Mycosis Fungoides Of The Tongue

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Citation

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Abstract

Although oral mycosis fungoides lesions have been rarely reported in the literature, incidental autopsy findings indicate a higher occurrence. We present two patients with mycosis fungoides of the tongue. Both patients had advanced tumor stage mycosis fungoides when they each developed a single tongue lesion. Tongue involvement has been associated with poor prognosis.

INTRODUCTION

Mycosis fungoides is a disease of clonal CD4+/CD45+ helper memory lymphocytes with an affinity for the skin. Of interest, mucosal membrane involvement is rarely encountered. We present two patients with mycosis fungoides of the tongue. The first patient had chronic lymphocytic leukemia and subsequently developed a tongue ulcer. The second patient had multiple biopsies over 13 years read as atopic dermatitis before a diagnosis of mycosis fungoides with large-cell transformation was made. Biopsy of both patients' tongue lesions revealed mycosis fungoides of the tongue, which often portends poor prognosis.

CASE ONE

A 70 year-old white male, with diabetes mellitus and a three-year history of B-cell chronic lymphocytic leukemia (CLL), presented with a two-year history of “itchy, scaly, red skin.” The patient had a four-month history of large tumors on his face, scalp, chest, and shoulders. On examination, he had erythroderma, keratoderma, and well-circumscribed, dome-shaped tumors on his scalp, chin, and chest. There were numerous pustules on the left scalp. Multiple scaly ring lesions on the anterior trunk were positive for dermatophyte fungi. The patient had severe scaling of his feet and hands, yellow discoloration of his nails, and bilateral ectropion with purulent discharge. Baseline involved body surface area was 27.15%, composed of 22% patches, 3.5% plaque, and 1.65% tumor.

Lesional biopsies demonstrated a superficial dermal infiltrate of medium and large atypical lymphoid cells, many with marked nuclear irregularity, and extensive epidermotropism with formation of Pautrier's microabscesses. This infiltrate was CD3+, CD4+, CD25+ and CD30+. These findings were consistent with large cell transformation of both plaque and tumor stage mycosis fungoides (MF). A deeper dermal infiltrate extending into the subcutaneous fat was composed of small, round lymphocytes with clumped chromatin and scant cytoplasm. These cells were weakly positive for CD5, CD79a, and CD23, supporting a B-cell CLL/small lymphocytic lymphoma immunophenotype coexistent with MF.

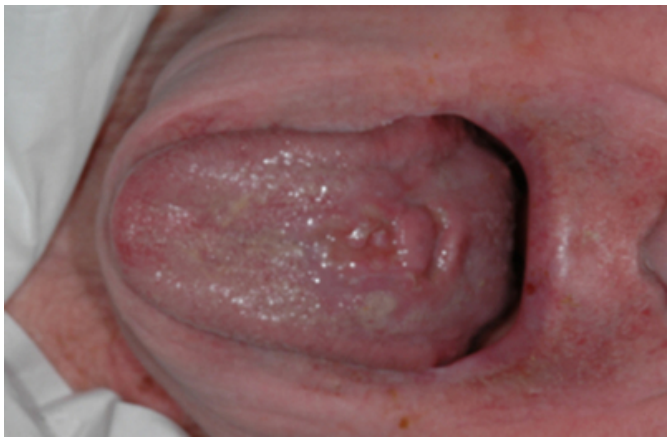
Routine laboratory tests were consistent with this dual diagnosis: elevated lactic dehydrogenase (1085 IU/L), elevated B2 microglobulin (3.2 MG/L), and elevated white blood cell count (64.3 K/UL) with 85% atypical, enlarged lymphocytes with irregularly clumped chromatin. Flow cytometry of peripheral blood revealed both T- and B-cell clones were CD25+. CT scans showed enlarged pelvic and abdominal lymph nodes. Skin cultures grew methicillin resistant staphylococcus aureus.

Levofloxacin, muciprocin, terbinafine, and econazole were initiated for the treatment of MRSA and tinea corporis. The patient's CLL responded to Denileukin diftitox (Ontak); unfortunately, his MF tumors progressed. Suberoylanilide hydroxamic acid (SAHA) initially stabilized the lesions, but the patient eventually worsened. Partial response was achieved with Gemcitabine (Gemzar), but when dosage was lowered secondary to grade III neutropenia, the patient's disease subsequently progressed. Finally, local radiation therapy resulted in complete response and resolution of skin tumors.

Two years after initial presentation, while maintaining his MF with oral bexarotene therapy, the patient noted a painful lesion on his tongue that interfered with his ability to eat.

The 1.5cm ulcer, located on the dorsal-central aspect of the tongue, was tender to palpation (Figure 1). There were no other masses or lesions on the patient's oral mucosa.

Figure 1



Cultures of the tongue grew Candida albicans and MRSA. Biopsy showed transformed mycosis fungoides (Figure 2). The infiltrate was CD3+, rare CD30+, and CD20-. The patient also had a low CD4 (52UL) and CD8 (92 UL) count. He was started on trimethoprim-sulfamethoxazole for PCP prophylaxis and fluconazole for the Candida infection. Because its central location and proximity to the lingual artery and hypoglossal nerve, excision was not favored and local radiation therapy was successful.

CASE TWO

A 56 yo black female presented with a 14-year history of pruritic, hyperpigmented patches on her legs. Multiple biopsies over the first 12 years of disease were read as atopic dermatitis or psoriasis. She was initially treated with only topical steroids, UVB, and PUVA. Because of suspicion for mycosis fungoides, she was eventually treated with oral bexarotene but could not tolerate this secondary to elevated lipids. One year before presentation, she developed large draining tumors on her trunk and groin. Biopsy at that time confirmed mycosis fungoides with large cell transformation: confluent sheets of large cells with highly irregular nuclear contours and frequent mitotic figures infiltrated the dermis and formed Pautrier's microabscessess. These cells stained positive for CD30 and CD25, and negative for CD3 and CD20. Monoclonal T-cell receptor gamma chain gene rearrangements were detected by PCR.

On her initial visit, she had generalized hyperpigmented plaques and multiple large prurulent tumors scattered over her trunk and extremities. Her total body surface area affected was 86 percent, composed of 2% patches, 80% plaques, and 6.4% tumors. Swab cultures of the tumors grew many staphylococcus aureus. By flow cytometry, the absolute CD4 count was 94, and the absolute CD8 count was 59. CT scans showed bulky axillary lymph nodes and enlarged superficial inguinal lymph nodes with MF by biopsy. Bone marrow biopsy was negative.

This patient received 6 cycles of cyclophosphamide, methotrexate, etoposide, and dexamethasone with progression of disease ([1]). Three courses of Gemzar was also unsuccessful. Total skin electron beam radiation resulted in partial response, complicated by multiple bacterial superinfections. She received boost radiation to unresponsive perineal tumors and to a biopsy-confirmed MF lesion on the tongue. Around this time, she developed epiglottitis and, because of difficulty swallowing, experienced a 40-pound weight loss. At the end of radiation, she had improvement in her dysphagia and partial response of all tumors. Unfortunately, one month later her tumors returned. Decadron and Roxicet elixir were somewhat helpful to alleviate her dysphagia. Fifteen years after her initial atopic skin symptoms began and four months after developing tongue involvement, she died.

DISCUSSION

We report two cases of mycosis fungoides of the tongue. Despite two independent studies finding oral MF lesions in 7% and 22% of CTCL patients at autopsy ([2,3,4]), clinical reports are rare. Sirois found only eight out of 824 patients seen at a CTCL center from 1968-1993 had oral lesions, an incidence of less then 1% ([5]). A recent review of the English language literature found only 31 reported cases of mycosis fungoides of the oral mucosa ([6]), primarily reported in the dental and oral surgery literature. This disparity between autopsy and clinical findings suggests oral MF may be subclinical or missed on examination.

The most common reported sites of oral mycosis fungoides involvement are the tongue and palate ([6]). Clinical presentation varies and includes ulcerated tumors, indurated plaques, papules, leukoplakia-like lesions, nodules, and multiple erosions ([4,5,6,7,8]). Dysphagia and odynophagia are commonly associated ([9]). Oral lesions appear to be a late manifestation of mycosis fungoides that arise, on average, eight years after the onset of cutaneous symptoms ([6]). In two cases, the oral lesions were found on initial examination before signs of cutaneous involvement; however, there is doubt about whether these lesions were actually mycosis fungoides ([6,10,11]). The tongue lesion of our first patient

appeared approximately four years after the onset of his initial cutaneous symptoms and two years after his diagnosis of mycosis fungoides. The tongue lesion of our second patient appeared 15 years after her initial cutaneous symptoms and one year after her diagnosis. In both patients, the development of tongue involvement occurred after the patients had failed multiple therapies.

The differential diagnosis of oral mycosis fungoides includes geographic tongue, benign eosiniphilic ulcers of the oral mucosa, trauma, lymphomatoid papulosis ([12]), malignancies, and infection. Squamous cell carcinomas are usually confined to the lateral edge of tongue, ventral surface of the tongue, or floor of the mouth. In this central dorsal location, infectious etiology was more probable. Histoplasmosis, herpes simplex, cytomegalovirus, tuberculosis, syphilis, aspergillus, cryptococcus, and candida albicans should be considered, especially in an immunocompromised patient ([5],[13]). A biopsy and culture is necessary to provide a definitive diagnosis. Histologically, the oral lesions of mycosis fungoides resemble the cutaneous lesions. Band-like infiltrates of atypical lymphocytes, exocytosis, and Pautrier's microabscesses are typical findings ([4],[6]).

In the reported literature, oral involvement is indicative of a poor prognosis. The mean survival time is 9.6 months from presentation of the oral lesion ([3]). One-half of patients die within one year, and almost all within three years ([5]). Historically, these lesions have been excised and treated with potassium iodine ([9]). Today, systemic chemotherapy, localized radiation therapy, and brachiotherapy can be successful, although lesions may recur ([9],[15]). Before radiation, patients should see a dentist: radiation in the setting of periodontal disease can result in osteonecrosis. Also, a mouth-opening/tongue-depressing stent can be made to focus radiation on the lesion. Thorough exam and early identification of oral MF lesions may increase the efficacy of treatment.

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