

## CASE REPORT

### **P16 and HPV discordance in metastatic carcinoma of cervical lymph nodes of unknown primary**

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#### **Funding Information**

No sources of funding were declared for this study.

Received: 6 May 2015; Accepted: 30 June 2015

*Clinical Case Reports* 2015; **3**(10): 817–818

doi: 10.1002/ccr3.338

#### **Key Clinical Message**

The prognostic utility of HPV in oropharyngeal squamous cell carcinoma (OPSCC) and non-OPSCC as has been well documented. Currently, a standardized IHC scoring system does not exist and is needed to define HPV positivity. We have recently seen a patient that provides a caution in using p16 status as a diagnostic aid.

#### **Keywords**

HPV, Oropharyngeal squamous cell carcinoma, P16, Unknown primary.

#### **Case**

A 44-year-old nonsmoking male presented with a tender neck mass of several weeks duration. CT Neck revealed two enlarged right cervical lymph nodes. Flexible laryngoscopy revealed no obvious primary. A fine needle aspiration of the neck mass was felt to be most consistent with squamous cell carcinoma. PET/CT revealed three FDG-avid lymph nodes in the right neck and no evidence of distant metastases. He underwent a right selective neck dissection with bilateral tonsillectomies and directed biopsies of the nasopharynx, base of the tongue, and pyriform sinuses. Pathology revealed no evidence of a primary tumor, and eight of 10 right cervical lymph nodes positive for poorly differentiated carcinoma most consistent with squamous cell carcinoma. The tumor was strongly positive for p16 on IHC staining, supporting the diagnosis of a squamous cell carcinoma of the head and neck region with unknown primary site. He was treated with a conventional 7-week course of concomitant cisplatin and radiation therapy.

Post treatment PET/CT revealed recurrence in a single cervical lymph node and new hepatic metastases. Biopsy of the hepatic metastasis revealed mucoepidermoid carci-

noma similar in morphology to the prior biopsy specimens. IHC was positive for p16. PCR testing was performed on both the original lymph node specimen and the liver metastasis; both were negative for HPV.

#### **Discussion**

P16, a cyclin-dependent kinase inhibitor, activates the cyclin D1 CKD4 and 6 complex, which prevents phosphorylation of the retinoblastoma protein (pRb) and leads to cell cycle arrest [1, 2]. Overexpression of p16 has been demonstrated in a wide range of human malignancies [3]. HPV infection can lead to overexpression of p16 by virally-expressed oncoprotein E7 binding to and inactivating pRb, thus leading to overexpression of p16 [1, 2].

In this case, the expression of p16 in the setting of a metastatic carcinoma to cervical lymph nodes with squamous differentiation was taken as supporting evidence of an unknown primary squamous cell carcinoma of the head and neck region. The subsequent biopsy revealed mucoepidermoid salivary gland carcinoma, which has been shown to overexpress p16 in the absence of HPV infection [4–12]. Thus, it is important to recognize that although IHC staining for p16 is a useful surrogate for HPV infec-

tion, discordance both due to testing inaccuracy as well as true p16 positivity without HPV infection exists and should be considered when evaluating a carcinoma originating in the head and neck region [1, 4–15, 17–20].

## Conflict of Interest

None declared.

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