

Case and Review

Oral Mycosis Fungoides: Report of 2 Cases and Review of the Literature

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Keywords

Oral mycosis fungoides · Mycosis fungoides · Cutaneous T-cell lymphoma · Case report

Abstract

Oral and laryngeal cutaneous T-cell lymphoma (CTCL) is rare and usually associated with poor prognosis. Here, we discuss 2 cases of oral CTCL that developed in heavily pretreated patients and provide a review of the literature. The first case is of a 46-year-old African American male with rapidly progressive disease, presenting with a lesion on his hard palate 6 months after being diagnosed with a CD4+CD8+ CTCL. His cutaneous disease was widespread with tumors on >80% of his body surface area. Unfortunately, the patient died 2 ½ years after his CTCL diagnosis and 7 months after developing the oral CTCL lesion. The second case is of a 38-year-old African American male with stage IIb CD3+CD4+CD30+ mycosis fungoides (MF), who developed a tumor on the hard palate 6 months after diagnosis. He received palliative radiation to the oral lesion and multiple lines of systemic therapy for pulmonary, laryngeal, esophageal, and gastric involvement. Biopsy of the gastric lesions showed a CD30+ T-cell lymphoma with the same clonal peak as in his skin but with large cell transformation. Brentuximab vendoin was started, and the patient is now in complete remission, 30 months later. From the 76 cases of oral CTCL that have been reported in the English language, six were of transformed MF. The most common sites affected were the tongue and palate, and the most common presentation were erythematous or ulcerated tumors, plaques, or nodules associated with dysphagia and pain. Oral CTCL typically occurs years after the initial diagnosis of CTCL and portend a poor prognosis with an average survival of just over 1 year after development of oral lesions.

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Historical Background

Cutaneous T-cell lymphoma (CTCL) is a term that encompasses various non-Hodgkin lymphomas of epidermotropic T cells. Mycosis fungoides (MF) comprises about 39% of all CTCLs, making it the most common subtype. Staging is dependent on the extent of skin involvement, and presence of atypical lymphocytes in lymph nodes, blood, and viscera as defined by the tumor-node-metastasis-blood classification, stratifying patients into nine stages (IA–IVB). CTCL has an unknown etiology. Diagnostic criteria are insensitive, and patients may often be undiagnosed for long periods of time [1]. The median age of diagnosis is in the mid-50s, tending to affect older patients who are male and those with darker skin tones [2]. A classic presentation includes waxing and waning erythematous, scaly, and/or itchy patches or plaques in non-sun-exposed areas. Some patients may also present with tumors or erythroderma. Early lesions are often preceded by non-diagnostic biopsies for many months to years [1]. Itch is common and can deeply affect the quality of life [3]. CTCL is mainly indolent, and most patients do not progress to later stages of the disease. However, disease progression is usually associated with a poor prognosis [4, 5]. The majority of patients present with stage I disease, and in these patients, MF is an indolent lymphoma with a 5-year disease-specific survival rate of 89–98% [5–7]. However, these T cells can also invade lymph nodes, blood, and other organs, thus having varied clinical presentations and prognosis. Extensive skin involvement, tumor stage disease, lymph node, and/or blood involvement, as well as other visceral involvement, are associated with later stages or more severe disease [8]. For example, extracutaneous involvement is more common [9] in those with tumors or generalized erythroderma [1]. Stage IVB disease, with visceral involvement, is uncommon. Even though any organ can be involved, typically the liver or spleen is affected. Patients with solid organ involvement (stage IVB disease) have a 5-year disease-specific survival rate of only 18% [5].

Introduction

Oral CTCL is rare. Since the publication of the first case in the late 1800s, there have been a total of 76 cases of oral MF reported in the English language [10–63]. Oral CTCL most commonly involves the tongue and/or palate and is usually treated with total skin electron beam radiation therapy. However, the features and clinical presentation of oral CTCL from prior case reports have not been previously summarized. Here, we report two additional cases of oral MF, one with large cell transformation, and give insight into the clinical presentation, survival, and the length of time for oral CTCL to appear after the development of cutaneous disease. The CARE Checklist has been completed by the authors for this case report and is attached as online supplementary material (for all online suppl. material, see <https://doi.org/10.1159/000530935>).

Case Report

Case #1

A 46-year-old African American male presented to our clinic after a 2-month history of tumors and plaques involving his face, neck, trunk, and extremities. These lesions were painful and pruritic and not responsive to topical corticosteroids. Biopsies of the back, neck, and scalp showed CD4⁺ and CD8⁺ epidermotropic T cells with a clonal T-cell receptor rearrangement diagnostic of MF. Less than 10% of the cells were positive for CD30. A positron emission tomography (PET) scan was significant for enlarged lymph nodes (≥ 1.5 cm) but showed no signs of visceral involvement. Peripheral blood did not show evidence of an aberrant T-cell population. The patient was thus diagnosed with stage IIB (T2NxM0B0) MF.

The patient received multiple lines of systemic therapy including bexarotene, brentuximab vedotin, gemcitabine, a CD30 chimeric antigen receptor T cell (CAR-T) product on a clinical trial, vorinostat, and mogamulizumab without significant improvement or durable responses and no significant adverse events. He had an excellent response to total skin electron beam therapy (TSEBT) twice, first with 15 Gy and the second time with 30 Gy. However, although he had almost complete skin clearing both times, the duration of response was on the order of months.

Six months after completing the second round of TSEBT (30 Gy), he had cutaneous progression and developed a lesion on his hard palate (as shown in Fig. 1) that was biopsy proven to be a T-cell lymphoma consistent with his MF. No large cell transformation was seen. He was started on oral etoposide with resolution of the lesion on his palate but not on his skin. He never developed other sites of visceral involvement but continued to have progression of his cutaneous disease with widespread plaque tumors on >80% of his body surface area. These were resistant to therapy, despite taking etoposide as prescribed and tolerating the medication well. After developing infectious complications, he transitioned to comfort care and died 2 ½ years after his MF diagnosis and 7 months after developing the oral MF lesion.

Case #2

Patient 2 is a 38-year-old African American male with a 4-year history of extensive cutaneous plaques and patches eventually progressing to widespread cutaneous tumors. At that time, he was diagnosed with CD3⁺CD4⁺CD30⁺ MF. The patient had no lymphadenopathy or visceral involvement. No positive clones were found in peripheral blood. Thus, at diagnosis, he was at stage IIb, T3N0M0B0.

The patient had disease progression while on systemic therapy with single agents brentuximab vedotin and gemcitabine. A complete clearance of his skin was achieved with 3,600 cGy of TSEBT, which has been durable on his skin. Despite this, 6 months after the radiation treatment, he developed an ulcerated tumor on the right hard palate. Biopsy of the mass showed a CD3⁺CD4⁻CD30⁻ lymphocytic infiltrate, different from the CD3⁺CD4⁺CD30⁺ phenotype of the prior skin biopsy. However, both skin and palate biopsies had identical clonal T-cell gene rearrangements consistent with involvement by his MF. There was no large cell transformation.

PET/CT done at the time the patient developed the tumor in the hard palate showed disease in the lungs, lymph nodes, and larynx. MRI of the brain and lumbar puncture were negative for central nervous system involvement. The patient started on dose-adjusted etoposide, prednisone, vincristine, cyclophosphamide, and doxorubicin with an initial partial response followed by regrowth of the tumor in his mouth after 4 cycles. Therapy was then switched to romidepsin, and even though there was a complete response in all other areas of involvement after two cycles, there was continued uptake in the oral mucosa, base of the tongue, and tonsils on PET scan. These were not responsive to 2 cycles of pralatrexate which he tolerated well. Ultimately, the patient received 30 Gy of radiation with complete resolution of the oral mass. Response lasted 4 months when the patient started to develop new lesions on the tongue outside of the radiation field (shown in Fig. 2). PET scan showed uptake in the base of the tongue, angle of the right mandible, pulmonary nodules, and subcutaneous lesions that subsequently completely resolved with 4 cycles of bendamustine. However, a PET scan done after the 5th cycle showed new esophageal involvement. He received 30 Gy of radiation to the esophagus for palliation of symptoms as it was the only site of disease. Three months later, he developed abdominal pain, and an EGD showed multiple gastric ulcers. Biopsy of these lesions demonstrated a CD30⁺ T-cell lymphoma with the same clonal peak as prior lesions but now with large cell transformation. At the time of writing this manuscript, 30 months after his initial diagnosis with MF, the patient has again achieved a complete remission with IV brentuximab vedotin therapy. Allogeneic transplant has been discussed with the patient, but thus far he has declined.



Fig. 1. Oral MF in patient 1.



Fig. 2. MF lesions on the tongue of patient 2.

Discussion/Conclusion

Upon review of the literature, oral CTCL was more common in men with a 1.6 male:female ratio (shown in Table 1). Race was only reported in 20 cases with more case reports in Caucasians (17) than in African Americans (2) or those of other races (1). The mean age at diagnosis of CTCL was 58 years old (range 12–85 years old). The most common type reported was MF ($CD4^+CD8^-$), followed by double-positive $CD4^+CD8^+$ MF. Only 6 cases of oral MF reported large cell transformation [54–56, 64]. Case 2 in this report will be the seventh case.

Table 1. Summary of reported characteristics of oral CTCL

Number of cases with oral MF	76
Sex (<i>n</i> = 65)	Total (%)
Male	40 (62)
Female	25 (38)
Male:female	1.6:1
Race, <i>n</i>	
Caucasian	17
African American	2
Other	1
Unknown	56
Age (<i>n</i> = 64)	
Mean in years (range)	57.8 (12–85)
CTCL type	Total (%)
MF	57 (75)
CD4 ⁺ CD8 ⁺	8 (10)
Transformed MF	6 (8)
Sézary Syndrome	3 (4)
CD4 ⁻ CD8 ⁻	2 (3)
Areas of involvement, <i>n</i>	
Tongue	37
Palate	35
Gingiva	19
Buccal mucosa	16
Tonsils	12
Pharynx	10
Esophagus	9
Larynx	7
Trachea	5
Uvula	4
Vestibule	2
Alveolar ridge	2
Primary lesion morphology, <i>n</i>	
Tumor	23
Plaque	17
Nodule	8
Papule	1
Secondary lesion characteristics, <i>n</i>	
Erythema	17
Ulcer	25
Firm	9
Edema	7

Table 1 (continued)

Erosion	6
Pseudomembrane	5
Necrosis	4
Soft/boggy	4
Leukoplakia	3
Perforation	1
Mobile	1
Gangrenous	1
Eruption	1
Fungating	1
Associated symptoms, <i>n</i>	
Dysphagia	14
Pain	11
Glossitis	7
Odynophagia	5
Hoarseness	1
Asymptomatic	2
Burning sensation	2
Painless	2
Difficulty in speaking	1
Nasal regurgitation	1
Length of time for oral CTCL to present from initial cutaneous lesions (<i>n</i> = 52)	
Mean in years (range)	6.4 years
Range	2 months –30 years
Outcome (<i>n</i> = 51)	
	Total (%)
Death	34 (67)
Alive	17 (33)
Causes of death (<i>n</i> = 33)	
	Total (%)
Sepsis	14 (42)
Advanced disease	11 (33)
Unknown	5 (15)
Other	3 (9)
Length of time from initial oral lesion to death (<i>n</i> = 30)	
Mean in months (range)	13.2 (0.5–48)
MF, mycosis fungoides.	

The most common sites affected by oral CTCL are the tongue and palate, consistent with what has been reported previously. The most common presentations of lesions in the oral cavity were tumors, plaques, and nodules that are erythematous or ulcerated. Plaques may be erythematous, edematous, and may often present as leukoplakia or with pseudomembranous changes. Nodules may be blue/purple in color, although pale lesions have also been reported. The most common symptoms associated with oral CTCL were dysphagia and pain.

Table 2. Characteristics of cases treated and not treated with total skin electron beam therapy

	TSEBT	Non-TSEBT
Number of cases	13	30
Age, years	60	56.9
Range	38–75	12–85
CTCL type	Total (%)	Total (%)
MF	7	17
Transformed MF	2	1
CD4 ⁺ CD8 ⁺	2	6
Unknown	2	0
Sézary syndrome	0	2
CD4 ⁻ CD8 ⁻	1	0
Length of time for oral CTCL to present from initial cutaneous lesions		
Mean in years	5.4	7.3
Range (months to years)	2–15	6–20
Outcome	Total (%)	Total (%)
Death	6 (43)	13 (57)
Alive	8 (57)	10 (43)
Causes of death	Total (%)	Total (%)
Advanced disease	3 (60)	4 (40)
Sepsis	1 (20)	5 (50)
Other	1 (20)	1 (10)
Length of time from initial oral lesion to death		
Mean in months (range)	10.3 (4–30)	10.5 (0.5–39)

TSEBT, total skin electron beam therapy.

On rare occasions, the oral lesions preceded cutaneous lesions, but in most cases, the patient had a known history of MF. The mean length of time for oral CTCL to appear after development of cutaneous disease was 6.4 years and ranged from 2 months to 30 years. Of the cases reported, 66% of patients were deceased, and the most frequent cause of death was due to sepsis (42%) or advanced disease (33%). Death occurred in a mean of 13.2 months (range: 2 weeks to 48 months) after initial presentation of the oral lesions.

In both of our patients, the oral lesions occurred shortly after completion of TSEBT. We were curious about this coincidence, so in the literature review, we paid close attention to prior treatment regimens, especially prior TSEBT (as shown in Table 2). There are a total of 43 cases that explicitly mention prior therapies received before the development of oral lesions. Of these, 13 cases (30%) received TSEBT (TSEBT group) [27, 28, 31, 35, 36, 38, 44–46, 54, 55, 57] and 30 cases (70%) did not receive TSEBT (non-TSEBT group) [13, 15, 16, 19, 21, 22, 26, 29, 33, 34, 36, 37, 39, 42, 43, 45, 47–50, 52, 53, 56, 58, 60–63] prior to developing oral lesions. The time for oral CTCL to develop after the initial presentation of CTCL was 5.4 years and 7.3 years for the TSEBT and the non-TSEBT groups, respectively. Only 6 cases in the TSEBT group and 13 cases in the non-TSEBT group reported death rates. Death rates were less in the TSEBT group (43%) and 57% in the non-TSEBT group. The length of time from the initial oral lesion presentation to death was similar among both groups, with 10.3 months for the TSEBT group versus 10.5 months for the non-TSEBT group. These numbers need to be interpreted

with caution, however, as establishing a correlation between TSEBT and non-TSEBT groups would need more controlled studies. There are several factors that could influence these variables, such as prior therapies received, disease subtype, and stage of disease.

Overall, MF lesions in the oropharynx are rare. Here, the characteristics of patients reported with oral MF reported so far are summarized and two additional cases of oral MF are presented, one with large cell transformation. Oral CTCL typically occurs years after the initial diagnosis of CTCL, but when present, they portend a poor prognosis with an average survival of just over 1 year after development of oral lesions.

Statement of Ethics

Ethical approval was not required for this study in accordance with local/national guidelines. Written informed consent was obtained from the patient's next of kin (Case #1) and patient (Case #2) for publication of the details of their medical case and any accompanying images.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

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Author Contributions

C.A.S., E.B.V., and A.W.B. participated in manuscript conception and design. C.A.S., A.B.D., and A.W.B. participated in data collection. C.A.S., A.B.D., E.B.V., and A.W.B. contributed to intellectual content, analysis, and manuscript preparation and review.

Data Availability Statement

All data generated or analyzed during this study is included in this article and its online supplementary material. Further inquiries can be directed to the corresponding author.

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