

High Risk SCC: What Factors Predict Recurrence and Metastasis?

Data shed light on risk factors associated with aggressive SCC, allowing dermatologists to identify and properly follow high-risk patients.

The vast majority of immunocompetent patients who undergo excision of a cutaneous squamous cell carcinoma (SCC) are at low risk for recurrence or metastasis. In fact, the risk of *de novo* SCC is typically the more pressing concern for patients and dermatologists, thus prompting regular follow-up skin exams. However, dermatologists must be vigilant for the minority of patients at highest risk for recurrence or metastasis, as aggressive SCCs are associated with significant morbidity and/or death. A recent publication provides an update on risk factors for recurrence and metastasis.

SCC History and Subsequent NMSC

Patients with a history of SCC are known to have an increased risk for development of new primary non-melanoma skin cancers (NMSC). A publication from early last decade advocated regular follow-up of all patients who undergo excision of an SCC, with recommended minimum follow-up at three-month intervals during the first year and twice a year for at least three more years.¹ The study followed 101 SCC patients annually for five years. Within five years of treatment for an initial SCC, 30 percent of patients developed additional SCCs, and just over half (52 percent) developed other NMSCs. Roughly half of all other NMSCs developed within the first year of follow-up, and all of the identified new

NMSCs had been identified by the fourth year.

The study suggested that the risk of subsequent NMSC was highest among patients who initially presented with multiple SCCs, an SCC greater than 1cm in diameter, an SCC requiring

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more than one Mohs surgery layer to remove, or an SCC occurring on the scalp, ear, nose, or extremities.¹

Aggressive SCC Risk

The risk of subsequent NMSC is relatively well established, however, there remains some question regarding risk for aggressive SCCs. More than 20 years ago, a proposed method for histologic microstaging of SCCs identified tumor thickness and level of inva-

sion as primary indicators of risk for recurrence or metastasis.² In a series of 63 patients who underwent excision of SCCs of the trunk or extremities (researchers excluded SCCs at “high-risk” settings), 14 percent had either local recurrence or metastases, and eight percent (five patients) died due to SCC. All tumors that recurred were 4mm or thicker and involved the deep half of the dermis or deeper structures. Among the patients who died, tumors were at least 10mm in maximum thickness; four of these tumors were evaluated for invasion, which extended into subcutaneous tissue or deeper structures.

When researchers looked specifically at cutaneous SCC of the head and neck, they concluded that thick lesions (greater than 4-5mm) in proximity to the parotid gland present increased risk for metastatic lymph node disease.³ This study retrospectively analyzed 266 patients who developed SCC metastasis to lymph nodes (parotid and cervical) of the head and neck following treatment for primary SCC from 1980 to 2005. The majority of metastatic lymph nodes (61 percent) were located in the parotid with or without cervical lymph node involvement. Roughly two-thirds of initial tumors had measured 5mm or more in thickness, while 30 percent were 2cm or more in greatest dimension. Fifteen percent of patients had recurrent SCC.

Last year researchers calculated,

based on their own data combined with pooled data from past studies (total of 83 patients), an Odds Ratio of 2.76 of finding positive sentinel nodes with an increase in tumor size from less than 2cm to 2.1-3cm to greater than 3cm (95percent CI 1.2-6.5; $p=0.02$).⁴ In their study group, sentinel node-negative patients had no recurrences during follow-up (median 17 months); the lone node-positive patient developed recurrences.

While they encourage further studies to determine the “role, utility, and cost-effectiveness of SNLB for high-risk SCC, their investigation showed that negative node status was not associated with recurrence while the lone node-positive patient developed recurrence.

This summer a published analysis of data from 615 patients who underwent excision of SCC with complete histological examination of three-dimensional excision margins (3D-histology) affirmed that key prognostic indicators (multi-variate analysis) for metastasis were: increased tumor thickness, immunosuppression, localization at the ear, and increased horizontal size.⁵ The authors concluded, “the risk of local recurrence depended on increased tumor thickness, and desmoplasia.”

Median follow-up was 43 months, during which time four percent of patients ($n=26$) developed metastases, and three percent ($n=20$) developed local recurrence. No tumor measuring 2.0mm or less in thickness metastasized, while the rate of metastasis among tumors 2.1-6mm was four percent (12 of 318 tumors). The rate of metastasis among tumors greater than 6mm thick was 16 percent (14 of 90 tumors.)

Assessing Risk in Practice

Each dermatologist has his or her own threshold for suspicion as well as specific protocols for follow-up and care of patients who present with a primary

NMSC. While these may vary somewhat, most patients treated for a primary SCC or other NMSC should return for re-evaluation at least every three to six months during the first 12 months and at appropriate intervals over the next several months for a total duration of at least four to five years. Ideally, such patients will see the dermatologist for a full skin examination annually or semi-annually for their remaining lifetime. Factors such as history of melanoma or NMSC as well as immunosuppression warrant more frequent evaluations.

A minority of patients who present with a primary SCC have aggressive disease. These individuals require frequent and careful follow-up, and in some cases SLN biopsy may be indicated. Patients at high risk for recurrence or metastasis appear to be those with tumors 2mm or thicker, tumors 2cm or wider, histopathologic evidence of desmoplasia, and/or proximi-

ty to the parotid. While there are as yet no clear guidelines for the use of SLN biopsy and staging in patients with primary SCC, data confirm the prognostic value of SLN status for risk of recurrence. ■

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NEW In Your Practice

Uncomplicated cSSI Therapy. A novel antibiotic that may prove useful in the fight against MRSA may be closer to approval, with recently reported Phase 3 data confirming that ceftaroline monotherapy achieved its primary endpoint of non-inferiority versus the combination of vancomycin and aztreonam in the treatment of complicated skin and skin structure infections (cSSSI). According to Forest Laboratories, data presented at the 48th Annual Interscience Conference on Antimicrobial Agents and Chemotherapy / Infectious Diseases Society of America 46th Annual Meeting (ICAAC / IDSA) in Washington, DC show ceftaroline is effective in a variety of monomicrobial and polymicrobial infections including those with phenotypes. Ceftaroline-treated patients had a clinical cure rate of 91.1 percent compared to a vancomycin-plus-aztreonam clinical cure rate of 93.3 percent at the test of cure (TOC) visit in the clinically evaluable population.

For Men, Too? A new report finds that the HPV vaccine Gardasil (Merck) may help prevent genital warts in men. In the study, researchers evaluated 4,065 men between the ages of 16 and 26 who received three shots of Gardasil or placebo over six months. Results of the study, presented to the European Research Organization on Genital Infection and Neoplasia (EUROGIN), indicated that treated participants were 90 percent less likely to develop genital warts related to the four HPV strains that Gardasil targets. The FDA hasn't approved Gardasil for use in male patients, but Merck says it plans to file an application this year for an indication of boys and men aged nine to 26 to prevent genital warts.