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Cutaneous manifestations associated with malignancy of the head and neck

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ABSTRACT

Most cutaneous malignancies of the head and neck (HN) are non-melanoma skin cancers, predominantly basal cell carcinomas (BCCs) and squamous cell carcinomas (SCCs). Less common entities include Merkel cell carcinoma (MCC), sebaceous carcinoma (SC), and angiosarcoma. Treatment is based on histology subtype, stage, and extent of involvement. Surgery is the primary means of treatment and includes wide local excision, Mohs micrographic surgery, sentinel lymph node biopsy, and cervical lymphadenectomy. Multidisciplinary management including radiation and targeted chemotherapy are critical adjuncts to surgery. Surgical planning must balance oncologic, functional, and cosmetic considerations. This review addresses cutaneous manifestations of primary malignancies of the HN and dermatologic complications of small molecule inhibitors used for targeted therapy. A working knowledge of both the cutaneous malignancies (CM) in the head and neck as well as the secondary dermatologic manifestations is relevant to multiple disciplines including dermatology, medical oncology, radiation oncology, and surgical oncology.

1. Introduction

Malignancies of the head and neck (HN) account for only 4% of all malignancies in the United States [1]. This includes malignancies of the upper aerodigestive tract, salivary gland cancers, and skull base tumors. This figure does not include endocrine malignancies nor cutaneous malignancies, which are tabulated separately [1]. Cutaneous malignancies (CM) have the highest incidence amongst all cancers in the United States. Furthermore, the incidence of CM, as a whole, has been increasing. While the total skin surface area of the head and neck is comparatively small, a large number of CM diagnoses occur in these sites due to the higher frequency of exposure to ultraviolet radiation (UVR) [2].

CM are generally divided into two broad groups: melanoma and non-melanoma. The majority of cases belong in the non-melanoma group. Basal cell carcinoma (BCC) and squamous cell carcinoma (SCC) are by far the most common non-melanomatous CM. BCC and SCC count for nearly 3,500,000 new diagnoses per year in the United States (80% *v* 20%) [1]. In 2014, 73,870 melanomas were diagnosed in the United States and there were 9,940 deaths due to melanoma. Other rarer CM such as Merkel cell carcinoma (MCC), sebaceous carcinoma (SC), and angiosarcoma accounted for 6,230 new diagnoses and 3,400 deaths in 2014 [1]. Though they result in comparably fewer deaths than melanoma and other non-melanomatous CM, when adjusted for rate of occurrence, BCC and SCC still pose a significant public health problem, especially when not recognized and treated early.

In this review, the focus will be to present a synopsis of the treatment options and challenges of cutaneous HN malignancies. CM when occurring in the HN often have separate considerations because of the proximity to functional or aesthetic structures. There are also several cutaneous considerations that result from the presence and treatment of even non-cutaneous HN cancers. Cutaneous eruptions from untreated cancer, Bazex syndrome, and those from treatment side effects, such as cetuximab-induced dermatitis will also be discussed. A working knowledge of CM in the HN and the secondary manifestations of HN malignancies requires understanding of relevant aspects of multiple disciplines including dermatology, medical oncology, radiation oncology, and surgical oncology.

2. Primary cancers of the head and neck

Risk factors for development of CM are fairly well known. Some of the most commonly cited include UVR, light skin, male sex, history of blistering sunburn, blonde or red hair, blue eyes, and family history (less so for BCC and SCC). Additional risk factors, but perhaps less commonly discussed, include outdoor occupation and

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hobbies, location relative to the equator, chronic inflammatory states, non-healing wounds, immunosuppression, burns, trauma, certain chemicals, and cigarette smoking. Details regarding the chronicity of the lesion, changes over time, associated discomfort, paresthesias, and presence of other cutaneous and non-cutaneous lesions can assist a clinician in the creation of a thorough differential diagnosis and appropriate plan for management.

3. Basal cell carcinomas

Common risk factors include UVR (though dose and duration are not well substantiated), blond or red hair, blue eyes, fair skin, poor ability to tan after prolonged sun exposure, more than one lifetime blistering sunburn, sun-induced freckling as a child, personal or family history of skin cancer, immunosuppressive therapy, childhood radiation therapy, smoking, and extended psoralen plus ultraviolet A treatment of psoriasis [3–7]. Prevention strategies primarily involve avoidance of UVR, use of sunscreen with an SPF rating of at least 30, and use of protective clothing [8].

BCCs have no known precursor lesion. The classically described lesion of a pearly, pink raised lesion with rolled borders and arborizing telangiectasia is seen mostly in the nodular variety, which accounts for the majority of BCC (Fig. 1A, B). Additional histologic subtypes include superficial multicentric, metatypical, and morpheaform. Superficial multicentric BCC is commonly mistaken for chronic dermatitis. It is characterized by small red patches with wispy borders and minimal dermal invasion. Metatypical BCC, also referred to as basosquamous, presents as an ulcerative lesion which progresses quickly and often times has perineural invasion. Patients frequently complain of formication and paresthesias associated with these lesions. Morpheaform BCC is the most invasive and least common of the subtypes. It is often mistaken for a scar with its off white to yellow appearance and firm feel [5]. The metatypical and morpheaform subtypes are considered high risk because of their propensity for perineural spread and invasive nature.

In addition to histologic subtype, size and location play a key role in determining risk. Up to 80% of all reported BCCs occur on the scalp, face, or neck [3]. In the absence of high risk histology, lesions of the neck less than 10mm and lesions of the face less than 6mm can be considered low risk. High-risk lesions are often found on the scalp, on/behind/in front of the ear, at the canthus or periorbital skin, at the lips, and along the mandible or nasolabial folds [9]. Rather than directly invading and violating tissue planes in these anatomical locations, BCC often spreads along the path of least resistance. This leads to elevated recurrence rates by a concept called the iceberg phenomenon; a situation in which the visible lesion and often excised lesion, represents only a portion of the actual tumor.

The mainstay of treatment for BCC remains surgical, either by electrodessication or excision [9]. BCC found in the HN is ideally suited for the application of Mohs micrographic surgery, allowing for real time examination for margins and feedback to the surgeon performing the excision. Mohs maximizes cosmesis and function by achieving the smallest margin that is oncologically sound. As with other CM of the HN, larger excisions or those in a challenging location should be performed by an experienced surgeon with expertise in reconstruction.

Radiation therapy is an appropriate alternative. Curative rates are excellent for primary lesions (90%–95%). However, tumors that are very large, significantly invasive, exhibit aggressive histology, or were previously irradiated, are far less responsive to treatment [10]. Radiation as primary therapy is more frequently used on tumors in the HN because of the proximity of critical structures. Primary radiation therapy is also appropriate in patients who are not considered surgical candidates because of comorbidities. It is also used as an adjunct therapy when there are positive margins, bone invasion, and/or extensive perineural involvement.

A number of novel medical therapies are being developed based on molecular signaling pathways. One such targeted therapy is vismodegib, a hedgehog inhibitor [11]. The hedgehog inhibitors have demonstrated promising therapeutic responses and results in advanced BCC. The hedgehog inhibitors are approved bu the US Food and Drug Administration (FDA) for advanced or multiply recurrent basal cell carcinomas. They represent a new development that has significantly improved treatment of advanced, metastatic, and recurrent disease.

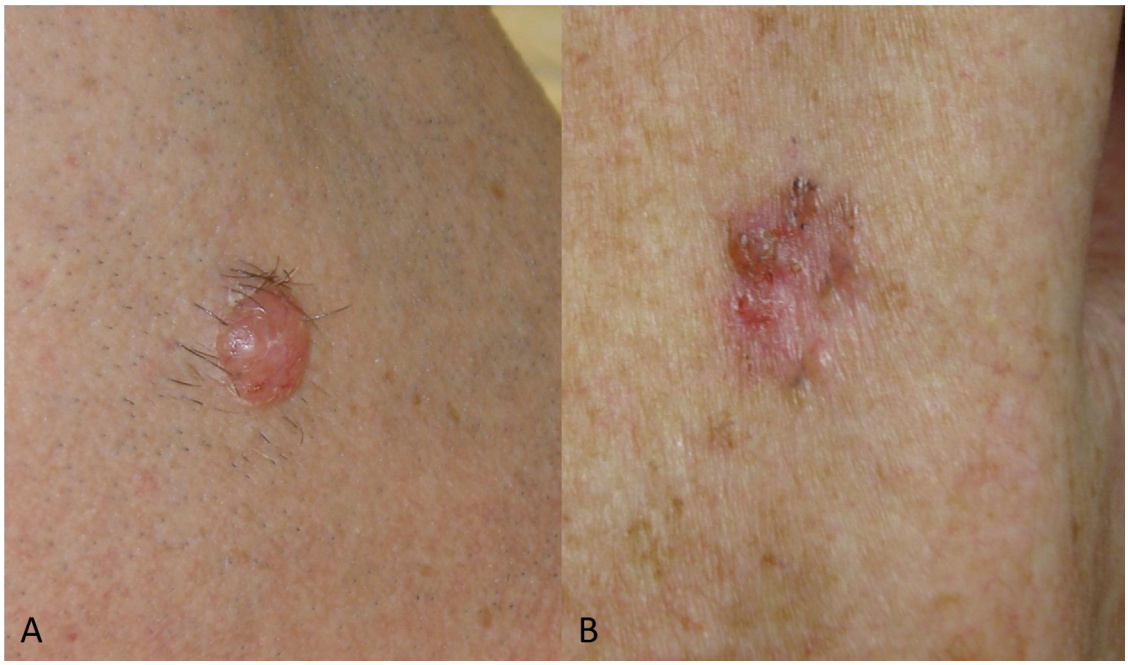

Fig. 1. Basal cell carcinoma (BCC). (A) Classic pearly papule with arborizing telangiectasia. (B) Sclerotic pink plaque with rolled borders.