



**ORIGINAL RESEARCH PAPER**

**Dermatology**

**BASAL CELL CARCINOMA: REVIEW**

**KEY WORDS:** carcinoma, skin

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**ABSTRACT** Basal cell carcinoma (BCC) is a common, locally invasive, keratinocyte cancer (also known as nonmelanoma cancer). It is the most common form of skin cancer. BCC is also known as rodent ulcer and basalioma. Patients with BCC often develop multiple primary tumours over time.

**INTRODUCTION**

Basal Cell Carcinoma is the most common type of cancer in the world, doctors diagnose millions of people with BCC every year. In the United States alone, it's estimated that about 2 million Americans each year.

Most people who develop this skin cancer have fair skin that they seldom protected with sunscreen or sun-protective clothing.

Before they developed skin cancer, they often noticed signs of sun damage on their skin, such as age spots, patches of discolored skin, and deep wrinkles.

Basal cell carcinoma (BCC) usually appears as a small, shiny pink or pearly-white lump with a translucent or waxy appearance. It can also look like a red, scaly patch.

There is sometimes some brown or black pigment within the patch.

The lump slowly gets bigger and may become crusty, bleed or develop into a painless ulcer.

The patched/hedgehog intracellular signaling pathway is responsible for regulating cell growth, and constitutive activation of this pathway leads to BCC development.

The most common mutations are inactivating mutations of PTCH1 or activating mutations of SMOM, which cause aberrant hedgehog pathway activation and tumor formation.

A loss-of-function mutation in SUFU, a negative regulator of

the hedgehog pathway, has also been identified in a small portion of BCCs.

Other common mutations include UV-specific defects in the p53 tumor suppressor gene, which are present in half of BCCs.

**Histologic subtypes**

Lower-risk histologic subtypes:

1. Superficial BCC
2. Nodular BCCs
3. Pigmented

Higher-risk histologic subtypes:

1. Morpheaform (sclerosing) BCCs
2. Infiltrative
3. Micronodular BCCs
4. Basosquamous carcinoma

**Clinical Factors**

Area H is considered the high-risk location, independent of tumor size. Tumors arising in the M and L areas can be classified as high risk, depending on the size, histologic subtype, and poorly defined borders.

BCCs developing in the setting of immunosuppression and recurrent tumors, irrespective of prior therapy, are also considered high-risk.

**Pathologic Factors**

Perineural involvement (PNI) is rare with an incidence of less than 1% but is an independent risk factor for recurrence and is more common with aggressive subtypes. MRI should be considered to evaluate nerve involvement if patients exhibit

neurologic symptoms.

**Treating non-melanoma skin cancer**

Surgery is the main treatment for non-melanoma skin cancer. It involves removing the cancerous tumour and some of the surrounding skin.

Other treatments for non-melanoma skin cancer include freezing (cryotherapy), anti-cancer creams, radiotherapy and a form of light treatment called photodynamic therapy (PDT).

The treatment used will depend on the type, size and location of the non-melanoma skin cancer you have.

Treatment for non-melanoma skin cancer is usually successful as, unlike most other types of cancer, there's a considerably lower risk that the cancer will spread to other parts of the body.

Basal cell carcinoma (BCC) does not usually spread to other parts of the body. There's a small risk (up to 5%) of squamous cell carcinoma (SCC) spreading to other parts of the body, usually the lymph nodes (small glands found throughout your body).

However, for both BCC and SCC there can sometimes be considerable skin damage if the tumour is not treated.

At least 9 out of 10 non-melanoma skin cancer cases are successfully cured.

**Cryosurgery**

Cryosurgery is a fast, destructive technique but lacks histologic assessment of tumor margin. The goal is to achieve -50°C to the tumor with a surrounding margin of 3 mm to 5 mm. Although multiple large case series report cures rates of 94% to 99%, careful patient and tumor selection is essential and should be reserved to superficial and low-risk tumors.

**Curettage and Electrodesiccation**

Curettage and electrodesiccation (CE) is recommended by the NCCN for properly selected, low-risk tumors. CE is fast and cost-effective; however, it does not allow for histologic margin assessment and is operator-dependent.

**Photodynamic Therapy**

Photodynamic therapy (PDT) with aminolevulinic acid (ALA) and methyl aminolevulinate (MAL) have similar outcomes and pain scores when used to treat nodular BCC. Cure rates range from 70% to 90%, although approximately all studies have short follow-up periods.

**Surgical Excision**

The NCCN recommends 4-mm clinical margins for low-risk tumors treated with standard excision with postoperative margin assessment (SEPMA). Primary tumors of any size on the neck, trunk, and extremities have in excess of 95% 5-year cure rate. Rates of incomplete excisions are estimated at 3% to 16.6% and are associated with a recurrence rate of approximately 38%. Surgical excision is less effective for BCCs arising in the H-area possibly due to narrower margins used, more aggressive histology, or increased subclinical spread

**Systemic Therapies**

Although a majority of BCCs are easily cured with local treatment, a subset of patients, including those with BCNS and locally advanced or metastatic disease, require systemic treatment. In 2012, the FDA approved vismodegib, a first-in-class hedgehog pathway inhibitor, for the treatment of locally advanced or metastatic BCCs.

Vismodegib can be taken with or without food and does not require laboratory work prior to or after initiation. There are

reports, however, of hepatotoxicity, so caution should be taken in patients with severe liver disease.

Sonidegib, the second hedgehog pathway inhibitor, is approved by the FDA for treatment of locally advanced BCCs that recur after surgery or RT or who are not candidates for surgery or radiotherapy.

Anti-programmed death-1 (PD-1) immunotherapy is another emerging treatment option for advanced BCC.

**REFERENCES**

- Lai V, Cranwell W, Sinclair R.: Epidemiology of skin cancer in the mature patient. *Clin Dermatol* 2018; 36: pp. 167-176.
- Kasper M, Jaks V, Hoh D, et al.: Basal cell carcinoma - molecular biology and potential new therapies. *J Clin Invest* 2012; 122: pp. 455-463.
- Cameron M.C., Lee E, Hibler B, et al.: Basal cell carcinoma: part 1. *J Am Acad Dermatol* 2018; [pii:S0190-9622(18)30775-8]
- Rogers H.W., Weinstock M.A., Feldman S.R., et al.: Incidence estimate of nonmelanoma skin cancer (Keratinocyte Carcinomas) in the US Population, 2012. *JAMA Dermatol* 2015; 151: pp. 1081.
- von Domarus H., Stevens P.J.: Metastatic basal cell carcinoma. Report of five cases and review of 170 cases in the literature. *J Am Acad Dermatol* 1984; 10: pp. 1043-1060.
- Morgan FC, Ruiz ES, Karia PS. Factors predictive of recurrence, metastasis, and death from primary basal cell carcinoma 2cm or larger in diameter. *In press.*
- Guy G.P., Machlin S.R., Ekwueme D.U., et al.: Prevalence and costs of skin cancer treatment in the U.S., 2002-2006 and 2007-2011. *Am J Prev Med* 2015; 48: pp. 183-187.
- Ruiz E.S., Morgan F.C., Zigler C.M., et al.: National skin cancer expenditure analysis in the United States medicare population, 2013. *J Am Acad Dermatol* 2018; [Epub ahead of print]
- Mofidi A., Tompa E., Spencer J., et al.: The economic burden of occupational non-melanoma skin cancer due to solar radiation. *J Occup Environ Hyg* 2018; 15: pp. 481-491.
- Sehgal V.N., Chatterjee K., Pandhi D., et al.: Basal cell carcinoma: pathophysiology. *Skinmed* 2014; 12: pp. 176-181.
- Bonilla X., Parmentier L., King B., et al.: Genomic analysis identifies new drivers and progression pathways in skin basal cell carcinoma. *Nat Genet* 2016; 48: pp. 398-406.
- Gallagher R.P., Hill G.B., Bajdik C.D., et al.: Sunlight exposure, pigmentation factors, and risk of nonmelanocytic skin cancer. *Arch Dermatol* 1995; 131: pp. 157.
- Robinson S.N., Zens M.S., Perry A.E., et al.: Photosensitizing agents and the risk of non-melanoma skin cancer: a population-based case-control study. *J Invest Dermatol* 2013; 133: pp. 1950-1955.
- Karagas M.R., McDonald J.A., Greenberg E.R., et al.: Risk of basal cell and squamous cell skin cancers after ionizing radiation therapy. *J Natl Cancer Inst* 1996; 88: pp. 1848-1853.
- Martinez V.D., Vucic E.A., Becker-Santos D.D., et al.: Arsenic exposure and the induction of human cancers. *J Toxicol* 2011; 2011: pp. 431287.
- Kricker A., Armstrong B.K., English D.R., et al.: Does intermittent sun exposure cause basal cell carcinoma? a case-control study in Western Australia. *Int J Cancer* 1995; 60: pp. 489-494.