Adv Ther (2019) 36:1511–1517
https://doi.org/10.1007/s12325-019-00978-7

REVIEW

Some Considerations on the WHO Histological Classification of Laryngeal Neoplasms

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Received: April 9, 2019 / Published online: May 22, 2019

ABSTRACT

A new edition of the World Health Organization (WHO) Histological classification of tumours of the hypopharynx, larynx, trachea and parapharyngeal space was published in 2017. We have considered this classification regarding laryngeal neoplasms and discuss the grounds for said revision. Many of the laryngeal neoplasms described in the literature and in the previous WHO edition from 2005 have been omitted from this current revision. Many are described elsewhere in the book but it may give the new generation of pathologists/surgeons/oncologists the false impression that these tumour entities do not exist in the larynx.

Keywords: Classification; Larynx; Oncology; Tumour; WHO; World Health Organization

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INTRODUCTION

While the crafting of a taxonomy scheme for laryngeal tumours might not seem to be so critical an endeavour, a well-constructed classification scheme actually serves as an essential foundation, allowing surgeons, pathologists and oncologists to use the same language for clarity and precision. As such, the classification of tumours is of considerable importance, and many attempts have been made to correlate the type of neoplasm with its biological behaviour. There are clinical, topographical and staging classifications and those based on the histological features of the individual neoplasms. The internationally applied TNM staging system is based on the anatomical extent of the respective tumours, but the histological features have been largely omitted. Early classifications were incomplete and too simple, only including a few types of malignant tumours, such as squamous cell carcinoma, undifferentiated carcinoma, adenocarcinoma and sarcomas.

Histological classification of laryngeal neoplasms is of essential relevance to treatment planning and evaluation of prognosis but the frequently changing terminology may lead to misunderstandings and even mistakes.

The earliest tumour classification schemes relied upon the gross and/or light microscopic features of different tumour types. Presently, those classic gross and light microscopic differentiating features are being supplemented, or even replaced, by molecular features of the tumours themselves [1, 2].

In an early attempt at standardizing the nomenclature of laryngeal tumours, the World Health Organization (WHO) published its Histological Typing of Upper Respiratory Tract Tumours (which included the larynx) in 1978 [3]. This classification was the result of a team effort by Drs. Shanmugaratnam and Sobin and pathologists from eight countries. The first version of this WHO classification is summarized in Table 1.

The WHO classification of upper respiratory tract and ear tumours [3] was reviewed by the following experts:

K. Shanmugaratnam (Singapore), L. H. Sobin (USA), L. Barnes (USA), A. Cardesa (Spain), A. Ferlito (Italy), I. Friedmann (England), D. K. Heffner (USA), H.B. Hellquist (Sweden), V. J. Hyams (USA), G.R.F. Krueger (Germany), C. Micheau (France) and A. Nascimento (Brazil). Several of these experts met in Dublin in 1988 and an amply illustrated, revised and updated second edition of the classification was published in 1991 [4] (Table 2).

In 2005 a third updated edition of the WHO Classification of Tumours was published, entitled Pathology and Genetics of Head and Neck Tumours [5]. The larynx was included within Chapter 3 and was entitled "Hypopharynx, larynx and trachea" containing the following sections (Table 3).

A 4th edition WHO Classification of Tumours, entitled Pathology and Genetics of Head and Neck Tumours, was published in 2017 [6]. The larynx was also included in Chapter 3, now entitled "Tumours of the hypopharynx, larynx, trachea and parapharyngeal space" (Table 4).

Table 1 Histological typing of laryngeal tumours (1978)

Epithelial tumours
Benign
Squamous cell papilloma/papillomatosis
Oxyphilic adenoma (oncocytoma)
Others
Malignant
Carcinoma in situ (intraepithelial carcinoma)
Squamous cell carcinoma
Verrucous (squamous) carcinoma
Spindle cell (squamous) carcinoma
Adenocarcinoma
Adenoid cystic carcinoma
Carcinoid tumour
Others
Undifferentiated carcinoma
Soft tissue tumours
Benign
Lipoma
Haemangioma
Leiomyoma
Rhabdomyoma
Granular cell tumour
Neurofibroma
Neurilemmoma (schwannoma)
Paraganglioma (chemodectoma)
Others
Malignant
Fibrosarcoma
Rhabdomyosarcoma
Angiosarcoma
Kaposi's sarcoma
Others

Table 1 continued

Tumours of bone and cartilage
Benign
Chondroma
Others
Malignant
Chondrosarcoma
Others
Tumours of lymphoid and haemopoietic tissues
Miscellaneous tumours
Secondary tumours
Unclassified tumours

Compliance with Ethics Guidelines

This article is based on the previously published WHO histological classifications and so does not involve any new studies of human or animal subjects performed by any of the authors.

CONSIDERATIONS

The application of immunohistochemical methods, with an ever-increasing arsenal of antibodies and recently developed molecular biology techniques, will obviously enable a more accurate identification and therefore a more reliable classification of neoplasms of the larynx. In the latest 2017 WHO Classification of Head and Neck Tumours [6], many of the laryngeal neoplasms described in the literature have been omitted. For example, only three salivary gland tumours are described, and acinic cell, salivary duct and myoepithelial carcinomas were not included. Similarly, unusual and rare tumours, such as NUT (nuclear protein in testis) midline carcinoma, synovial sarcoma, alveolar soft sarcoma and intestinal-type adenocarcinoma, are also not listed [7]. Therefore, one has to refer to the earlier versions of the WHO Classification (2nd edition 1991 and 3rd edition

Table 2 Histological typing of laryngeal tumours (1991)

Epithelial tumours and precancerous lesions
Benign
Papilloma
Papillomatosis
Pleomorphic adenoma[a]
Basal cell (basaloid) adenoma[a]
Dysplasia and carcinoma in situ
Squamous cell dysplasia
Mild dysplasia
Moderate dysplasia
Severe dysplasia
Carcinoma in situ
Malignant
Squamous cell carcinoma
Verrucous squamous cell carcinoma
Spindle cell carcinoma
Adenoid squamous cell carcinoma[a]
Basaloid squamous cell carcinoma[a]
Adenocarcinoma
Acinic cell carcinoma[a]
Mucoepidermoid carcinoma[a]
Adenoid cystic carcinoma
Carcinoma in pleomorphic adenoma[a]
Epithelial-myoepithelial carcinoma[a]
Clear cell carcinoma[a]
Adenosquamous carcinoma[a]
Giant cell carcinoma[a]
Salivary duct carcinoma[a]
Carcinoid tumour
Atypical carcinoid tumour[a]
Small cell carcinoma[a]
Lymphoepithelial carcinoma[a]

Table 2 continued

Soft tissue tumours
Benign
Aggressive fibromatosis[a]
Myxoma[a]
Fibrous histiocytoma[a]
Lipoma
Leiomyoma
Rhabdomyoma
Haemangioma
Haemangiopericytoma[a]
Lymphangioma[a]
Neurilemmoma
Neurofibroma
Granular cell tumour
Paraganglioma
Malignant
Fibrosarcoma
Malignant fibrous histiocytoma[a]
Liposarcoma[a]
Leiomyosarcoma[a]
Rhabdomyosarcoma
Angiosarcoma
Kaposi's sarcoma
Malignant haemangiopericytoma[a]
Malignant nerve sheath tumour[a]
Alveolar soft part sarcoma[a]
Synovial sarcoma[a]
Ewing sarcoma[a]
Tumours of bone and cartilage
Benign
Chondroma
Malignant
Chondrosarcoma
Osteosarcoma[a]
Malignant lymphomas
Miscellaneous tumours
Benign
Mature teratoma[a]
Malignant
Malignant melanoma[a]
Malignant germ cell tumours[a]
Secondary tumours
Unclassified tumours

[a] Oncotypes new to the second edition

2005) to obtain a comprehensive view of the neoplasms that have been described in the larynx.

The histological classification is intended to facilitate the comparison of results in various fields of oncology and should be useful to pathologists, laryngologists, radiotherapists and oncologists as well as epidemiologists. A histological classification of neoplasms is extremely important for establishing a reliable prognosis, and this classification forms the foundation for appropriate clinical management of patients with laryngeal tumours.

Establishing the phenotype gives us a qualitative diagnosis of the disease. Different phenotypes have different biological behaviours, so only similar histopathological tumour types should be compared for their prognostic implications.

Specific histological types also give an indication of potential prognostic features. For example, small cell neuroendocrine carcinoma metastasizes more frequently than squamous cell carcinoma, which is in turn more aggressive than verrucous squamous cell carcinoma. These differences are further evidenced by the differing survival rates. The 5-year survival rates are approximately 68% for squamous cell carcinoma of the larynx [8] and 5% for small

Table 3 Histological typing of laryngeal tumours (2005)

Malignant epithelial tumours
Squamous cell carcinoma
Verrucous carcinoma
Basaloid squamous cell carcinoma
Papillary squamous cell carcinoma
Spindle cell carcinoma
Acantholytic squamous cell carcinoma
Adenosquamous carcinoma
Lymphoepithelial carcinoma
Giant cell carcinoma
Malignant salivary gland-type tumours
Neuroendocrine tumours
Carcinoid
Atypical carcinoid
Small cell carcinoma, neuroendocrine type
Combines small cell carcinoma, neuroendocrine type, with non-small cell carcinoma (squamous cell carcinoma, adenocarcinoma, etc.)
Paraganglioma
Epithelial precursor lesions
Benign epithelial tumours
Papilloma/papillomatosis
Benign salivary gland-type tumours
Malignant soft tissue tumours
Fibrosarcoma
Malignant fibrous histiocytoma (MFH)
Liposarcoma
Leomyosarcoma
Rhabdomyosarcoma
Kaposi's sarcoma
Peripheral nerve sheath tumour (PNST)
Synovial sarcoma
Inflammatory myofibroblastic tumour
Benign soft tissue tumours
Lipoma
Leyomyoma
Haemangioma and lymphangioma
Granular cell tumour
Haematolymphoid tumours
Non-Hodgkin lymphoma
Plasmacytoma
Tumours of bone and cartilage
Chondrosarcoma
Osteosarcoma
Chondroma
Giant cell tumour
Mucosal malignant melanoma
Secondary tumours

cell neuroendocrine carcinoma [9], considering all stages of the disease. Taking squamous cell carcinoma as a yardstick for comparison, verrucous squamous cell carcinoma, low-grade mucoepidermoid carcinoma, well-differentiated neuroendocrine carcinoma and chondrosarcoma all have a more favourable prognosis, whereas poorly differentiated neuroendocrine carcinoma (both small and large cell neuroendocrine carcinoma), moderately differentiated neuroendocrine carcinoma, NUT midline carcinoma and basaloid squamous carcinoma are likely to have a less favourable outcome.

If the histological type is properly identified, then specific and personalized tumour treatment protocols can be implemented. The phenotype should therefore be considered the most important factor in determining therapeutic decisions [10, 11]. In conclusion, confirming both the histological diagnosis and clinical characteristics of every tumour will form the basis for accurate, personalized and effective treatment planning.

Table 4 Histological typing of laryngeal tumours (2017)

Malignant surface epithelial tumours
Conventional squamous cell carcinoma
Verrucous squamous cell carcinoma
Basaloid squamous cell carcinoma
Papillary squamous cell carcinoma
Spindle cell squamous cell carcinoma
Adenosquamous carcinoma
Lymphoepithelial carcinoma
Precursor lesions
Dysplasia, low grade
Dysplasia, high grade
Squamous cell papilloma
Squamous cell papillomatosis
Neuroendocrine tumours
Well-differentiated neuroendocrine carcinoma
Moderately differentiated neuroendocrine carcinoma
Poorly differentiated neuroendocrine carcinoma
Small cell neuroendocrine carcinoma
Large cell neuroendocrine carcinoma
Salivary gland tumours
Adenoid cystic carcinoma
Pleomorphic adenoma
Oncocytic papillary cystadenoma
Soft tissue tumours
Granular cell tumour
Liposarcoma
Inflammatory myofibroblastic tumour
Cartilage tumours
Chondroma
Chondrosarcoma
Chondrosarcoma grade 1
Chondrosarcoma grade 2/3
Haematolymphoid tumours

ACKNOWLEDGEMENTS

Funding. No funding or sponsorship was received for this study or publication of this article.

Authorship. All named authors meet the International Committee of Medical Journal Editors (ICMJE) criteria for authorship for this manuscript, take responsibility for the integrity of the work as a whole and have given final approval for the version to be published.

Disclosures. Alfio Ferlito, Kenneth O. Devaney, Jennifer L. Hunt and Henrik Hellquist have nothing to disclose.

Compliance with Ethics Guidelines. This article is based on the previously published WHO histological classifications and so does not involve any new studies of human or animal subjects performed by any of the authors.

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