Head and neck squamous cell carcinoma

- Kynurenine enhances aryl hydrocarbon receptor signaling and expression levels of multidrug resistance genes in head and neck squamous cell carcinoma cell lines but does not change the potency of antineoplastic drugs
- Spatial Distribution and Prognostic Value of T Cell Subtypes and Immune Biomarkers in p16-Negative HNSCC
- Molecular patterns and mechanisms of tumorigenesis in HPV-associated and HPV-independent sinonasal squamous cell carcinoma
- In vivo CRISPR screening identifies NF1/RASA1/TP53 co-mutations and downstream MEK signaling as a common key mechanism of sinonasal tumorigenesis
- An integrated machine learning-based prognostic model in head and neck cancer using the systemic inflammatory response index and correlations with patient reported financial toxicity
- Primary intracranial squamous cell carcinoma arising in epidermoid cysts: A case report and review of literature
- Commentary: Disulfidptosis-related gene signatures as prognostic biomarkers and predictors of immunotherapy response in HNSCC
- Survival analysis of patients with metastatic head and neck squamous cell carcinoma treated with metastasis-directed radiotherapy and immunotherapy

1. Includes cancers of the oral cavity, oropharynx, larynx, and nasopharynx.
2. Risk factors include tobacco use, alcohol consumption, and human papillomavirus (HPV) infection, particularly for oropharyngeal cancers.
3. HPV-positive SCCs tend to have a better prognosis compared to HPV-negative ones.

Epidemiology

Head and neck squamous cell carcinoma (HNSCC) affects nearly 500,000 individuals globally each year. With the rise of human papillomavirus (HPV) in the general population, clinicians are seeing a concomitant rise in HPV-related HNSCC.

Classification

1. By Anatomical Subsite

HNSCC includes cancers originating from squamous epithelium in different regions. Common subsites include:

- **Oral Cavity:** Tobacco, alcohol, poor hygiene; includes tongue, floor of mouth, buccal mucosa.
- **Oropharynx:** HPV, smoking, alcohol; involves base of tongue and tonsils – p16 testing is important.
- **Larynx:** Smoking, alcohol; subdivided into supraglottic, glottic, and subglottic regions.
- **Hypopharynx:** Smoking, alcohol; typically seen in the pyriform sinus and postcricoid area.
- **Nasopharynx:** Associated with EBV and genetics (especially in Asia); often non-keratinizing.
- **Sinonasal Tract:** Less common; linked to occupational exposures.

2. By Molecular Profile

Different subtypes based on molecular characteristics:

- **HPV-positive:** Mainly oropharyngeal, p16 positive, and typically has a better prognosis.
- **HPV-negative:** Associated with tobacco/alcohol use, p16 negative, and generally exhibits a worse prognosis.
- **EBV-positive:** Characteristic of nasopharyngeal carcinomas.
- **p53-mutant:** Frequently observed in tobacco-associated cancers.
- **CDKN2A-inactivated:** Common in cancers of the oral cavity and larynx.

3. By Histopathology

Histological variations of HNSCC include:

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^ Type                  ^ Description                                    ^
^ Keratinizing SCC      ^ Classic pattern; more differentiated           ^
^ Non-keratinizing SCC  ^ Seen often in HPV+ and EBV+ tumors               ^
^ Basaloid SCC          ^ An aggressive variant                          ^
^ Papillary SCC         ^ Frequently found in sinonasal/oropharyngeal area^
^ Spindle Cell SCC      ^ Displays a sarcomatoid appearance; aggressive  ^
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4. Clinical Staging (AJCC 8th Edition)

Staging of HNSCC is based on the TNM system and also considers HPV status, especially in oropharyngeal cancers:

- **T (Tumor size)**
- **N (Nodal involvement)**
- **M (Metastases)**

For HPV-positive oropharyngeal SCC (OPSCC), a separate staging system is used that typically reflects a less aggressive prognosis for similar tumor burdens.

Etiology

PI3K pathway is the most frequently mutated pathway in head and neck squamous cell carcinoma (HNSC), which plays a crucial role in tumorigenesis and progression. The PI3K pathway mutation status could be considered as a potential biomarker to predict better immunotherapeutic efficacy and clinical outcomes after immunotherapy in HNSC patients [1].

Clinical features

Notably, a hallmark of HPV-related HNSCC is a predilection for unique biological and clinical features, which portend a tendency for hematogenous metastases to distant locations, such as the brain. Despite the classic belief that HNSCC is restricted to local spread via passive lymphatic drainage, brain metastases (BMs) are a rare complication that occurs in less than 1% of all HNSCC cases. Time between initial diagnosis of HNSCC and BM development can vary considerably. Some patients experience more than a decade of disease-free survival, whereas others present with definitive neurological symptoms that precede primary tumor detection [2)].

Diagnosis

The clinical role of perfusion-weighted MRI (PWI) in head and neck squamous cell carcinoma (HNSCC) remains to be defined. The aim of this study was to provide evidence-based recommendations for the use of PWI sequence in HNSCC with regard to clinical indications and acquisition parameters.

Methods: Public databases were searched, and selected papers were evaluated by applying the Oxford criteria 2011. A questionnaire was prepared including statements on clinical indications of PWI as well as its acquisition technique and submitted to selected panelists who worked in anonymity using a modified Delphi approach. Each panelist was asked to rate each statement using a 7-point Likert scale (1 = strongly disagree, 7 = strongly agree). Statements with scores equal or inferior to 5 assigned by at least two panelists were revised and re-submitted for the subsequent Delphi round to reach a final consensus.

Results: Two Delphi rounds were conducted. The final questionnaire consisted of 6 statements on clinical indications of PWI and 9 statements on the acquisition technique of PWI. Four of 19 (21%) statements obtained scores equal or inferior to 5 by two panelists, all dealing with clinical indications. The Delphi process was considered concluded as reasons entered by panelists for lower scores were mainly related to the lack of robust evidence so that no further modifications were suggested.

Conclusions: Evidence-based recommendations on the use of PWI have been provided by an independent panel of experts worldwide, encouraging a standardized use of PWI across university and research centers to produce more robust evidence [3)].

Outcome

Head and neck squamous cell carcinoma (HNSCC) is notorious for local recurrence and metastatic spread to regional lymph nodes. Distant spread is uncommon, and brain involvement is rare.

Case series

Cases of metastatic squamous cell carcinoma (SCC) to the brain were identified from a computerized search of the surgical pathology files of The Johns Hopkins Hospital between 1985 and 2012. The medical records were reviewed to document primary site of tumor origin, treatment, and patient outcome. P16 immunohistochemistry and HPV in situ hybridization were performed on those

metastases arising from the head and neck. Of the 38 metastatic SCCs, 7 (18 %) originated in the head and neck. HPV-16 was detected in 4 (57 %) of the metastatic HNSCCs. All 4 HPV-positive metastases were from oropharyngeal primaries. The time from treatment of the primary to development of the brain metastases ranged from 19 to 57 months (mean, 45). Following aggressive treatment (surgery and radiation), two patients died of disease progression (7 and 34 months), and two are alive with recurrent brain metastases (4 and 10 months). Although HPV positivity is regarded as a favorable prognostic indicator, it does not safeguard from spread to the brain. In our experience, just over half of the HNSCCs that metastasized to the brain were HPV-related. The potential for developing a brain metastases long after curative therapy argues for extended patient follow-up. The development of a brain metastases is an ominous finding signaling rapid clinical deterioration [4)]

1)
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