



From biomolecular aspects to treatment strategies of HPV + OPSCC: a critical review.

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OBJECTIVES

Patients with cystic metastasis in the neck lymph nodes and no obvious primary tumor, neck cancer with unknown primaries (NCUP), represent a very complex management challenge, especially today in the HPV era. It is estimated that a relevant part of these cases are related to p16 positive OPSCC, with the primary tumor often involving palatine or lingual tonsils or the base of the tongue. However, given the increasing incidence of HPV-related SCC in the oropharynx, HPV testing is crucial. An HPV-positive status can localize the tumor to the oropharynx, a common site for occult tumors. It is important to identify the primary tumor because tumor identification influences treatments administered, reducing radiation fields and providing possible de-escalation to primary surgical management.

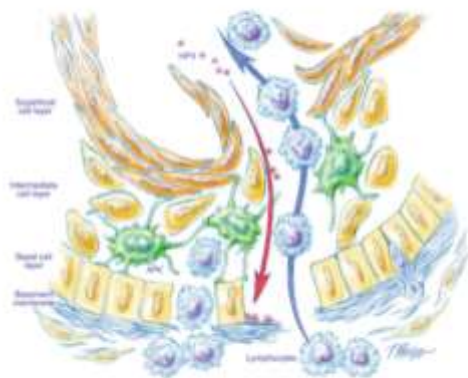
METHODS

We present a systemic review regarding biomolecular and clinical-prognostical aspects of OPSCC patients. A pub-med literature research was performed and relevant studies of the last 2 decades are critically discussed to provide an overview of biomolecular, clinical-prognostical and therapeutical aspects regarding HPV+ OPSCC. The aim of our work is to stimulate debate in order to facilitate a more precise diagnosis of HPV OPSCC related cases and to guarantee the best prognostic-therapeutic process to the patients affected by OPSCC.

GRAPHS AND TABLES

THE MORPHOLOGIC PROFILE OF HPV-RELATED HEAD AND NECK SQUAMOUS CARCINOMA: IMPLICATIONS FOR DIAGNOSIS, PROGNOSIS, AND CLINICAL MANAGEMENT

Wilson H. Westra

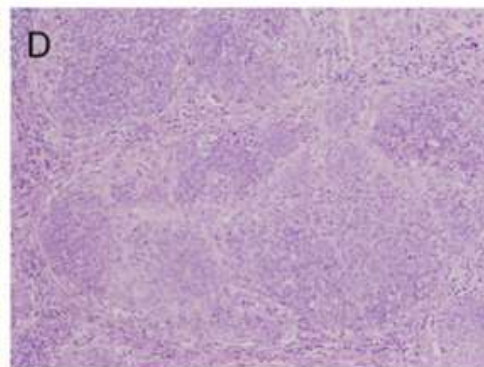
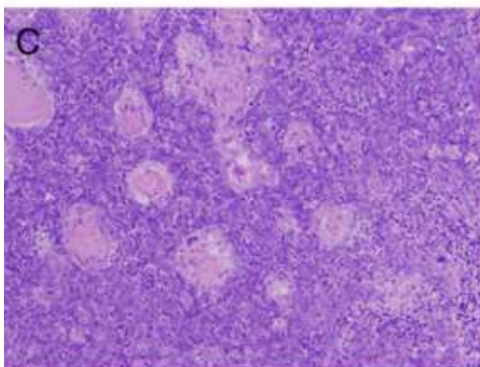


Schematic representation of the reticulated epithelium lining the tonsillar crypts. A porous basement membrane facilitates the migration of lymphocytes and antigen presenting cells (APCs). This lack of structural integrity of the basement membrane confounds the distinction between in situ and invasive disease

Photo by Pai SI, Westra WH. Molecular pathology of head and neck cancer: implications for diagnosis, prognosis and treatment of patients with head and neck squamous cell carcinoma. Annual Rev Pathol. 2009;4:49-70

	P16+ OPSCC	P16- OPSCC
	<u>Squamous Carcinoma.</u>	<u>Squamous Carcinoma.</u>
	Age <60, <u>males, non-smokers</u> with <u>numerous sexual partners.</u>	Older patients, <u>smokers</u> and/or <u>drinkers.</u>
Why?	<u>Good radiotherapy response</u> <u>Better prognosis</u> <u>Better survival</u>	<u>Worst Prognosis</u> <u>Worst Survival</u>
Actions?	<u>Higher risk of metastasis(60% unknown primaries)</u>	<u>Lower risk of metastasis</u>
Is it correct?	<u>Lymph nodes extracapsular extension(ENE) is not considered in pathological lymph nodes stadiation in HPV+ patients</u>	<u>Lymph nodes extracapsular extension (ENE) is considered in pathological lymph nodes stadiation</u>

Some patients can show within the same sample, a share of non keratizing squamous cell carcinoma, presumtively related to the HPV, and a share of keratizing squamous cell carcinoma, presumtively related to tobacco exposure. In these cases it might be very important to look for the p53 status (mutated or wild type)



RESULTS

Bilateral tonsillectomy is the diagnostic gold standard for identifying HPV-related OPSCC presenting with cystic laterocervical lymph node metastasis. This procedure ensures better post-operative control due to oropharyngeal symmetry.

Further detection methods, besides immunohistochemistry (p16), are necessary for an early and correct identification of HPV-related OPSCC.

Not all HPV-positive cancers respond completely to radiotherapy. Among the negative predictors we have identified:

- N size (especially ENE+);
- Alcohol and tobacco use;
- Mutations of the p53 protein;
- Old age;
- keratinizing and small cell histology.

CONCLUSION

Especially at a biomolecular level, a more accurate diagnosis is required in order to adequately stage and manage HPV+ OPSCC neck metastasis.

Inducing specific onco-suppressive mutations, the role of tobacco exposure is fundamental and should be taken into consideration in the prognostic staging of HPV + OPSCC.

OPSCC patients who are HPV positive and have a tobacco exposure history might not have good outcomes, and this is probably due to p53 mutations induced by tobacco exposure.

Until the diagnosis is not more accurate, extracapsular extension should be considered in HPV+ OPSCC, like in all head and neck cancers.

Given the numerous pitfalls caused by these Head and Neck cancers, a multidisciplinary team is absolutely indispensable for the management of these neoplasms, guaranteeing the correct planning of the diagnostic therapeutic procedure.

At present, for the same reasons, today it is inappropriate and risky to propose de-escalation protocols in clinical routine.

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