Esophageal Squamous Cell Carcinoma, Human Papillomavirus and p16

Dear Editor,

Esophageal cancer is the eighth most common cancer worldwide and the sixth most common cause of cancer-related death.[1] Among the Asian countries, India has a high burden of esophageal cancer.[1] Esophageal cancers are mainly two histopathologicaal types: adenocarcinoma and squamous cell carcinoma.[2] Esophageal squamous cell carcinoma (ESCC) is the predominant histological subtype worldwide with high incidence rate in Asia.[2] Esophageal carcinogenesis is a multifactorial process with influence of local environmental conditions, lifestyle, and genetic predisposition.[3] ESCC is usually associated with tobacco and alcohol intake.[1] In northeastern India, where the tobacco and areca nut use is rampant, the incidence of ESCC is relatively high.[1,2]

Human papillomavirus (HPV) infection as one of the possible etiological factors in ESCC was reported by Syrjänen *et al*. in 1982.[4] Like HPV-associated head and neck squamous cell carcinoma, HPV-associated ESCCs are associated with favorable prognosis.[1] HPV detection in ESCC is done through polymerase chain reaction, but it is expensive and requires a setup, which may not be available in all the centers. Again, immunohistochemistry for HPV in ESCC gives conflicting results.[1] In such a scenario, p16 expression by immunohistochemistry is usually used as a surrogate marker for HPV infection.[1,3] The biological rationale underlying this surrogacy stems from the fact that the HPV E7 viral protein triggers degradation of the retinoblastoma tumor suppressor protein in infected cells, which in turn initiates a feedback loop that results increased expression of p16. Immunohistochemical expression of p16 is cost-effective and technically straightforward with high sensitivity.[1]

However, the use of p16 as a surrogate marker of HPV has few disadvantages. As with any surrogate biomarker, there is a risk of discordance between p16 status and the actual HPV status due to failure to use a stringent cutoff for p16-positive tumor cells.[5] Moreover, p16 expression does not discriminate between HPV16 and non-HPV16 subtypes.[5]

Expression of p16 is usually used as surrogate marker for HPV in ESCC and is associated with relatively better outcome.

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Conflicts of interest

There are no conflicts of interest.

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