Squamous Cell Carcinoma of the Hand in Solid Organ Transplant Patients

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Learning Objectives

- Discuss the prevalence of squamous cell carcinoma (SCC) of the hand in transplant patients.
- Describe the role of immunosuppression in the pathophysiology of SCC.
- Review operative treatment measures for SCC.
- Highlight the differences in SCC caused by ultraviolet exposure and organ transplant.
- Assess preventive measures and the importance of early detection of SCC in transplant patients.

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BACKGROUND

As hand surgeons, it is important to know about the high risk of squamous cell carcinoma (SCC) in the upper extremity of solid organ transplant recipients. Skin cancer is overwhelmingly the most common malignancy in transplant recipients; SCC is the most prevalent. In 2011, 17,671 kidney transplants were performed in the United States, adding to the 181,469 Americans currently living with kidney transplants.[1] As long-term survival with solid organ transplantation increases, diseases related to transplants have become more prevalent. Cancer is the third leading cause of death in organ transplant recipients, accounting for 9.8% of mortality, behind only cardiovascular disease and infection, respectively.[1]

In developed countries, up to 70% of patients will present with a nonmelanoma skin cancer by 20 years

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posttransplantation, most of which is SCC.[2,3] Transplanted patients have a 65 to 200 times greater risk of developing SCC and a 10 times increased risk of developing basal cell carcinoma compared with the general population.[2] Ultraviolet (UV) radiation is the leading cause of all skin cancers; 90% occur in sun-exposed areas.[4] The dorsum of the hand and head are the 2 most common sites of SCC.[3,5,6] In patients younger than 40 years of age at the time of transplant, 80% of SCC lesions occur on the dorsum of the hand, forearms, and upper trunk.[3]

Squamous cell carcinoma in kidney and other organ transplant recipients is more aggressive than in nonimmunocompromised patients. These tumors grow more rapidly, are often characterized by multiple lesions, and have a high rate of local recurrence and a greater tendency to be invasive and metastatic. Local recurrence is 13.4% within 6 months of excision and metastases occur in 5% to 8% of patients.[3] Because of the more aggressive nature of SCC in these patients, close surveillance by dermatologists is recommended.

Studies have shown a bimodal distribution of relative risk based on the patients' age at the time of transplant. Patients who are 50 of age or older have a steady increase in the rate of SCC, with a peak incidence occurring 6 to 8 years posttransplant. Younger patients have an initial lower risk of SCC, which peaks 10 to 12 years posttransplant.[5] One theory for this bimodal distribution is that in older patients, the initial increase in cancer rates represents preexisting malignant cells that can proliferate in a now immunosuppressed patient, whereas in the younger patients, new malignancy develops after immunosuppression.[5]

Ultraviolet radiation has long been accepted as the leading cause of SCC. Ultraviolet rays cause mutations in DNA directly, both by induction of mutations in tumor suppressor genes such as p53 and by release of immunosuppressive mediators (interleukin [IL]-1, IL-4, IL-6, and IL-10), thereby initiating, promoting, and sustaining skin cancer.[4] Conventional risk factors for skin cancer include history of skin cancer or actinic keratosis, fair skin, advanced age, male sex, sun exposure, previous sunburns, and genetic predisposition.[7] The development of SCC in kidney transplant recipients is multifactorial because of the induced immunosuppression needed to prevent organ rejection. In addition to preventing organ rejection, these drugs decrease the body's immunosurveillance. Patients requiring higher levels of immunosuppressive agents have a greater risk of developing skin cancer.[4] Certain immunosuppressive drugs have been associated with a higher risk of developing SCC posttransplant than other medications, which may be accounted for by their differing mechanisms of action, such as sensitizing DNA to the effects of UV radiation or suppressing the antitumor immune response.[5] Opportunistic viral infections, such as oncogenic human papillomavirus may also contribute co-carcinogenic factors by encoding DNA sequences that immortalize epithelial cells.[8] Interestingly, recent literature has shown genetic evidence that SCCs in solid organ transplant patients may be derived from donor cells.[8]

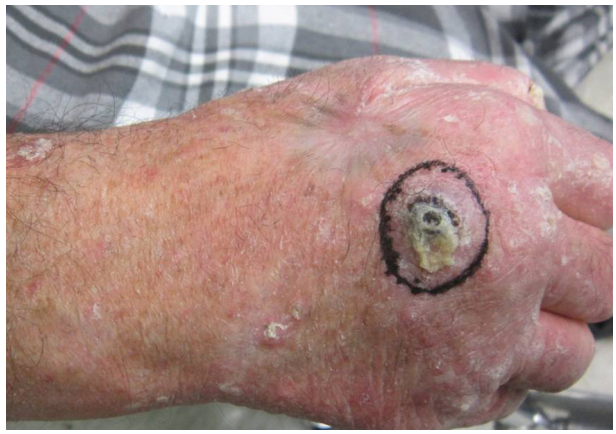

FIGURE 1: Characteristic squamous cell carcinoma lesion on the dorsum of the hand of a solid organ transplant recipient. (Figure courtesy of Joel Cohen, MD, AboutSkin Dermatology and DermSurgery, Denver, CO.)

TREATMENT

Squamous cell carcinoma is classically a papulosquamous tumor with a rounded, erythematous, thickened appearance, with scales and ill-defined margins (Fig. 1). Lesions frequently have ulcerations, plaques, and a tendency to bleed when hyperkeratotic scale is removed. These lesions may be asymptomatic but can be painful or pruritic. Local neurologic symptoms, including paresthesia, pain, dysesthesia, burning, or stinging, are present in one third of patients with perineural invasion. History of change in size or appearance, rate of growth, tendency to bleed, and previous treatments can help make the diagnosis. Biopsy is used to confirm the diagnosis of SCC, providing information regarding perineural invasion, tumor differentiation, and tumor depth, which is needed for staging.[9]

Total surgical excision with wide margins (Fig. 2) is the recommended treatment for these lesions in the general population. There are multiple published margin guidelines as low as 4 mm and as high as 20 mm,[2,10–12] based on the aggressiveness of the tumor (Table 1). A recent consensus recommended excision

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