

## Abstract

This doctor thesis comprises two studies. (i) A retrospective study was performed on 22 patients who presented with cystic head and neck squamous cell carcinoma (SCC) metastases. The purpose of the study was to find out whether histomorphology, p16 protein expression, HPV and EBV status could be useful in predicting the localization of the primary tumor. The primary site was identified in 20 of 22 patients and included the oropharynx in 14 patients (63.6%), the nasopharynx in 3 patients (13.6%), the lungs in 2 cases (9%), and the skin of the auricle in one case (4.5%). No primary was found in two patients (9%). Sixteen of 17 cases (94.1%) originating in Waldayer's ring, and both cases with an unknown primary showed morphology of non-keratinizing SCC or non-keratinizing SCC with maturation. All tumors with oropharyngeal primary and both cases with unknown primary showed diffuse p16 staining and presence of HPV DNA. All three cystic metastases of nasopharyngeal carcinoma (NPCa) were EBV-positive and p16/HPV negative. In contrast, cutaneous and pulmonary metastases showed morphology of a well differentiated keratinizing SCC and poorly differentiated keratinizing SCC, respectively, and were HPV/EBV-negative. We confirmed that cystic SCC lymph node metastases of the head and neck region are strongly associated with the occult oropharyngeal primary. The oropharyngeal origin should always be corroborated by p16 immunohistochemistry and HPV-specific testing because SCC arising in other sites may manifest with cystic neck metastases as well. Addition of EBV testing in p16/HPV-negative cases can disclose the nasopharyngeal origin of the cystic neck metastases in a subset of cases.

(ii) NPCa is a rare malignancy in the Czech Republic and Slovakia and EBV/HPV status of NPCa is currently unknown. In a retrospective study, we evaluated the presence of EBV and HPV in 62 NPCa cases and performed meta-analysis separately for proportion of EBV-positive cases, PCR-detected HPV-positive cases and p16/in situ hybridization -detected HPV-positive cases in the Caucasian patients with NPCa. Sixty-one studied cases showed non-keratinizing morphology and one was keratinizing SCC. Only one non-keratinizing SCC was p16/HPV-positive and the DNA PCR confirmed the presence of HPV18 type. EBV was detected in 85.5% (53/62) of cases. In contrast with previous reports on the prevalence of EBV-positivity in Caucasian patients with NPCa, the majority of patients coming from this non-endemic region show EBV-positivity; therefore, they may be candidates for novel EBV-targeting therapies. Conversely, HPV-positive NPCa is very rare and HPV does not seem to play a significant role in the etiopathogenesis of NPCa in these populations. The probability that HPV-positive cervical metastasis from an unknown origin comes from an occult nasopharyngeal primary is very low in our population and HPV detection should direct attention to oropharynx.