Ancillary studies (Non-core)

Reason/Evidentiary Support

Ancillary testing for head and neck cancers most commonly refers to testing for high-risk human papilloma virus (HPV) status in tumours of the oropharynx (typically using the surrogate marker of p16 immunohistochemistry or in situ hybridization) and EBV status in tumours of the nasopharynx (typically using in situ hybridization for EBV-encoded RNA or EBER). If ancillary testing is performed, it is recommended to include the type of testing, the result and interpretive guidelines if applicable.[1]

Oropharyngeal carcinoma is frequently human papillomavirus associated, with these tumours having improved survival versus human papilloma virus (HPV)-negative cases.[2] Testing for p16 status in oropharyngeal squamous cell carcinoma is a requirement of the 8th edition of the American Joint Committee on Cancer (AJCC) TNM staging system[3] and Union for International Cancer Control (UICC) TNM staging system,[4] and separate staging categories have been devised for p16 – and p16+ tumours.[3]

p16 overexpression by immunohistochemical analysis is a reliable surrogate for high-risk HPV associated squamous cell carcinomas of the oropharynx (including types 16, 18 and others). Overexpression of p16 is defined as diffuse, strong nuclear and often cytoplasmic expression (2-3+ intensity) in ≥70% of tumour cells. P16 expression is not applicable as a surrogate for HPV in other head and neck subsites (i.e. oral cavity, sinonasal, hypopharynx skin, etc.) as HPV is infrequent and p16 expression is non-specific.

Strong p16 expression in non-HPV associated squamous cell carcinoma of non-oropharyngeal sites does occur with unclear significance. Thus while HPV specific testing would be ideal in the assessment of neck nodes in patients with unknown primary squamous cell carcinoma, the lack of testing availability and cost makes this impractical. p16 status should be reported in all oropharyngeal primary squamous cell carcinomas (testing either the primary site or from a metastatic focus). Additionally, metastatic squamous cell carcinomas to cervical upper– or mid–jugular chain neck lymph nodes (levels II and III) with an unknown primary site should also be tested for p16 over expression by immunohistochemistry.[5] In situ hybridisation for EBER is recommended for p16-negative, non-keratinizing or undifferentiated carcinomas, or if there is clinical suspicion of a nasopharyngeal primary.

References

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