Diagnostic concordance lacking in poorly differentiated SCC

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A recent study underscores the need for a consistent scale to grade risk levels of cutaneous squamous cell carcinoma (SCC), particularly poorly differentiated tumors, according to study authors who presented at the 2020 virtual American Society for Dermatologic Surgery (ASDS) meeting.

A recent study underscores the need for a consistent scale to grade risk levels of cutaneous squamous cell carcinoma (SCC), particularly poorly differentiated tumors, according to study authors.

"We believe the topic is incredibly important because right now, there are multiple grading scales for assessing risk for squamous cell carcinoma," says co-author James Prezzano, M.D. He is a third-year dermatology resident at the University of Rochester Medical Center in Rochester, New York.

Additionally, little literature examines inter-rater reliability among dermatopathologists in grading poorly differentiated tumors.

"We wanted to assess how reliable one dermatopathologist's poorly differentiated tumor was from another's," says Dr. Prezzano.

Investigators also wondered how Mohs surgeons compare in grading the differentiation of tumors. In clinical practice, Mohs surgeons sometimes receive partially sampled tumors, or patients with tumors labeled as SCC-invasive, with no differentiation assessment. Upon examination, surgeons may find an extremely poorly differentiated tumor.

"So the question is whether their assessment is accurate in terms of upstaging those potential patients," says Dr. Prezzano.

Investigators selected 131 slides of H&E, formalin-fixed cutaneous SCC as determined by a single dermatopathologist, with approximately one-third rated well, moderately or poorly differentiated, respectively. Then the samples were rated by two additional dermatopathologists and three Mohs surgeons in an independent, randomized and blinded manner. Investigators used the most commonly cited interpretation of Fleiss' kappa statistic to determine inter-rater concordance.

"We've shown that there is not very good correlation between different reviewers," says fellowship-trained Mohs surgeon, assistant professor of dermatology at the University of Rochester Medical Center, and senior author Sherrif Ibrahim, M.D. Reviewers were highly concordant in selecting well-differentiated SCCs.

"But it was very hard to distinguish between those that were moderately or poorly differentiated," he adds.

"Moderate concordance is not ideal when you're looking at a grading scale," says Dr. Prezzano.

In clinical practice, adds Dr. Ibrahim, moderate concordance could mean that a patient who actually has poorly differentiated histology might be understaged and undertreated, and vice versa.

Dr. Prezzano continues, "A better understanding of the concordance of different dermatopathologists is always important. Moving forward, efforts to standardize histological grading scales may assist in more consistent tumor staging. There is room for improvement in concordance. But as of now, there is no accepted, standardized histological grading scale."

Whereas both the American Joint Cancer Commission (AJCC) 7 and the Brigham and Women's Hospital systems classified poor differentiation as a high-risk factor for SCC, AJCC 8 does not.

"It was thought that since there is no standardized histological grading scale, poor differentiation is subjective," he says. "That's why it was dropped."

In two recent studies, the BWH grading scale more accurately predicted outcomes than did AJCC 8.

"So we believe that poor differentiation is important as a marker of high-risk disease," says Dr. Prezzano.

But this level of differentiation is difficult to classify, he notes. While other features used to measure SCC risk levels — such as size and depth — are more objective, the poorly differentiated category relies on subjective interpretation of factors such as low keratinization, pleomorphic cells and disorganized architecture.

"If a tumor has all those elements," says Dr. Prezzano, "most raters would grade it as poorly differentiated."

However, he says, the most difficult challenges arise when tumors have some but not all of these features, or if only part of a tumor displays poor differentiation.

Disclosures: Drs. Ibrahim and Prezzano report no relevant financial interests.

References:
James Prezzano MD, Sherrif Ibrahim MD. "[Making the Grade: Squamous Cell Carcinoma Histological Concordance amongst Dermatopathologists and Mohs Micrographic Surgeons]," American Society for Dermatologic Surgery Virtual Annual Meeting. October 10, 2020.