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EDITORIAL

# Ocular surface squamous neoplasia: terminology that is conceptually friendly but clinically perilous

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In 2000, Powsner *et al*[1] reported the results of an open-book examination that analyzed the comprehension of written surgical pathology reports by clinicians. They found that surgeons misunderstood reports 30% of the time, and that many discordant interpretations involved major findings. Although little empirical literature had existed on the subject, the results were not entirely unexpected given past problems in communicating the results of cervical cytology and other types of diagnostic biopsies.[2–4] Multiple factors likely contribute to this communication gap, including the diverse backgrounds that many clinicians have in surgical pathology. The use of ambiguous terminology may also lead to miscommunication in pathology reports. We receive requests from surgeons to clarify pathology reports that were produced elsewhere because the diagnosis ocular surface squamous neoplasia (OSSN) leaves them confused. Most queries revolve around whether OSSN refers to *in situ* disease or squamous cell carcinoma, questions that we are unable to answer in any given case without reviewing the slides directly. We take the position that the diagnosis of OSSN serves no purpose in routine surgical pathology, and can result in mismanagement when the distinction of premalignant squamous epithelial dysplasia (including carcinoma *in situ*) from squamous cell carcinoma is considered clinically relevant.

The phrase OSSN was coined by Lee and Hirst[5] in 1995 to describe the continuum of mild epithelial dysplasia to squamous cell carcinoma. In clinical studies of OSSN, lesions that fall along this continuum of severity are moderately positively correlated with important clinical outcomes (eg, rates of recurrence, regional metastasis, and so on), but the associations have not been consistently demonstrable.[5–7] This lack of consistency may be due to the fact that biopsy interferes with the natural history of the disease process. This model of neoplastic progression, however, is biologically plausible and conveys sufficiently well the multistep process of cancer development. As a pedagogical tool OSSN can be useful, but the term has no role in diagnostic pathology.

According to current usage, OSSN can refer to premalignant disease, to squamous cell carcinoma, or to both conditions. It does not provide clinicians with as much information that would be available to them through traditional vocabulary that subdivides epithelial dysplasia by severity, and identifies cancer, with its potential to metastasize, as the distinct entity of squamous cell carcinoma. When OSSN is reported along with other overlapping (and traditional) histopathologic diagnoses, it may have less elucidating effects than anticipated. When studied in a standardized manner, the addition of histological descriptions to general pathology reports appear to diminish the comprehension of surgeons rather than improve it.[1]

The American Joint Committee on Cancer (AJCC) Cancer Staging Manual, seventh edition, recognizes squamous cell carcinoma of the conjunctiva and two histologic variants (mucoepidermoid carcinoma and spindle cell carcinoma).[8] Conjunctival intraepithelial neoplasia (CIN), which embraces the range of keratinocyte dysplasias through *in situ* squamous cell carcinoma, is designated Tis, according the TNM system. This portion of the neoplastic spectrum is precancerous having no metastatic potential as dysplastic keratinocytes lack access to lymphatic and vascular channels. It is assigned stage 0 according to AJCC guidelines.[8] (see p6) Primary conjunctival squamous

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cell carcinoma tumor (T) stages are also stratified by increasingly larger size and degree of invasive growth (Table 1). The term OSSN is not used in the AJCC manual.

Misunderstandings attributed to OSSN from pathology reports are difficult if not impossible to measure, but can be inferred from the confusion related to the phrase in the area of clinical research. Take, for example, a recent clinical series of 75 patients with clinically suspicious OSSN.[9] Thirty-three patients had histologically confirmed 'malignant OSSN' and 22 had benign or premalignant OSSN.[9] Upon inspection of the methodology, the distinction between malignant OSSN (supposedly squamous cell carcinoma) and premalignant OSSN was not invasive carcinoma and *in situ* disease but rather the transition between moderate dysplasia and severe dysplasia.[9] This redefinition of cancer is lost in the term malignant OSSN, which discards over 80 years of evidence that supports intraepithelial neoplasia as a premalignant stage of development when cells do not have the capacity to metastasize.[10]

Another illustration is offered to emphasize how OSSN terminology undermines, if not invalidates, potentially important clinical research by contributing to serious errors in tumor staging. A major study of 389 patients with conjunctival intraepithelial squamous neoplasia and squamous cell carcinoma treated by excisional biopsy refers to both conditions as OSSN;[11] it also describes these lesions in traditional histopathologic terms.[11] The purpose of the study (and one of the largest published series to date) was to identify predictors of recurrence after treatment. These 389 patients were selected from 612 consecutively diagnosed cases of OSSN occurring over nearly a 10-year period.[12] The clinical and histopathologic features of this larger cohort of cases were published as a companion article the month before.[12] The primary cohort of 612 patients included 69 cases of squamous cell carcinoma (11.6%) and 527 cases of intraepithelial squamous neoplasia (mild, moderate, and severe dysplasia, and carcinoma *in situ*).[12] Sixteen cases (2.6%) were judged indeterminate histologically and excluded. In the analytical study of 386 patients who underwent excisional biopsy, however, the authors reported 377 patients with squamous cell carcinoma, which were broken down according to AJCC classification into three cancer tumor (T) stages: T1 = 201; T2 = 140; and T3 = 36.[11] The data from these two papers are inconsistent with one another. Three hundred and seventy-seven cases of squamous cell carcinoma reported in the excisional biopsy study cannot be derived from a primary cohort in which only 69 cases existed originally. We suspect whether the authors and the persons who reviewed the study before publication had not been befuddled by the term OSSN, a misclassification error of this magnitude would never have occurred. If such a gross error in classification of OSSN can go undetected by experts in the field of ocular oncology, imagine how this medical argot might baffle less experienced clinicians.[13]

We recommend the term OSSN be avoided in surgical pathology reports and that the stage of conjunctival neoplasia be described in terms that minimize the potential for misinterpretation. For premalignant conjunctival dysplasia this would include mild, moderate, and severe dysplasia, and carcinoma *in situ*. The diagnosis of squamous cell carcinoma is applicable once cells have breached the epithelial basement

**Table 1** Carcinoma of conjunctiva primary tumor (T) stage[a]

| *Designation* | *Description* | *Comment* |
|---|---|---|
| TX | Primary tumor cannot be assessed | |
| T0 | No evidence of primary tumor | |
| Tis | Carcinoma *in situ* | Would include lesser degrees of dysplasia collectively referred to as conjunctival intraepithelial squamous neoplasia |
| T1 | Squamous cell carcinoma 5 mm or less in greatest dimensions | T1 stage and beyond represent invasive cancer |
| T2 | Squamous cell carcinoma >5 mm in greatest dimension, without invasion of adjacent structures | Excludes carcinomas that invade cornea, eye, forniceal conjunctiva, tarsus, lacrimal punctum, canaliculi, plica, caruncle, anterior or posterior eyelid lamella, or eyelid margin |
| T3 | Squamous cell carcinoma invades adjacent structures but not orbit | Includes involvement of adjacent structures excluded in T2 |
| T4 | Squamous cell carcinoma invades orbit with or without further extension | |
| T4a | Squamous cell carcinoma invades bone | |
| T4c | Squamous cell carcinoma invades paranasal sinuses | |
| T4d | Squamous cell carcinoma invades brain | |

[a] Modified from AJCC Cancer Staging Manual.[8]

membrane, invading the substantia propria.
The complete microscopic description of squamous cell carcinoma of the conjunctiva should follow the guidelines outlined by the *ad hoc* committee of the Association of Directors of Anatomic and Surgery Pathology.[14]

## Conflict of interest

The authors declare no conflict of interest.

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