SKIN

BRIEF ARTICLE

A Case of Systemic Fungal Infection Diagnosed After Tongue Mass Biopsy

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ABSTRACT

Introduction: Coccidioidomycosis is a fungal infection transmitted by inhalation of spores that primarily presents with pulmonary symptoms, but disseminated disease may manifest in the skin, subcutaneous tissue, joints, bone, and meninges. It is common in its endemic regions of the southwest United States as well as parts of Mexico and South America.
Case Presentation: We present a unique case of systemic coccidioidomycosis diagnosed after a tongue mass biopsy for suspected carcinoma revealed granulomatous inflammation and the presence of fungal organisms. The patient reported a recent self-limiting rash and a hospitalization one year prior due to presumed community-acquired bacterial pneumonia that may, in retrospect, have suggested fungal disease. This case demonstrates an important potential presentation of disseminated coccidioidomycosis that should be included in dermatologists' differential diagnoses for non-healing tongue masses.

INTRODUCTION

Coccidioidomycosis is a fungal infection transmitted by inhalation of spores that primarily presents with self-limiting pulmonary symptoms or pneumonia, but may also produce night sweats, fatigue, and pulmonary nodules or hilar/mediastinal lymphadenopathy on radiography.[3,11] However, disseminated disease may manifest in the skin, subcutaneous tissue, joints, bone, and meninges.[2] It is becoming increasingly common in its endemic regions of the southwest United States as well as parts of Mexico and South America; in fact, the incidence of coccidioidomycosis in California increased approximately 800% from 2000 to 2018.[1,11] Our patient presented with a persistent, enlarging lateral tongue mass that raised suspicion for malignancy. However, a diagnosis of coccidioidomycosis was made after biopsy revealed granulomatous inflammation and the presence of fungal organisms. The patient reported a recent history of a self-limiting rash as well as a hospitalization one year prior for presumed community-acquired bacterial pneumonia that may, in retrospect, have suggested fungal disease. This case demonstrates an important potential presentation of disseminated coccidioidomycosis that should be included in dermatologists' differential diagnoses for non-healing tongue masses.

CASE PRESENTATION

A man in his 50s presented to our clinic in southern California with a 3-month history of increasing oral pain and enlarging lateral tongue mass. He did not smoke or drink alcohol and denied fevers, chills, shortness of breath, cough, nausea, vomiting, diarrhea, or dysuria. The patient reported a bilateral upper and lower extremity rash one month ago with intermittent, sharp RUQ pain that resolved spontaneously. One year ago, he had a hospital admission due to 30-pound weight loss and spiking fevers, with a diagnosis of community acquired bacterial pneumonia and endocarditis. His past medical history included past intravenous drug use (IVDU) 15 years ago, untreated Hepatitis C infection, and latent tuberculosis infection treated with isoniazid for 1 year. He had no history of diabetes mellitus and tested negative for human immunodeficiency virus. Physical exam demonstrated a 3x3x2 cm raised nodular left lateral tongue mass with ulcerated borders that was not tender to palpation (**Figure 1**). The rest of the physical exam was unremarkable, including a soft neck with no palpable lymphadenopathy.

Chest CT with contrast showed multiple necrotic mediastinal lymph nodes and mass-like consolidations along broncho-vascular bundles of the left lower lung with sub centimeter, near-diffuse, centrilobular, and tree-in-bud nodules suspicious for a concurrent infectious process.

A tongue mass biopsy performed for evaluation of possible carcinoma is pictured (**Figure 2)**. The H&E-stained tissue showed multinucleate giant cell formation along with mixed inflammation in the background indicative of granulomatous inflammation. The overlying squamous epithelium displayed pseudoepitheliomatous hyperplasia. Silver staining (GMS) highlighted organisms with a thick-walled spherule containing endospores, later identified as coccidioidomycosis (**Figure 3**).

DISCUSSION

Our patient presented with a 3-month history of a non-healing lateral tongue nodular mass with indurated borders that raised our concern for a malignant neoplasm. However, histologic evaluation revealed coccidioidomycosis. Interestingly, our patient's medical history included an admission for a presumed community acquired pneumonia and a skin rash that may, in retrospect, have suggested a systemic fungal disease. Additionally, our patient lived in a Coccidioides endemic area.[1,2]

As in our patient, chest CT in coccidioidomycosis often demonstrates multiple nodules. The diagnosis of primary pulmonary coccidioidomycosis is suggested by a history of night sweats or profound fatigue as well as peripheral-blood eosinophilia and hilar or mediastinal lymphadenopathy on chest radiography. In most patients, primary pulmonary coccidioidomycosis usually resolves without sequelae in several weeks. However, a variety of pneumonic complications may ensue. Pulmonary nodules are residua of primary pneumonia, and coccidioidal pulmonary nodules can be difficult to distinguish radiographically from pulmonary malignancies.[3]

When encountering any oral fungal infections, it is imperative to explore the possibility of an underlying immunocompromised state. Evaluation may include a complete blood count, urine

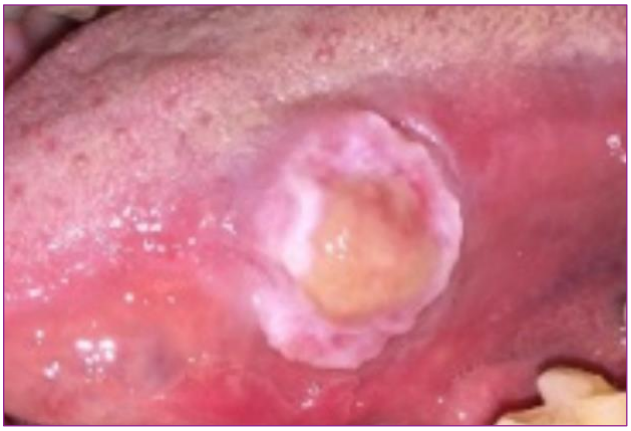

Figure 1. 3x3x2 cm raised nodular left lateral tongue mass with ulcerated borders that was not tender to palpation

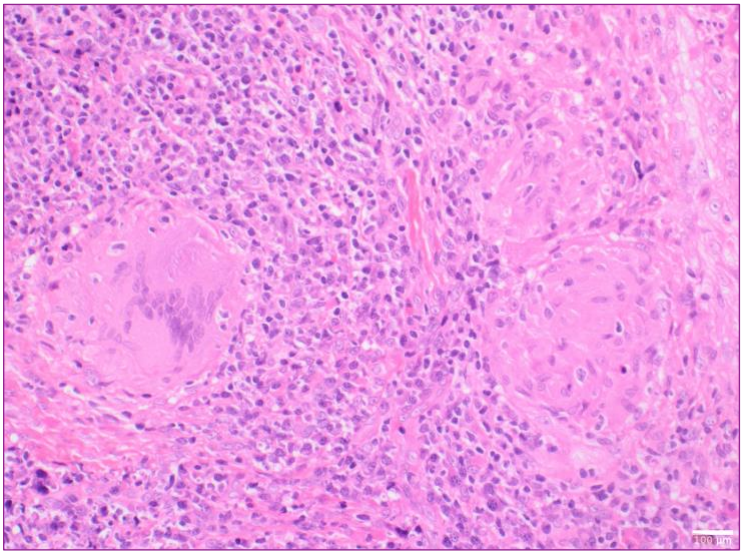

Figure 2. The H&E-stained tissue showed multinucleate giant cell formation along with mixed inflammation in the background indicative of granulomatous inflammation. The overlying squamous epithelium displayed pseudoepitheliomatous hyperplasia

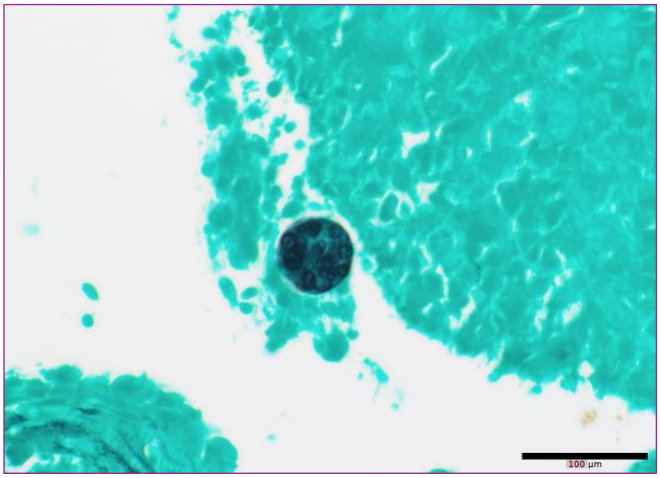

Figure 3. Silver staining (GMS) highlighted organisms with a thick-walled spherule containing endospores, later identified as coccidioidomycosis.

analysis, white blood cell count, sputum culture/Gram strain, glycosylated hemoglobin (HBA1c), HIV levels, CD4 count, albumin/prealbumin, and possibly fungal or blood cultures.[4] Additionally, brush biopsy/smear or incisional biopsy may be obtained for accessible lesions.

Clinical observations and data from animal studies strongly support a critical role of robust cellular immune response in the host's control of coccidioidomycosis. Necrotizing granulomas containing spherules are typically identified in patients with resolved pulmonary infection. In disseminated disease, granulomas are poorly formed or do not develop at all, and a poly-morphonuclear leukocyte response occurs frequently.

Currently, diagnosis can be established using immunologic assays, culture, or histopathology of tissues involved.[3] Most clinical infections are diagnosed serologically in the setting of a compatible clinical syndrome. Several techniques are available, including the traditional tuberculin precipitin and complement fixation assays, immunodiffusion, and enzyme immunoassay to detect IgM and IgG antibodies. Immunodiffusion for the detection of IgG and IgM-specific antibodies is a preferred test for detection of exposure to C. immitis with high specificity. Complement fixation tests for IgG-specific antibody are most useful in immunocompetent patients, both for diagnosis and long-term disease assessment.[5] Molecular assays and DNA probes for identifying species that cause specific fungal infections still require additional research to validate use as a standard diagnostic tool.[6] Nucleic acid amplification is still being evaluated and developed for use in clinical diagnosis, with several centers using novel primers. Its potential ability to effectively detect organisms in culture-negative samples would be welcome but is yet unproven.[7-10]

Unfortunately, the patient did not return to the clinic and was lost to follow-up.

Conflict of Interest Disclosures: None

Funding: None

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