The Utility of Liquid Biopsy for Diagnosis and Surveillance of Non-Oropharyngeal HPV+ Squamous Cell Carcinoma of the Head and Neck

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Abstract:

Background: The application of tumor tissue-modified viral (TTMV) HPV DNA measurement for head and neck squamous cell carcinoma (HNSCC) has primarily been studied in the context of oropharyngeal disease. However, the utility of the liquid biopsy measurement in HPV-associated SCC of other head and neck subsites remains largely unexplored.

Objective: This study aims to assess the value of TTMV DNA measurements for non-oropharyngeal head and neck subsites, specifically the oral cavity, nasal cavity, hypopharynx, and larynx, in two clinical settings: pre-treatment diagnostics and post-treatment surveillance.

Methods: A single institution database of patients with confirmed HNSCC who underwent TTMV HPV DNA measurement between April 2020 and September 2023 was analyzed. Patients with primary cancer of the oropharynx or an unknown primary site were excluded. Diagnostic and surveillance cohorts were established. For the diagnostic cohort, patients with a liquid biopsy within 8 weeks of diagnosis were included. For the surveillance cohort, patients with a TTMV HPV DNA measurement after completion of the initial treatment course were included. Surveillance measurements were considered true positives if a recurrence was detected via imaging or tissue biopsy within 3 months of a positive TTMV HPV DNA test. In both diagnostic and surveillance settings, metrics of sensitivity and specificity of TTMV HPV DNA measurement were assessed.

Results: 27 patients met inclusion criteria with the following subsite distribution: hypopharynx n=6, larynx n=6, nasal cavity n=12, and oral cavity n=3. In the diagnostic cohort, 18 patients received pretreatment liquid biopsy tests, 18 tests were conducted that yielded a sensitivity for diagnosis of HPV-associated SCC 72.7% (8/11 tests), specificity of 100% (7/7 tests). In the cohort of 14 patients undergoing surveillance post-treatment using liquid biopsy measurements, 26 tests were conducted. Molecularly confirmed recurrences were confirmed in 10 patients. Surveillance TTMV HPV DNA measurements yielded a sensitivity for recurrence of 85.7% (12/14 tests), specificity of 100% (9/9 tests), PPV of 100% (12/12 tests), and NPV of 82% (9/11 tests).

Conclusion: TTMV HPV DNA measurement likely has clinical utility in both the diagnostic and surveillance settings for HPV-positive cancers in head and neck in subsites outside of the oropharynx. While HPV status is not prognostic in non-oropharyngeal subsites, tissue-agnostic liquid biopsy testing for HPV-positive tissue DNA, may serve as a reliable marker of disease. How to incorporate circulating tumor testing in the management of HPV-associated cancers in subsites outside of the oropharynx will need to be explored in larger studies.