

Cutaneous metastasis of tonsillar carcinoma: Report of a rare case



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INTRODUCTION

Cutaneous metastases (CM) occur in 1% to 2.4% of all patients with squamous cell carcinoma of the head and neck (SCCHN) and rarely originate from a tonsillar primary tumor.^{1,2} To date, only 4 prior cases have been described in the literature.³⁻⁶ The diagnosis of tonsillar carcinoma CM may be unexpected, as clinical presentation varies widely, and cases can present after a disease-free interval. Dermatologists, therefore, are uniquely positioned to be the first to identify disease recurrence. Here we describe the fifth documented case of CM in tonsillar carcinoma managed with a unique therapy, review the clinical presentation of all known cases, and discuss risk factors and prognostic implications.

CASE REPORT

A 70-year-old man with a history of prostate cancer and recurrent head and neck cancer presented for evaluation of an asymptomatic cutaneous eruption. The patient had T4b, N2b, M0 squamous cell carcinoma (SCC) of the right tonsil in June 2015 and treated with chemoradiation (70 Gy and weekly cetuximab). Disease recurred to a right axillary lymph node in August 2016, for which he completed 5 cycles of docetaxel. After this regimen, there was no evidence of disease on a restaging positron emission tomography/computed tomography, and the patient began a treatment break in February 2017.

In June 2017, the dermatology department was consulted for a rash that was present for many months. On examination, there were 2 distinct morphologies. The first was a large blanchable erythematous patch involving the right chest and

Abbreviations used:

CM:	cutaneous metastases
DM:	distant metastasis
HPV:	human papillomavirus
SCC:	squamous cell carcinoma
SCCHN:	squamous cell carcinoma of head and neck

upper abdomen that extended across the midline (Fig 1). Another morphology was observed overlying the right lateral chest, shoulder, and clavicle in the form of reddish-yellow papules (Fig 1, inset).

A punch biopsy of a papule (Fig 2) found SCC with basaloid morphology (p40⁺, p16⁺, high expression PD-L1). A punch biopsy of the erythematous patch (Fig 3) found minute foci of SCC seen only in angiolymphatic spaces (p40⁺, p16⁺, high expression PD-L1). Histopathology results were consistent with the primary tonsillar carcinoma (p16⁺; Fig 4) and the axillary lymph node biopsy that previously found disease recurrence (p40⁺). Given the patient's history of prostate cancer and increasing prostate-specific antigen (PSA), both skin biopsies were evaluated and stained negative for PSA and NKX3.1.

Restaging positron emission tomography/computed tomography found interval development of mild to moderate metabolic right supraclavicular, right axillary, mediastinal, bilateral hilar, periportal, and para-aortic nodes concerning for metastases. Given the high expression of PD-L1 in his recent biopsies, the patient was started on nivolumab in July 2017. As of January 2018, the patient's cutaneous

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Fig 1. Large blanchable erythematous patch involving the right chest and abdomen extending across the midline. Reddish-yellow papules on the right lateral chest (inset).

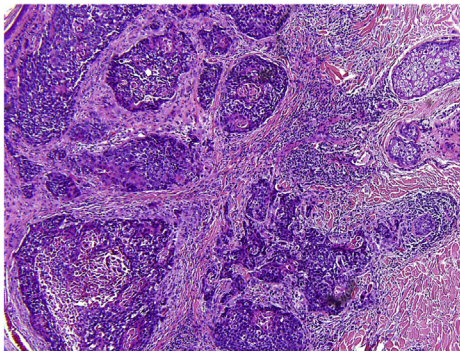


Fig 2. Right clavicle punch biopsy of a papule found SCC with basaloid morphology p40⁺, p16⁺, PSA⁻, NKX3.1⁻, and high expression PD-L1. (Hematoxylin-eosin stain; original magnification: ×10.)

eruption had resolved, and repeat imaging was improved.

DISCUSSION

According to the literature, 0.7% to 10.4% of all patients with cancer will have cutaneous metastases.^{7,8} Cutaneous involvement can occur in two ways: by direct extension from the primary tumor or by metastasis, which can be local or distant.^{2,7} Local spread occurs through dermal lymphatics whereas distant metastasis (DM) arises from hematogenous spread.² Compared with other malignancies, the incidence of CM from SCCHN primary tumors is relatively small.^{1,2} A retrospective review of 798 patients with SCCHN found that only 19 patients (2.4%) went on to have CM, none of which were tonsillar in origin.² To our knowledge, there are only 4 previously documented occurrences of CM from a tonsillar primary (Table 1).³⁻⁶

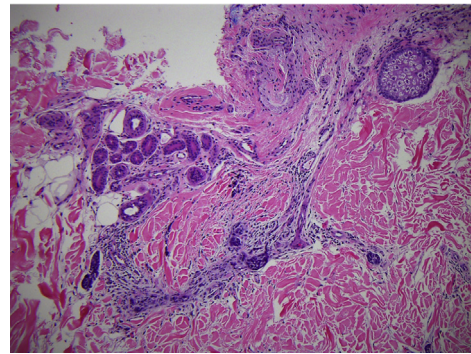


Fig 3. Right chest punch biopsy of the patch found minute foci of SCC seen only in angiolympathic spaces p40⁺, p16⁺, PSA⁻, NKX3.1⁻, and high expression PD-L1. (Hematoxylin-eosin stain; original magnification: ×10.)

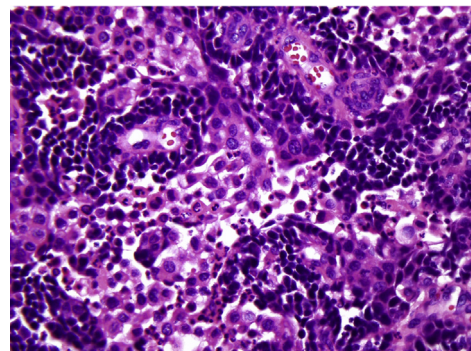


Fig 4. Right tonsil lesion biopsy found invasive moderately differentiated SCC with basaloid features p16⁺ (Hematoxylin-eosin stain; original magnification: ×40.)

The incidence of DM in SCCHN is directly related to the stage of the primary tumor and the presence or absence of regional control above the clavicle.¹ Primary tumors with advanced T stages in the oropharynx, hypopharynx, or oral cavity are the most likely to develop DM.¹ In the previously cited retrospective review of SCCHN, only 15.8% of CM occurred outside the head and neck region, and all such cases occurred on the chest.² Our patient, with a stage IVB primary tumor, had CM across the chest and abdomen, making this the third of 5 reported cases of tonsillar carcinoma CM with involvement outside the head and neck region. Basaloid squamous cell carcinoma is known to metastasize widely.¹ Advanced staging, absence of regional control, and basaloid features on pathology support extensive metastatic workup.

Risk factors for CM from tonsillar SCC will be better identified as case volume increases. All 5 cases of tonsillar carcinoma occurred in men 40 to 70 years of age.³⁻⁶ Three patients were chronic smokers, a significant risk factor for human papillomavirus (HPV)⁻ tumors.⁹ HPV infection has been implicated

Table I. Characteristics of patients with cutaneous metastasis of tonsillar carcinoma

Study	Age*/sex	Tobacco use	TNM stage at diagnosis	Time to CM (mo)	Clinical presentation of CM	Initial sign of recurrence?	Metastatic treatment and follow-up
Dasmajumdar et al ⁶ (2002)	40/M	Chronic smoker	T3, N2c, M0	26	Confluent erythematous papules and plaques in the left periorbital, temporal, and malar region	Yes [†]	Palliative XRT; reduced size by 50% after 4 months
Chikkannaiah et al ⁵ (2015)	70/M	Chronic smoker	T2, N0, M0	16	Swelling of the right fronto-parietal scalp	Yes	Palliative XRT planned; died 2 days after CM diagnosis before receiving therapy
Singh et al ⁴ (2016)	55/M	Chronic smoker	T3, N1, M0	6	Ulcerative proliferative growths on the scalp and left thigh	Yes [†]	Palliative MTX
Bari and Cohen ³ (2017)	59/M	Nonsmoker	Stage IV	54	Confluent erythematous papules and plaques on the neck and proximal chest	No	Declined treatment
Current case (2017)	68/M	Nonsmoker	T4b, N2b, M0	24	Blanchable erythematous patch across right chest and abdomen, reddish-yellow papules on the right chest, shoulder, and clavicle	Yes [†]	Nivolumab; cutaneous eruption resolved at 6 months

CM, Cutaneous metastasis; MTX, methotrexate; XRT, radiotherapy.

*Age at diagnosis of tonsillar carcinoma.

[†]No sign of residual or recurrent local disease noted.

in the pathogenesis of oropharyngeal cancers and, according to a meta-analysis of data, has a prevalence of 48%.⁹ It is the strongest prognostic factor in recurrent or metastatic SCCHN and predicts an improved prognosis over HPV⁻ tumors.¹⁰ Our patient's original tonsil biopsy and skin biopsies stained p16⁺, although this was not reported in the 4 prior patients. HPV testing should be considered in future cases, as the results may influence treatment decisions.⁷

CM may represent the first evidence of recurrent malignancy.^{7,8} In 4 of the 5 cases, CM were the initial presenting sign of disease recurrence.³⁻⁶ The time to presentation ranged widely from 6 to 54 months.³⁻⁶ In a study by Yoskovitch et al, the time to presentation of CM in SCCHN averaged 17.65 months with 75% of cases appearing by 18 months. Eighty-three percent of patients had locoregional control of their disease at the time of CM diagnosis.²

Clinical presentation varies. In the literature, tonsillar carcinoma CM have presented as confluent erythematous papules and plaques, ulcerative proliferative growths, and even as subtle swelling of the scalp.³⁻⁶ Our patient's case uniquely presented

with two morphologies: confluent reddish-yellow papules and an erythematous patch. Therefore, dermatologists should consider the possibility of metastases when evaluating cutaneous lesions in patients with a history of malignancy, regardless of morphology.

Cutaneous metastases represent advanced disease and portend a very poor prognosis. Data on survival time are limited. One retrospective review of SCCHN found the average survival time among patients after the development of cutaneous metastasis was 7.2 months; the 1-year survival rate was 0%.² In all 4 prior cases of a tonsillar primary, radiation or chemotherapy was offered with palliative intent.³⁻⁶ This is the first documented case in which checkpoint immunotherapy, with nivolumab, was pursued and resolution of skin findings was achieved.

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