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Perspective

Basal Cell Carcinoma and Its Treatment

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DESCRIPTION

More than 3.5 million skin cancers are diagnosed in more than two million Americans annually, making it the most common form of cancer in this country. Basal cell carcinoma (BCC) is the most common cancer in the United States with an estimated annual incidence of 0.5%. BCC is generally thought to affect men and women equally. Overall, the age-adjusted incidence of basal cell carcinoma per 100,000 persons was 25.9 for women and 20.9 for men; however, one analysis shows the incidence of BCC has increased significantly among women only. Compared to squamous cell carcinoma (SCC), BCC is more common on areas of only moderate exposure, e.g. upper trunk in men and women and lower legs in women. Yet, up to 85 percent of BCCs occur in the sun-exposed head and neck region. Several studies have illustrated the link between UV exposure and BCC to be weaker than the link between UV exposure and AK or squamous cell carcinoma.

Pathogenesis elucidating the pathogenesis of basal cell nevus syndrome (BCNS), also known as Gorlin's syndrome, has greatly enhanced our understanding of the pathogenesis of BCC. This genetic syndrome is inherited as an autosomal dominant trait and is typically expressed in young adulthood with patients presenting with multiple basal cell cancers. Mutation of the tumor suppressor gene PTCH, which is located on chromose 9 q22-q31, has been implicated in 40 to 80 percent off cases of BCNS mutations have now been implicated in both sporadic and hereditary forms of BCC.8 Although BCC is felt to originate from mutation of the basal epithelial cell, there is evidence to suggest that it may also originate from actinic keratoses (AKs), common dysplastic keratinocytic epidermal lesions caused by chronic ultraviolet light (UV) exposure.9 AKs primarily affect fair skinned, middle-aged people, and have a reported prevalence of up to 60 percent in individuals over 60 years of age.10 Historically, AK was classified as a pre-malignant lesion; in recent years it has been determined that AKs are part of a spectrum of disease progression, ranging from sun-damaged skin to squamous cell carcinoma in situ (SCC).11-13 Despite the common belief that AKs evolve only into SCC, in one large study, BCC was shown to evolve from lesions previously diagnosed as AK. There was a one year risk of evolution of 0.48% and a four year risk of 1.56% (compared to 0.60% and 2.57% for SCC, respectively).

KEY POINTS

Basal cell carcinoma (BCC) is the most common cancer in the US. PTCH gene mutations have now been implicated in both sporadic and hereditary forms of BCC. The PTCH gene functions as a transmembrane receptor for the sonic hedgehog protein (SHH) (which normally acts to inhibit another transmembrane protein Smoothened (SMO)), leading to aberrant cell proliferation. BCC generally is a slowly progressing, locally invasive malignancy with a low rate of metastasis (0.0028 to 0.5%). Generalized dissemination of BCC is very rare cases of metastasis to the lymph nodes, lung, bone, and liver have been described. Some experts suggest current data may underestimate the incidence of metastatic BCC Most local BCCs are treated with surgical excision, though scarring, tissue loss, and pigmentation changes are possible. Other available treatments include destruction, photodynamic therapy (PDT), imiquimod cream, and 5-fluorouracil. Investigational agents for localized BCC include ingenol mebutate (PEP005) and celecoxib. Vismodegib (GDC-0449) has been submitted to the FDA for treatment of advanced BCC. Oral alpha-difluoromethylornithine (DFMO) is under investigation as a preventive agent.

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