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Non-surgical management of early basal cell carcinoma

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Abstract

In the case of a suspicious mole on the skin, the question always arises as to whether it is benign or malignant. Is it a harmless mole, a capillary malformation or a basal cell carcinoma, squamous cell carcinoma or even a melanoma? Often the nevus can be assessed just by a close examination of the lesion and a few questions about its origin. However, every dermatologist knows all too well the problem that very different lesions can look extremely similar to the naked eye and even on dermatoscopy. Therefore, the question arises: how should dermatology deal with and communicate in such cases? This article identifies ways forward in this difficult situation, which occurs tens of thousands of times a day around the globe.

Overview

Basal cell carcinoma (BCC) is the most common cancer in fair-skinned people and continues to increase rapidly. Not least in the context of increased patient vigilance, physicians from various specialties are increasingly confronted with BZK, which accounts for about 80% of all cases of white skin cancer. BZK is often misdiagnosed due to its light color and low symptomatology and develops over months to years due to its slow growth. Metastatic spread is extremely rare with an estimated incidence of <0.45%. However, the invasive growth can destroy cartilage and bone tissue and reach vital structures (main vessels, CNS) - sometimes with a lethal outcome. Therefore, early detection of this particular type of cancer is of particular importance. For a long time, the only therapy was complete surgical removal. In case of inoperability or postoperatively expected functionally limiting or aesthetically disfiguring results, radiotherapy is an alternative. In recent years, other therapies have been developed, especially substances to be applied topically. These new therapeutic options should truly ease the fear and anxiety of any patient with a small lesion. BCC is the most common non-benign tumor in fair-skinned people, with about two million new cases annually worldwide. It accounts for the largest proportion of light skin cancers (80%) and is increasingly occurring in younger patients (<40 years), with an average age of 60 years at initial diagnosis. Meta-analyses show regional variations, reported with incidences of 115 in the UK, 80 in Germany, Switzerland, and Italy, 170 in sen USA, and >800 in Australia, each based on 100,000 person-years. Incidence has increased at least 2- to 3-fold within the past 30 years. The predilection site is the chronically light-exposed head and neck area, but BCC also frequently occurs on the trunk as a multicentric superficial growing subtype. In addition to fair skin type and UV radiation, immunosuppression, arsenic exposure, scars, and hereditary diseases such as nevoid BCC syndrome (syn. Gorlin-Goltz syndrome) and xeroderma pigmentosum are risk factors. Clinically and histologically, the most common subtype, solid (synonym: nodular) BCC, is distinguished from the infiltrative variants (sclerodermiform BCC and micronodular BCC) and from multicentric superficial BCC (syn.: trunk skin basal cell carcinoma), each with an incidence of about 25%. Other rarer forms are pigmented BCC (1%) and feral, ulcerating-destructive growing subtypes (ulcus terebrans, ulcus rodens). Depending on the growth pattern and localization, various therapeutic options are available; in the following, we present topical treatment.[3,6,8]

Topical treatment of BCCs

For several years, various topical agents have been available for the therapy of superficially growing BCCs. The immunomodulator imiquimod binds to Toll-like receptor-7, inducing the release of pro-inflammatory cytokines, such as IFN-alpha, TNF-alpha, and IL-12. Imiquimod is approved as a 5% cream for the treatment of small (<7.25 cm2) superficial BCC and is applied to the skin overnight five times per week for six weeks. The histologically controlled complete cure rate was approximately 80% in the pivotal randomized controlled trial.[19-23]

Topical photodynamic therapy (PDT) with 5-aminolevulinic acid or with its methyl ester (MAL, 160 mg/g cream) in combination with red light is another therapeutic option for BCC. The MAL cream is applied to the BCC and left there for three hours by means of an occlusive dressing. During this time, increased photosensitizer (protoporphyrin IX) is synthesized in the tumor cells, and subsequent exposure to red light initiates a chain of reactions with the formation of reactive oxygen species that have a cytotoxic effect. PDT for BCC should be repeated at intervals of 1-4 weeks. Complete remission was seen in 92% in a randomized controlled trial for superficial BCCs. The cytostatic agent 5-fluorouracil is available as a 5% prescription cream and is usually applied twice daily for 3-12 weeks until erosions occur. Although the drug has been on the market for many years, no prospective randomized studies of healing and recurrence rates have been available. Systemic side effects may occur with this preparation, necessitating treatment discontinuation. In a multicenter, single-blind, controlled, randomized comparative study of 601 patients with superficial BCC published in 2013, complete cure rates were 83% for imiquimod, 80% for 5-fluorouracil, and 73% for MAL-PDT. A systematic review of clinical trials of therapy for superficial BCC reported average healing rates for imiquimod of 86% (95% confidence interval 82-90%) and for PDT of 79% (71-87%), whereas for 5-fluorouracil the study data were too limited. Advantages of topical cream treatment and PDT are scar-free healing and the possibility of area therapy. Disadvantages of 5-fluorouracil and imiquimod are the sometimes very strong inflammatory and erosive reactions (although these are beneficial with regard to the antitumor effect) after individually very different time periods (several days to several weeks) and the dependence on good patient compliance. Disadvantages of PDT are painfulness during irradiation and local reactions (redness, erosions, pustules, sloughing) lasting for 1-2 weeks. Disadvantages of all topical cream applications and of PDT are the lack of histological control and the limited depth of penetration, so that the risk of residual tumor at depth with the risk of clinically late recurrence should not be underestimated in view of the success rates given above.[17,19,23]

Conclusion

Various topical therapies as an alternative to excisional biopsy for uncomplicated BCC have quickly gained a foothold in dermatology. This is welcome as it can address the inhibition of many patients with "scalpel anxiety". However, very rare systemic side effects should be kept in mind and the preparations should not be promoted as "healing ointment". Both the physician and the patient should be aware of the strength of the preparations.

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Conflicts of interest

None.

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