Back to basics : Hematoxylin and eosin staining is the principal tool for histopathological risk assessment of oral cancer

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Letter to the editor

Back to basics: Hematoxylin and eosin staining is the principal tool for histopathological risk assessment of oral cancer

Despite the discovery of several biomarkers that have been introduced for risk assessment of oral squamous cell carcinoma (OSCC) [1], daily practice still depends on morphological assessment of histopathologic parameters/prognosticators. Parameters that are identified using routine hematoxylin and eosin (HE) staining include, for example, depth of invasion, perineural and lymphovascular invasion among others. Of note, in the recent issue (December 2020) of *Oral Oncology*, two interesting studies [2,3] focused on such prognosticators and confirmed their clinical significance and underlined some important methodological considerations such as the optimal cutoff point for risk stratification based on depth of invasion. Also in mind, the traditional WHO grading system which is routinely included in pathology reports is evaluated using HE staining and is the cornerstone for histopathologic classification of OSCC [4]. Moreover, the eighth edition of the American Joint Committee on Cancer (AJCC 8) incorporated depth of invasion as a modifier of T stage, typically assessed using HE staining in daily practice. In addition, evidence from recent research has highlighted many other promising prognosticators that can be identified by HE staining. Such emerging histologic markers include tumor budding, tumor-stroma ratio and infiltrating lymphocytes, and all have been discussed in a recent article published in *Oral Oncology* [5]. Furthermore, cannibalistic activity presented as cell-in-cell invasion has also been evaluated using HE staining and it has shown a valuable risk stratification in many cancers including OSCC [6]. Again, the assessment of these newly introduced histopathologic markers of OSCC is cost-effective and can be easily included in pathology reports. In addition, the above-mentioned markers reveal tumor-related features (e.g. tumor budding reveals tumor dissociation and active invasion) and also stroma-related features (e.g. estimation of lymphocytes reveals the status of stromal immune response).

It is well documented that deeper invasion of OSCC tumors is associated with worse survival compared with superficial invasion. In a recent attempt to recognize the optimal cutoff point for the depth of invasion in early OSCC, van Lanschot et al. [2] recommended elective neck dissection for tumors with invasion depth of 4 mm or more. In another recent study, Noorlag et al. [7] reported that intraoral ultrasound can be used accurately in cases with depth up to 10 mm; and magnetic resonance imaging was a better tool for tumors more than 10 mm in depth. Such assessment of depth using preoperative imaging tools can guide clinicians during treatment planning and therefore require further confirmatory studies.

Lymphatic and vascular invasion of OSCC were recently confirmed by Spoerl et al. [3] as promising prognosticators in a large population-based cohort. Similarly, multifocal perineural invasion showed a promising value in risk assessment of OSCC in a recent study [8]. Invasion of cancer cells in vital structures such as lymphatic vessels, blood vessels and nerves is associated with worse survival in many other cancers as well. Indeed, the possibility of assessing such invasion using HE staining is well documented and therefore it is ready for routine assessment in daily practice.

HE is the gold standard in histopathologic diagnosis of solid tumors including the OSCC. As a routine staining, it has many advantages (including easy and simple protocol, cheap costs and fast processing) that makes it the staining of choice for risk assessment. Notably, recent research efforts have successfully used machine learning techniques for automated microscopic image analysis of some markers and this can assist in reducing variability among pathologists during the evaluation of HE-related markers (e.g. estimation of the infiltrating lymphocytes [9]). In addition, machine learning was used recently to analyze clinicopathologic data allowing clinicians to consider all markers together in risk stratification by a web-based tool [10]. Altogether, existing recent literature strongly supports the utility of conventional HE staining in prognostication of OSCC helping in decision making and treatment planning. For those histologic prognosticators that are not yet established in daily practice of OSCC (e.g. tumor budding and stroma ratio), it is necessary to consider multi-institutional studies and prospective studies. Indeed, that will warrant collaborative efforts. We support such initiatives and recommend to benefit from experience gained in studies [11] that established tumor budding for daily practice of colorectal cancer.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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