Published in final edited form as:

Otolaryngol Head Neck Surg. 2018 September ; 159(3): 593–594. doi:10.1177/0194599818774756.

HPV-positive Oropharyngeal Squamous Cell Carcinoma among Patients Taking Adalimumab for Autoimmune Disorders

Douglas R. Farquhar¹, James M. Taylor², Angela L. Mazul³, and Jose P. Zevallos⁴

¹Department of Otolaryngology/Head and Neck Surgery, University of North Carolina at Chapel Hill School of Medicine, Chapel Hill, NC

²Department of Internal Medicine, Moses Cone Hospital, Greensboro, NC

³Department of Epidemiology, Gillings School of Global Public Health, University of North Carolina at Chapel Hill, Chapel Hill, NC

⁴Department of Otolaryngology-Head and Neck Surgery, Washington University School of Medicine, St. Louis, MO

Introduction

The incidence of human papillomavirus (HPV)-associated oropharyngeal cancer (OPSCC) is rising and now accounts for the majority of oropharyngeal carcinomas. Recent evidence has linked immune dysregulation to both the reactivation of viral infections such as HPV and the risk of viral-associated cancers.¹ However, this association has not been investigated in oropharyngeal cancer. In addition, many patients with autoimmune disease are now treated with biopharmaceuticals (biologics), potent immunosuppressants that may compound this risk. TNF-alpha-blocking agents in particular have been associated with reactivation of latent viruses including HPV.² However, a link between biologics and oropharyngeal carcinoma also remains unexplored.

The purpose of this study is to characterize the presentation, treatment course, and outcomes in HPV-positive OPSCC patients on biologics treated at a single tertiary care cancer center.

Methods

The electronic medical records of all HPV-positive OPSCC patients treated between 2003 and 2013 at our institution were reviewed for patients who had taken TNF-alpha-blocking agents at the time of diagnosis. Their presentation and treatment were then described. The study was approved by the University of North Carolina Institutional Review Board.

Results

Of 262 HPV-positive OPSCC patients, three were taking adalimumab (Humira), a TNF-alpha inhibitor, for autoimmune disease.

Corresponding author: Douglas R. Farquhar, drfarquhar@gmail.com.

Disclosure: The authors have no disclosures.

Case 1

Case 1 is a 32-year-old male with a 2-year history of adalimumab use for severe psoriasis who presented throat pain. Tonsillectomy revealed a 3 cm HPV and p16-positive OPSCC. The patient underwent a transoral robotic resection and a selective neck dissection, followed by 60 Gy of radiation therapy. He is now disease-free after 12 months.

Case 2

Case 2 is 63-year-old man with a 12-year history of adalimumab use for psoriatic arthritis who presented with otalgia and odynophagia. Biopsy diagnosed an HPV and p16-positive OPSCC (staged T3N2b). He underwent concurrent cisplatin chemotherapy and 60 Gy of radiation therapy.

PET scan at 12 weeks revealed persistent tumor in his base of tongue and left neck. He underwent salvage surgery, but repeat scans and biopsies at 4 months revealed squamous cell carcinoma in his lung, likely representing a metastasis. He is currently undergoing palliative chemotherapy.

Case 3

Case 3 is a 57-year-old man with a long history of adalimumab use for rheumatoid arthritis who presented to the ED after a fall; a head CT incidentally revealed bilateral cervical adenopathy and an oropharyngeal mass. He had a distant 10 pack-year smoking history. A biopsy revealed p16 and HPV positive OPSCC, staged T4N2c. He recently began treatment with cisplatin and 70 Gy of radiation.

Discussion

In this series, we report three cases of HPV-positive OPSCC in patients with longstanding autoimmune disorders taking adalimumab. They provide preliminary evidence of a potential association between HPV-positive OPSCC, autoimmune conditions and immunosuppressive medication. These results are in line with evidence that immune dysregulation may play a role in HPV infection and carcinogenesis. A recent study demonstrated that persistent HPV cervical infection was associated with an impaired HPV-specific T-cell response.¹ In a mouse model, an HPV-specific T-cell response was associated with HPV-related tumor development and clearance in immunodeficient mice.³

Autoimmune disease, the most widespread form of immune dysregulation in the US, has recently been linked with HPV-related cervical cancer in several studies.^{2,4} Nonetheless, an epidemiologic link with HPV-related OPSCC has not been investigated. This risk may be exacerbated by the rapidly increasing use of TNF-alpha blocking biologics to treat autoimmune disease. Recent evidence has also linked TNF-alpha blocking agents in particular to the risk of viral infection or reactivation,² and multiple case reports have documented cutaneous HPV infections after patients received TNF-alpha blocking therapy.^{2,5}

Of note, the patients in our series all shared a uniquely aggressive presentation or disease course for HPV-positive OPSCC. Case 1 was the youngest in our institutional database at 32,

Case 3 presented with a T4 tumor, and Case 2 had a rapidly progressive course of disease requiring palliative therapy. Only two other HPV-positive OPSCC patients in our institutional series had received palliative therapy after initial treatment failure.

A large epidemiology study is warranted to investigate potential associations between autoimmune disease, biologics, and the incidence and survival of HPV-related OPSCC. The results could affect screening for HPV-positive OPSCC among patients taking TNF-alpha inhibiting medications, and affect treatment decisions for those found to have disease.

References

1. Andersen AS, Solling ASK, Ovesen T, Rusan M. The interplay between HPV and host immunity in head and neck squamous cell carcinoma. *Int J Cancer*. 2014; 134(12):2755–2763. [PubMed: 23913554]
2. Kim SY, Solomon DH. Tumor necrosis factor blockade and the risk of viral infection. *Nat Rev Rheumatol*. 2010; 6(3):165–174. [PubMed: 20142812]
3. Lin CT, Chang TC, Shaw SW, et al. Maintenance of CD8 effector T cells by CD4 helper T cells eradicates growing tumors and promotes long-term tumor immunity. *Vaccine*. 2006; 24(37–39): 6199–6207. [PubMed: 16824651]
4. Kim SC, Glynn RJ, Giovannucci E, et al. Risk of high-grade cervical dysplasia and cervical cancer in women with systemic inflammatory diseases: a population-based cohort study. *Ann Rheum Dis*. 2015; 74(7):1360–1367. [PubMed: 24618265]
5. Antoniou C, Kosmadaki MG, Stratigos AJ, Katsambas AD. Genital HPV lesions and molluscum contagiosum occurring in patients receiving anti-TNF-alpha therapy. *Dermatology*. 2008; 216(4): 364–365. [PubMed: 18285688]