Malignant Risk–Based SCC Classification Proposed

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MONTEREY, CALIF. — Cutaneous squamous cell carcinoma can take many forms, with vastly different biological behaviors and risk profiles.

Yet, "with relatively few exceptions, they have a tendency to simply be lumped by the nondermatologist clinician, the general surgeon, and the general pathologist," said Dr. Ronald Barr in calling for a comprehensive clinicopathologic classification of cutaneous SCC subtypes based on malignant potential.

Subtypes of SCC are not "histological curiosities," but distinct entities that offer important clues as to management and prognosis of individual patients, maintained Dr. Barr during a presentation to the annual meeting of the California Society of Dermatology and Dermatologic Surgery.

A system of histologic subtypes of SCC has been proposed by Dr. Barr, professor emeritus of dermatology and pathology at the University of California, Irvine, and his colleagues (J. Cutan. Pathol. 2006;33:191-206, 261-79). The suggested subtypes include low-risk SCCs, which carry a less than 3% risk of metastasis; intermediate-risk SCCs, which have a 3%-10% risk of metastasis; high-risk SCCs, with a greater than 10% risk of metastasis; and SCCs of indeterminate malignant potential, explained Dr. Barr.

These subtype categories would include:

► **Low-risk, invasive SCCs.** These would include SCCs arising in sun-damaged skin of elderly patients (95% of cases), verrucous carcinoma and other human papillomavirus–related SCCs in immunocompetent patients, spindle cell SCC (unrelated to radiation exposure), and trichilemmal carcinoma.

► **Intermediate-risk SCCs.** Suggested category inclusions are acantholytic SCC, lymphoepitheliomalike carcinoma of the skin (LELCS), intraepidermal epithelioma (IEE), and Borst-Jadassohn tumor with invasion.

► **High-risk SCCs.** This subtype category would include invasive Bowen's disease; desmoplastic SCCs; malignant proliferating pilar tumor/cyst; de novo SCC; adenosquamous cell carcinoma; and SCC arising in association with radiation, burn scars, chronic conditions, or immunosuppression.

► **SCCs of indeterminate malignant potential.** Proposed subtypes for this category include signet-ring and clear cell SCC; pigmented, papillary, and follicular SCC; SCC arising in adnexal cysts; and possibly keratoacanthoma.

Dr. Barr acknowledged that many of the tumors he categorized as intermediate- or high-risk are rare, and there have been few studies to accurately determine their malignant potential. However, this classification system would help to structure research by subtype and help to clarify future research by separating out entities that carry a higher risk potential than a superficially invasive, well-differentiated SCC arising within actinic keratoses on sun-damaged skin.

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In addition to histologic subtypes, he called for more pathologic reporting of prognostic factors in individual SCC cases including the grade of differentiation (Broders' grades I-IV), tumor size and depth of invasion, and presence or absence of perineural or hematolymphatic invasion.

Fewer than 35% of patients with metastatic SCC survive for 5 years, in stark contrast to the generally excellent prognosis of SCC. "When squamous cell carcinoma metastasizes, the literature just clumps [these cases]," but clearly, individual characteristics make a difference, he said.

With regard to depth of invasion, one study found that tumors less than 2 mm thick never metastasized, those 2 mm to 6 mm metastasized at a rate of 4.5%, and those deeper than 6 mm metastasized at a rate of 15% (Am. J. Clin. Pathol. 1990;94:624-7). Low- versus high-grade differentiation carries a highly variable rate of metastasis as well (33% vs. 9%), Dr. Barr said. Perineural invasion is associated with rates of metastasis between 35% and 80%. ■