Current role of human papillomavirus in head and neck oncology

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Tobacco and alcohol were, until recently, considered to be the major risk factors in carcinogenesis of head and neck cancer (HNSCC). However, during the past decade a causal association between infection with human papillomavirus (HPV) and HNSCC has been established [1], and this 'new' aetiological factor has changed the conventional understanding of HNSCC because of the extensive influence of the virus on the epidemiology, clinical presentation and treatment outcome for patients with HNSCC.

Association with HPV is predominantly a matter of concern in tumours of the oropharynx, especially in tonsillar cancer [2,3], and a dramatic increase in the incidence of oropharyngeal cancer (OPC) has been reported in several Western countries over the past 30 years [4–8]. Based on the observations that, simultaneously, there has been an increase in the frequency of HPV-positivity among OPCs [4,9], infection with HPV seems to be the dominant cause of this development. Moreover, in the same time period a decrease in tobacco-smoking seems to be responsible for a reduction in the incidence of HNSCC outside the oropharynx [6], at least in Western countries. The natural history of oral HPV infection remains to be fully elucidated, and although the exact mechanism is not known, oral–genital contact is assumed to be the primary mode by which HPV is transmitted to the oral mucosa, and several case–control studies have shown an association between HPV-related HNSCC and sexual behaviour (reviewed by Gillison et al. [3]). The optimal method for detecting HPV in tumours is controversial, and both in-situ hybridisation and the polymerase chain reaction (PCR) are commonly used; p16-immunohistochemistry has gained broad acceptance as a surrogate marker and is also widely used in the clinical setting [10,11].

HPV-related HNSCC constitutes a clinically distinct subgroup of cancers in terms of molecular biology, patient characteristics and sensitivity to treatment, and this on the whole differentiates it markedly from HPV-negative tumours. The molecular profile of HPV-related HNSCC is distinct, with P53 degradation, retinoblastoma RB pathway inactivation and p16 up-regulation. By contrast, HPV-negative tumours are characterised by TP53 mutation and down-regulation of p16 [12,13]. Patients with HPV-related HNSCC tend to be younger, have less comorbidity and a better performance status [14–16], and are less declined to be abusers of tobacco and alcohol [6,15] compared with HPV-negative patients.

Tumour HPV status has a major impact on outcome for patients with HNSCC, and compared with HPV-negative patients, tumour-control and survival are highly significantly better for patients with HPV-positive tumours. This has been shown repeatedly in several clinical trials and with the use of a variety of different treatment schedules [17–22] and is believed to be caused in part by a higher sensitivity to radiotherapy of HPV-positive tumours, presumably because of the distinct molecular profile [23], combined with a better general health status in this group of patients. Smoking negatively affects survival in HNSCC, and the accumulated lifetime number of pack years independently impacts prognosis for both HPV-positive and -negative tumours [21,24]; implementation of smoking history in the risk stratification of HNSCC is under consideration.

As a consequence of this profound impact of HPV in HNSCC, this 'new' type of cancer has attracted a lot of attention, and separate therapeutic treatment strategies based on tumour HPV status are in the pipeline. In light of the enhanced sensitivity to treatment of HPV-related HNSCC, de-intensification of present treatment strategies in order to avoid excessive toxicity has been proposed for selected patients with minimal risk of distant metastasis [25]. On the other hand, patients with HPV-negative tumours have a very poor prognosis, and efforts should be made to improve treatment efficacy and compliance in this group of patients.

Conflict of interest statement

None declared.

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