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EDITORIAL

The importance of histological types for treatment and prognosis in laryngeal cancer

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The classification of neoplasms is an important matter, with correlation of a tumor's type with its biological behavior. To provide internationally acceptable criteria for the histological diagnosis of tumors, the World Health Organization (WHO) published an updated Pathology and Genetics of Head and Neck Tumours Classification of Tumours in 2005, which included tumors of the hypopharynx, larynx and trachea [1].

The histological classification is intended to facilitate the comparison of results and outcomes between various fields of oncology and should be useful to pathologists, laryngologists, radiotherapists and oncologists, as well as to epidemiologists. A histological classification of neoplasms is extremely important for a reliable prognosis to be established and it provides the basis for clinical management of patients. The histologic or morphologic cell type provides a critical *qualitative* assessment of the biologic aggressiveness of the tumor whereas the extent of disease represents an important *quantitative* assessment [2]. Approximately 85 to 90 % of malignant neoplasms of the larynx are squamous cell carcinomas, but other tumor types must be distinguished pathologically from the more commonly encountered squamous carcinoma. Different phenotypes have different biological behavior, so only phenotypically similar tumors should be compared for their prognostic implications.

The revised histological WHO classification is more comprehensive than the two previous classifications [3, 4] and, like the previous editions, it is based on the histological features of lesions as seen by conventional light microscopy. However, ancillary techniques, such as immunohistochemistry and electron microscopy and molecular techniques have proved helpful in further

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clarifying diagnoses. Immunohistochemistry and electronic microscopy are valuable adjuncts in the diagnosis of neuroendocrine neoplasms. Detection by in situ hybridization of HPV DNA integration in the neoplastic genome of a small subset of laryngeal squamous cell carcinomas has become a key indicator of better prognosis, as compared with the much more common group of tobacco smoking and alcohol drinking related squamous cell carcinomas, which show frequent disruptive mutations of the TP53 gene and have a more aggressive course [5, 6].

Molecular studies aid in classification of inflammatory myofibroblastic tumor, as an example, with the identification of anaplastic lymphoma kinase (ALK-1) (on chromosome 2p23), even though not all laboratories perform these techniques routinely [7]. Nuclear Protein in Testis (NUT) midline carcinoma is a recently described aggressive carcinoma that mainly involves the head and neck (including the larynx), characteristically associated with chromosomal rearrangement of NUT gene [8], giving rise to the translocation (15, 19).

There are still a few neoplasms which have been described but are not included in the current classification, such as large cell neuroendocrine carcinoma [9–12] and alveolar soft part sarcoma, [13–16] among others. In the most recent WHO classification, large cell neuroendocrine carcinoma was technically grouped with atypical carcinoid, a situation that was specifically addressed as follows: "some atypical carcinoids may fulfill the diagnostic criteria of large cell neuroendocrine carcinoma of lung," but then they were not specifically separated out as a distinct entity. Their biological behavior is similar to small cell neuroendocrine carcinoma [9, 12, 17] and so it is our position that large cell neuroendocrine carcinoma should be considered distinct from moderately differentiated neuroendocrine carcinoma (atypical carcinoid) and, specifically, should be considered a high grade neoplasm [17]. Mucoepidermoid carcinoma has to be mainly distinguished from adenosquamous carcinoma, the latter having a more aggressive course [18].

Specific histological types are associated with different prognoses and survival rates: for e.g., small cell neuroendocrine carcinoma metastasizes more frequently than conventional squamous cell carcinoma; and conventional squamous cell carcinoma has a more aggressive behavior than verrucous squamous cell carcinoma. However, hybrid verrucous cell carcinoma follows a similar aggressive course as conventional squamous cell carcinoma [19]. Likewise, there are different responses by each tumor type to different treatment modalities. Each tumor has its own unique intrinsic aggressiveness related to and driven by specific environment and inherent molecular alterations. The 5-year survival rates for verrucous squamous cell carcinoma are 95 %, but decrease to 80 % for mucoepidermoid carcinoma, 48 % for typical carcinoid, 20 % for melanoma, and 5 % for small cell neuroendocrine carcinoma of the larynx, taking into consideration matched stages for these tumor types [20]. The exact identification of the type of cancer enables clinicians to plan specific and individual tumor staging (tumor staging evaluation in verrucous squamous cell carcinoma is not the same as in small cell neuroendocrine carcinoma) and treatments for the specific tumor.

In conclusion, first there must be an accurate morphological classification of a neoplasm before effective therapy can be implemented, taking into consideration different responsiveness and outcomes for each therapeutic modality. At present, the histological subtype combined with tumor stage should be considered the "gold standard" for determining appropriate treatment. Other factors such as: the presence of another malignancy, comorbidities, environmental aspects, and previous treatment can then be added to the management decisions.

Conflict of interest None

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