carcinoma



Source: Courtesy of Dr. Christian Murray.

Figure 5: Morpheaform/Sclerosing Basal Cell Carcinoma



Source: Courtesy of Dr. Christian Murray.

Occasionally, atrophy or scarring is present.

Morpheaform or Sclerosing Basal Cell Carcinoma

Morpheaform (sclerosing / fibrosing / infiltrating) BCC presents as a flat, slightly atrophic, indurated white or red plaque (Figure 5). Overlying telangiectasia may be present. The margins appear indistinct, and the actual size of the cancer is often much larger than what is clinically visible.

Table 2: Characteristics of Major Basal Cell Carcinoma Variants

Nodular	Superficial	Morpheaform/Sclerosing
Most common (70–80%)	10%	5%
Mostly head and neck	Mostly trunk/limbs	Mostly head and neck
Ddx: nevi, sebaceous hyperplasia	Ddx: psoriasis, eczema	Ddx: scar
May be pigmented	May respond to topical therapy	High risk for recurrence

Ddx = differential diagnosis.

Prevention

The main modifiable risk factor for BCC development is UV exposure. Unfortunately, little is known about the actual benefits of sun avoidance or sunscreen use in older adults. Sunscreen trials have almost exclusively used young, healthy volunteers, and there is little evidence describing sunscreen's ability to protect older adults from skin cancer. However, although sun protection later in life may not reduce BCC incidence, it likely helps protect against developing SCC.[20] It does seem prudent to continue to advise older adults to reduce UV exposure because this is expected to lower premalignant lesions, such as actinic keratoses, which may transform to SCC.

Newer preventative techniques to reduce early actinic damage such as photodynamic therapy or chemotherapies such as 5-fluorouracil or imiquimod creams may be useful, but evidence remains limited. A recent trial looking at topical retinoids to reduce skin cancer in American veterans unfortunately noted a higher mortality in the treatment arm and had to be stopped prematurely.[21]

Evaluation

Although rarely life threatening, BCC can destroy the skin and neighbouring tissues causing significant functional impairment and cosmetic disfigurement. While some patients are told that the slow growth of BCC means they should consider palliative measures instead of active therapy, given the effectiveness and limited morbidity associated with BCC management, there is usually no reason why older adults cannot be offered the same treatment options as younger patients. In fact, comorbidities are uncommonly a contraindication to effective therapy.

Evaluation of a suspected BCC requires a history taking, a physical examination, and usually a biopsy of the lesion. This evaluation should primarily establish the diagnosis and the complexity of the case, especially looking for evidence of previous failed therapy. It is also prudent to examine the surrounding skin and do a full-body skin examination to look for other cutaneous malignancies.

Treatment

The management of a BCC depends on whether it is a high- or low-risk lesion (Table 3), as well as access to treatment.[22]

Table 3: Characteristics of High- and Low-Risk Basal Cell Carcinomas

Features	Low Risk	High Risk
Location	Extremities, trunk	Face
Subtype	Superficial, nodular	Sclerosing/morpheaform
Size	Small (<2 cm body, <1 cm face)	Large (>2 cm body, >1 cm face)
Clinical margins	Well defined, feels thin	Poorly defined, or has depth on palpation
Previous treatment	None (primary lesion)	Recurrent
Histology	Nodular, superficial	Micronodular, sclerosing, basosquamous, perineural, perivascular
Treatment options	Topicals for superficial BCC, cryosurgery, ED&C, excision	Mohs' micrographic surgery, radiation
Patient factors	Healthy	Immunosuppressed, multiple lesions, past radiation nearby

BCC = basal cell carcinoma; ED&C = electrodesiccation and curettage.

Table 4: Treatments for Basal Cell Carcinoma

Topical Immunomodulators Imiquimod is a topical immune-response modifier that acts through toll-like receptors to induce an immune response against tumour cells. A local inflammatory reaction is associated with a higher clearance rate, and erythema and erosion are common side effects. Studies of this modality have shown clearance rates of 80% for superficial BCC, but long-term data on recurrence rates are limited.[22] Topical 5-fluorouracil has also been used for the treatment of superficial BCC, with 5-year cure rates of >80%. Topical treatments are limited by depth of penetration and should only be used for superficial BCC.
Cryosurgery Liquid nitrogen cryosurgery uses low temperatures (–50°C) to destroys tumour cells and surrounding tissues. The success of treatment depends on the appropriate selection of low-risk lesions and has been reported as high as 99%.[22]
Electrodessication and Curettage ED&C combines the physical removal and thermal damage of cancer cells. This commonly used modality is a good choice for primary small nodular BCCs, with cure rates of 92–98% for appropriate low-risk lesions.[23] This modality should not be used in morpheaform BCC.
Surgical Excision In standard surgical excision, the tumour is excised with a margin of clinically normal surrounding tissue. Wide excision with 4 mm margins gives a 90–98% cure rate for primary nonmorpheaform BCC <2cm.[24,25] This technique is very effective for most primary BCCs, but has higher recurrence rates for high-risk BCCs compared with MMS.
Mohs' Micrographic Surgery MMS combines staged resection with intraoperative surgical margin examination and results in extremely high cure rates (even for high-risk lesions) combined with maximal preservation of normal tissue.[26] Indications for MMS include (1) tumours with high recurrence rates following standard skin cancer treatment (recurrent tumours, large tumours, high-risk locations, aggressive histology, poorly defined clinical margins) and (2) tumours for which maximal conservation of normal tissue is important (i.e., tumours around the eyelid, nose, lip, ear; tumours in young patients; and tumours around vital structures such as extraocular muscles). MMS has a 99% cure rate for primary BCCs and a 95% cure rate for recurrent lesions.[22,27]
Radiotherapy Radiotherapy is effective in the treatment of primary and recurrent BCCs (but not radiorecurrence) and as adjuvant therapy after an incompletely excised BCC. Radiotherapy is the treatment of choice for high-risk BCCs in patients who are unable to tolerate surgery. Besides the challenges of accessibility, disadvantages for radiotherapy include radiodermatitis, worsening scar cosmesis over time, and secondary carcinogenesis. Five-year recurrence rates are between 90 and 93%.[22,23,28]
Other Other less common treatment modalities for BCC include photodynamic therapy for superficial BCC, intralesional interferon, oral retinoids, and various combination therapies.

BCC = basal cell carcinoma; ED&C = electrodesiccation and curettage; MMS = Mohs' micrographic surgery.

Cryotherapy, topical treatments, electrodesiccation and curettage, and simple excision are generally good options for low-risk lesions. Mohs' micrographic surgery, wide surgical excision with margins, and radiotherapy remain the mainstay of treatment for most high-risk lesions. Table 4 provides a summary of BCC treatments.

Follow-Up

Patients with a diagnosis of BCC should have follow-up skin examinations regularly, which often means every 6–12 months for life. Patients should be educated about sun safety and clinical signs of nonmelanoma skin cancer during self-examination.[9] Low-risk BCC may be managed adequately by experienced primary caregivers; however, more aggressive or recurrent BCC should be referred to a specialist such as a dermatologist for definitive management.

Conclusion

Basal cell carcinoma is the most common human cancer and appears destined to become an even more important health care issue as the population continues to age. Older adults benefit from the same effective therapies as younger patients and should be expected to achieve good outcomes despite advanced age. It is important to recognize and treat BCC early to avoid significant morbidity, and to follow up all skin cancer patients with regular skin checks.

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Key Points

Basal cell carcinoma (BCC) is a very common, slow-growing, and locally destructive skin malignancy.

The main risk factors are childhood exposure to sunlight, fair skin type, and advanced age.

Therapeutic options for BCC include surgery, electrodesiccation and curettage, radiotherapy, and topical creams.

Treatment of each BCC must be tailored to the individual patient and take into account specific tumour characteristics.

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Clinical Pearls

Once a patient has been diagnosed with his or her first BCC, there is a high chance of the patient developing another BCC in the next 5 years. Regular follow-up with skin examination is particularly important in this patient population.

A BCC that has recurred after electrodesiccation and curettage, cryotherapy, or topical therapy generally requires more definitive management for cure, and referral to a specialist with expertise in skin cancer, such as a dermatologist, is warranted.