



Human papilloma virus (HPV) in lung cancer: Unanswered questions

Dear Editor,

We read with interest the review by Klein et al. [1] highlighting the presence of human papilloma virus (HPV) in lung carcinoma samples and indicating its potential role in lung carcinogenesis. In this review, it was shown that the overall incidence of HPV in lung cancer up to date is 24.5%, which essentially renders HPV the second commonest risk factor for lung cancer if the cause–effect link is indeed valid. Interestingly, there is geographic variation with higher mean incidence rates reported in Asia (35.7%) compared to Europe (17%) and America (15%). This variation has been attributed to the different detection methods used and possibly to the epidemiology of the HPV itself, although information on HPV prevalence worldwide is absent.

The main questions therefore that need to be answered are: what is the route of transmission of HPV to lung tissue and how can it be potentially tumourigenic? It is known that HPV normally invades healthy tissue by direct mucosal contact [2] and it is postulated that it reaches the lung site via blood circulation [3], while the possibility of transmission from the cervix to the oral cavity and then to the larynx and lung is also plausible [4]. Once it presents to the host cells it is believed that it attaches to those cells expressing heparin sulphates, that act as primary receptors for HPV [5] and it is internalised to interfere with p53 and Rb proteins. This is achieved by E6 proteins, encoded by HPV, binding to the host cellular tumour suppressor proteins and triggering its degradation through the ubiquitin pathway [6]. Contrary to this theory is evidence of HPV in normal lung tissue of patients with HPV positive lung cancer and the question that arises is whether HPV is easily integrated to tumour genome than healthy cells and therefore is an epiphenomenon rather than the cause of the tumour. This remains to be answered. However, if the cause–effect link is true then molecular HPV typing could potentially be used as a marker of lung cancer [7] as well as to discriminate primary from metastatic squamous cell carcinoma [8]. In addition, early evidence shows that it can have a prognostic importance in stage I non-small cell lung carcinomas [9]. As a result, the implications for the prevention, management and prognosis of these tumours are vast and currently remain to be determined. It can be safely concluded that evidence for a causative link between HPV and lung cancer is mounting but the jury is still out.

Conflict of interest statement

There is no conflict of interest.

References

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