



Case Report

A SCITECHNOL JOURNAL

Human Papillomavirus Induced Adenocarcinoma of Tonsil: A Rare Entity

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Abstract

Oropharyngeal carcinoma or tonsil cancers are mainly squamous cell cancers. Smoking, alcohol consumption and Human Papilloma Virus (HPV) infection are leading causative factors Oropharyngeal Squamous Cell Carcinoma (OPSCC). Locally advanced head and neck cancers are usually treated with combination of surgery and chemoradiation. We report a case of a 60 year old caucasian man with HPV induced primary adenocarcinoma of tonsil and its clinical course.

Keywords

Adenocarcinoma; Human papilloma virus; Oropharyngeal cancer; Tonsil cancer; Keynote 040; Checkmate 141 trials; p16

Introduction

Tonsillar carcinoma is the second most common malignancy of the head and neck after laryngeal cancer [1]. Majority of tonsil cancer or oropharyngeal malignancy is Squamous Cell Carcinoma (SCC). Smoking and alcohol usage are commonly associated with tonsil cancer. Also, there has been a rise in the number of cases of tonsil cancer occurring secondary to the HPV infection. HPV 16 subtype has the greatest association with oropharyngeal cancers [2]. Diffuse pattern of p16 immunostaining is considered a highly sensitive marker for the identification of HPV type cancers [3]. We report a rare case of a 56 year old caucasian man presenting with HPV induced primary adenocarcinoma of tonsil and its clinical course which is rarely documented in the medical literature.

Case Presentation

A 60-year-old Caucasian male presented with complaints of neck swelling and dysphagia of two months duration [Figure 1]. Patient was a former chronic smoker for 25 years and consumed alcohol occasionally. Patient had a good overall performance status at the time of initial presentation. Left cervical lymphadenopathy and enlarged left tonsil were positive findings on physical examination [Figure 1, Figure 2]. Computed tomography (CT) of neck with contrast showed left cervical lymphadenopathy in continuity with the tonsillar mass. Tonsillar mass was adjacent to internal carotid artery, encroaching the carotid sheath. Patient was not a surgical candidate based on

CT findings. Tumor size measured 1.5 cm × 1.1 cm. Endoscopy and colonoscopy performed were inconclusive for malignancy. Initial Positron Emission Tomography (PET) scan illustrated left tonsillar mass of Standardized Uptake Values (SUVs) of 14.2, retropharyngeal node of SUV 7.2, left cervical nodal mass with right sided adenopathy which was consistent with malignancy. No other features of malignancy was seen on PET scan below the neck. The histopathological biopsy analysis of the left tonsillar fossa revealed poorly differentiated adenocarcinoma which was positive for p16, suggestive of tumor being HPV-related [Figure 3]. Biopsy slides were



Figure 1: Cervical lymphadenopathy/submandibular mass.

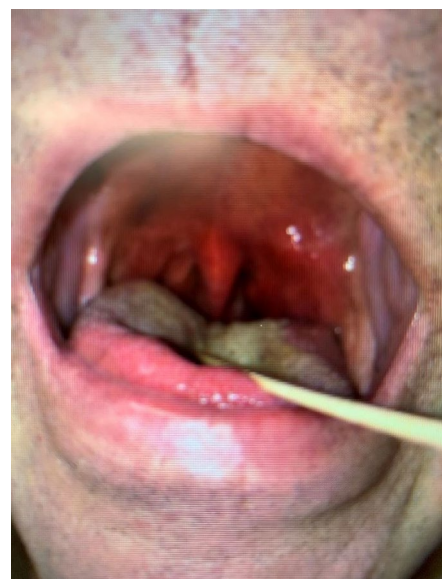


Figure 2: Enlarged left tonsil.

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Received: January 16, 2022, Manuscript No: M-51793; Editor Assigned: January 25, 2022, PreQC No: P-51793; Reviewed: February 21, 2022, QC No: Q-51793; Revised: February 24, 2022, Manuscript No: R-51793; Published: February 28, 2022, DOI: 10.4172/coocr.5(2).215

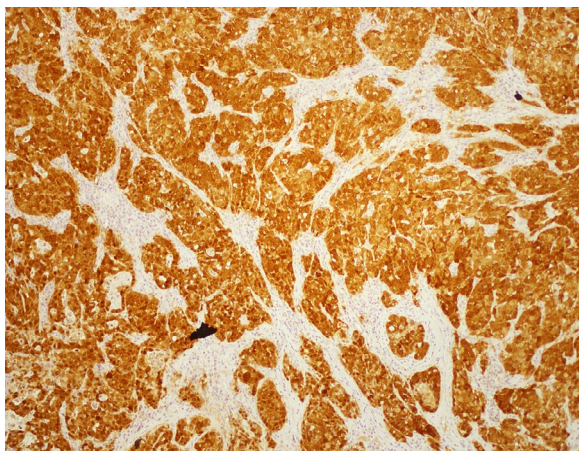


Figure 3: Immunohistochemical stains for p16 on tonsillar biopsies show diffuse, strong positivity (100 X): A mucicarmine stain shows positivity in tumor cells. Adenocarcinoma of Tonsil: Immunohistochemical stains on tumor show it to be positive for cytokeratin 7 and p16, and negative for p40 and cytokeratin 20 favoring adenocarcinoma.

Table 1: Patient demographics and initial management.

Characteristic	Case
Age	60
Gender	Male
Race	Caucasian
Smoking	Yes
Alcohol	Occasional (Socially)
Tumor grade	T1, N3, M0
Tumor stage	III
Treatment plan	Induction chemotherapy with Cisplatin+Docetaxel+fluorouracil every 21 days followed by carboplatin with concurrent radiation

reviewed by three different pathologists to confirm the diagnosis of adenocarcinoma. The patient’s demographics, tumor characteristics, and the treatment details are illustrated below [Table 1].

Adenocarcinoma of Tonsil: Immunohistochemical stains on tumor show it to be positive for cytokeratin 7 and p16, and negative for p40 and cytokeratin 20 favoring Adenocarcinoma.

After completing six cycles of carboplatin with concurrent radiation, three months later patient’s disease progressed with PET scan revealing increased hypermetabolic activity of the known palatine malignancy, new and worsening bilateral cervical lymphadenopathy, pulmonary metastases, thoracic lymphadenopathy, and osseous metastatic disease. Later, biopsy performed on left cervical lymph node after disease progression also revealed metastatic poorly differentiated adenocarcinoma positive for p16 protein. Next generation sequencing (NGS) from the cervical lymph node biopsy was inconclusive for targeted therapy. Palliative treatment with carboplatin, 5-fluorouracil and pembrolizumab every twenty one days was further planned and has currently completed one cycle at the time of writing this case report.

Discussion

Lump in neck, otalgia, dysphagia hoarseness, persistent sore throat

are frequently associated complaints in patient with tonsil cancer. However, clinical presentation varies with many patients remaining asymptomatic at the time of diagnosis. Not all cases of primary tonsil cancer presents with a visible lesion and tumors may be hidden in the tonsil crypts [4].

HPV-positive patients are predominantly seen in younger population group and those who use less alcohol and tobacco. As a group, they respond favourably to radiotherapy or surgery when compared to HPV-negative cancers in terms of improved locoregional tumour control, disease-specific survival, and Overall Survival (OS) [5-8]. Prognosis of HPV positive tonsil cancer showed a 5-year OS of 71% compared to 46% in HPV negative disease [9]. Unfortunately, up to 66% of patients with head and neck cancers are diagnosed at advanced stages- III and IV with about 10% of patients presenting as distant metastases [10]. Carcinoma of tonsil accounts for 10% of all head and neck cancers and local spread or neck node involvement are the usual mode of metastasis. Locally advanced oropharyngeal cancer or staged III and IV have high chances of recurrence and has poor prognosis. Meta-analysis of chemotherapy in head and neck cancer (MACH-NC) study included 19,248 patients which concluded that addition of concomitant chemoradiation decreased 5 -year mortality of 6.5% (hazard ratio for death, 0.83; 95% CI, 0.79 to 0.87; P<0.001) and loco regional failure rates [11,12]. Also, it concluded that adding induction chemotherapy did not improve OS, when compared with chemoradiation alone. Extensive elective neck dissection with adjuvant therapy is an alternative in treating T3 or T4 staged head and neck tumors [11,12].

Platinum drugs regimens vis cisplatin and carboplatin or sometimes Epidermal Growth Factor Receptor [EGFR] antibody cetuximab with concurrent radiation is the standard of care for patients with good performance status in locally advanced oropharyngeal cancers. Recent randomized trials have showed decreased survival with cetuximab and radiotherapy in patients with HPV positive oropharyngeal cancer compared to high dose cisplatin or carboplatin with radiation. Also, induction chemotherapy followed by chemoradiation in oropharyngeal cancers is mainly approached in those with the bulky disease or with high risk for loco regional relapse. However, many studies did not improve survival with upfront induction chemotherapy as compared with chemoradiotherapy alone., Immunotherapy has also influenced the treatment in metastatic head and neck cancers particularly squamous cell type. Keynote-040 and Checkmate 141 trials illustrated that programmed death-ligand 1 (PD-L1) expression (>50%) on tumor cells improved survival with anti-programmed cell death protein (PD-1) antibody treatment in such aggressive cancers [13,14].

Conclusion

Adenocarcinoma of tonsil is a rare entity. Its treatment approach is mainly extrapolated as per the guidelines followed for locally advanced head and neck cancer. Targeted therapies based on NGS may help in the treatment in the metastatic setting.

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