Non-melanoma skin cancer management - a literature review

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ABSTRACT

Background. As our population ages, the increasing incidence of non-melanoma skin cancer presents significant financial and logistical challenges. Around 90% of all cases are initiated by UV light exposure. Non-melanoma skin cancer includes squamous cell carcinoma and basal cell carcinoma, in addition to many uncommon tumors.

Aim. The aim of this article is to review and analyze scientific publications, including indications and different treatment options for non-melanoma skin cancer.

Materials and methods. A search of scientific articles was performed in PubMed, UpToDate, and Google Scholar databases using the terms “non-melanoma skin cancer”, “white skin cancer” and “management” or “treatment”. Articles were included if they were in English and no more than 10 years. Finally, 21 articles in all were analyzed.

Results. One of the most common types of cancer in the world is skin cancer, with non-melanoma skin cancer being the most common form. Management options are operative treatment, chemical destruction, physical destruction, and immunomodulatory therapy. Photodynamic treatment and several topical medications offers promise for superficial basal cell carcinoma. Nowadays photodynamic treatment provides better cosmetic results compared to surgery.

Conclusions. Non-melanoma skin cancers are generally considered treatable, but their increasing incidence has led to a growing global health problem. More and more advanced non-melanoma skin cancers are being treated with immunotherapy. Despite the development of innovative non-surgical therapies, surgical excision remains the most commonly used treatment option for non-melanoma skin cancers.

Keywords: Basal cell carcinoma, squamous cell carcinoma, operative treatment, radiotherapy, cryotherapy, curettage, photodynamic treatment.

1. Introduction

The aging population and increased UV radiation exposure from trips abroad and sunbed use are the main causes of the rising prevalence. Non-melanoma skin cancer (NMSC) encompasses a variety of uncommon skin tumors in addition to its primary constituents, squamous cell carcinoma (SCC) and basal cell carcinoma (BCC). Three-quarters of NMSC cases that are registered are caused by BCC. In white populations, BCC is the most prevalent type of malignant tumor (1). Despite the low death rates, there is a considerable amount of morbidity since sun-exposed areas like the face are frequently the site of lesions (2). The following are risk factors for non-melanoma skin cancer: pale skin, genetic predisposition, residing in high UV radiation areas, age, male sex, and prior incidence (3,4).

2. Materials and methods

The UpToDate clinical database, Google Scholar, and PubMed databases were searched. The search was conducted using the phrases “non-melanoma skin cancer” or “white skin cancer” in combination with “management” or “treatment”. A total of 285 English-language publications were found. After an initial title screening, 170 articles were classified as unsuitable. Duplicate publications were also excluded. After a comprehensive review of the selected publications, 94 more were excluded due to inconsistencies in the subject matter, leaving a final selection and in-depth analysis of 21 scientific references published between 2013 and 2023. The following sources were used: systematic literature reviews, meta-analyses, full-text articles, and literature reviews.

3. Results

3.1. Presentation

3.1.2 Presentation of basal cell carcinoma

The majority of BCC cases-80% on the head and neck and 15% on the trunk occur in sun-exposed areas (5). Although metastases are uncommon and lesions grow slowly, if they are left untreated, they may invade other structures locally and cause them to collapse. BCC has multiple histopathological subtypes. The pink, pearly papule with rolling edges, telangiectasia overlaying, and sometimes core ulceration is a typical nodular subtype. Typically found on the trunk, superficial BCCs are developing slowly erythematous plaques that may appear like discoid eczema, psoriasis, or Bowen's disease. Because morphemic BCCs appear as pale, poorly delineated plaques, they are more invasive and manifest later in life (5).

3.1.2 Presentationsquamous cell carcinoma

On sun-exposed areas, SCC can manifest as indurated keratinising lesions or ulcers. Bowen's disease, also known as SCC in situ, actinic keratoses (AKs), and pre-malignant lesions can all lead to SCC development. A sign of UV-damaged skin, AKs develop into invasive SCC in about 1-10% of cases (6). Usually, nodule, keratinising lesions, and keratoacanthomas evolve over several months before spontaneously inverting. Because they are histologically identical to well-differentiated SCCs, removal is necessary in every instance.

3.2 Management

3.2.1 Surgery

Historically, surgery has always been the mainstay ("gold standard") of treatment. The whole tumor is removed during surgery with the best possible cosmetic outcome. The original tumor should be removed in 95% of cases when well-defined, low-risk SCCs with a diameter of less than 2 cm are excised, maintaining a 4 mm margin. Excision with a 4 mm margin is another successful treatment for primary BCC, resulting in a 5-year recurrence rate of less than 2% (7). For larger and poorly differentiated lesions, wider margins or alternative methods of therapy are needed (7,8).

The best method for fully examining surgical margins is micrographically controlled surgery. It is a safe and effective way to ensure the complete removal of invading tumors while protecting surrounding tissue, particularly at troublesome locations. Compared to non-surgical methods, this provides aesthetic results that are either superior or equivalent (9).

3.2.2 Physical destruction

For SCC, radiotherapy has been shown to have cure rates as high as 90%. For primary BCC, it has 5-year cure rates of 91,3%, while for recurrent BCC, it has 90,2%. Radiotherapy is frequently the chosen method of treatment for patients for whom surgery is contraindicated, for bony or cartilaginous sites, and when tissue preservation is crucial (lip, lower eyelid, and inner canthus of the eye) (6). Although current techniques have improved, radiation was once a less appealing alternative for younger people due to inferior cosmetic results. Cryotherapy and curettage are also physically invasive treatments that can be used to treat some low-grade BCC and SCC. However, these methods may not provide good cosmetic results and do not allow for histological examination of the margins (8).

3.2.3 Chemical destruction

Methyl aminolevulinate (MAL) or 5-aminolevulinic acid is a photosensitising substance used in topical photodynamic treatment (PDT), which is activated by light. When malignant keratinocytes are exposed to light, the photosensitiser causes the production of photoactive porphyrins, which in turn causes the release of reactive oxygen species and the generation of free radicals (6). In randomized studies, MAL-PDT has demonstrated better clinical and cosmetic results than cryotherapy. It is not advised, therefore, for high-risk tumors unless the patient refuses or is unable to get more appropriate treatment. PDT is useful in the treatment of premalignant lesions but is not authorized for SCC because of the risk of metastasis and recurrence (10,11).

Another thoroughly researched treatment for pre-malignant lesions, AKs, Bowen's disease, and small superficial BCCs is 5-fluorouracil (5-FU) (12). It is allowed to treat sBCC with two daily applications of the 5% formulation of the antimetabolite 5-FU for a duration of three to six weeks (13,14). Other topical medications that are chemically damaging for AKs are gel diclofenac and gel ingenol mebutate (6).

3.2.4 Immunomodulatory therapy

Imiquimod stimulates dendritic cells and monocytes to produce cytokines and chemokines by binding to toll-like receptors. Immune response modifier imiquimod is prescribed once daily, five times a week for six weeks to treat sBCC in immunocompetent people (15). The combination of different forms of therapy is an innovative approach to the treatment of cancer. It is more beneficial to use ALA-PDT with imiquimod twice a week for 16 weeks than PDT alone (16). However, the majority of studies conducted

include only a limited number of patients, the results are assessed only clinically and without histological confirmation. Knowledge of the molecular mechanisms underlying PDT for the different NMSC will improve and allow us to identify the most promising treatment combinations (16).

Anti-PD1 drugs such as cemiplimab and pembrolizumab have shown remarkable results in terms of response rate in patients with locally advanced or metastatic SCC who are not eligible for surgery or radiotherapy (17). Pembrolizumab, an anti-PD-1 medication, was approved in 2020 for the treatment of patients with metastatic or recurrent SCC who do not respond to radiatiotherapy or curative surgery (18). Many advanced-stage NMSC patients now have a better chance of survival rates due to anti-PD-1 drugs. Treatment of advanced disease is increasingly dependent on immunotherapy. In order to maximize the number of patients and achieve continuous improvements, it is important to constantly review the status of clinical trials (19–21).

4. Conclusions

The standard treatment for non-melanoma skin cancer is surgical excision. Other alternatives include non-surgical techniques such as topical chemotherapeutic agents, cryotherapy and immunomodulatory treatment. A successful treatment for superficial BCC is photodynamic therapy. Response rates for nodular BCC and Bowen's disease are satisfactor, but recurrence rates are higher for these two NMSC subtypes. For nodular BCC, MAL-PDT is a more effective treatment than ALA-PDT. Numerous studies have shown that PDT leads to better cosmetic results than surgery. The treatment and survival of advanced skin cancers have been transformed by immunotherapy and targeted therapy.

The selection of patients who will benefit from these treatments will pose new challenges in the future, regardless of the efficacy of these new drugs.

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