Unexpected Blastomyces dermatitidis Etiology of Fungal Sinusitis and Erosive Palatal Infection in a Diabetic Patient

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We present what is believed to be the initial report of hard-palate infection caused by Blastomyces dermatitidis. The organism was cultivated from biopsy material obtained from a diabetic patient presenting with complaints of headache and malaise. Radiologic findings revealed a malignant-appearing soft-tissue mass with paranasal sinus base destruction.

CASE REPORT

A 79-year-old female presented for evaluation of a 4- to 5-day history of malaise and bilateral frontal lobe headache. Associated pain was characterized as moderate to severe. The patient was withdrawn and uncooperative during the examination. Weakness, dizziness, loss of appetite, and dysphagia also characterized the course of illness. Family members intimated that the patient had lost 30 to 40 pounds over the previous month. Past medical history was significant for type 2 diabetes mellitus, aortic valve replacement, depression, osteoarthritis, and hyperlipidemia. The patient was a nonsmoker and did not consume alcohol. No history of chronic headaches, cerebrovascular accident, transient ischemic attack, and psychiatric or neurologic maladies was revealed. At the time of presentation, the patient resided in a Wisconsin assisted-living facility. The patient was also a past resident of Tennessee, though the timing of this was unclear.

Vital signs were stable upon presentation (temperature, 98.3°F; heart rate, 67 beats per min; blood pressure, 143/66), with the exception of slight tachypnea (20 inhalations per min). Pulse oximetry was 98% on 2 liters of supplemental oxygen. A chest X-ray indicated mild chronic obstructive pulmonary disease without acute disease. The patient had elevated laboratory values for peripheral leukocytes (15,800/µl, with increased neutrophils [79.0%] and decreased lymphocytes [11.0%] upon differential), serum glucose (226 mg/dl; upper limit of normal, 99 mg/dl), serum C-reactive protein (135.4 mg/liter; upper limit of normal, 8 mg/liter), and Westergren sedimentation rate (92 mm/h; upper limit of normal, 20 mm/h). A decreased serum albumin level (2.8 g/dl; lower limit of normal, 3.2 g/dl) was also documented. Two sets of blood cultures yielded no growth. Due to leukocyte esterase and microscopic leukocyte (5 to 10 per high-power field) findings from a urinalysis, diagnosis of a urinary tract infection was entertained, but culture was not pursued. The patient was treated with empirical vancomycin at 1,250 mg administered intravenously (i.v.) every 12 h (q12h) and levofloxacin at 750 mg i.v. q48h and subsequently discharged.

During the hospitalization, the physical finding of an approximately 4-cm-diameter soft granulomatous mass on the hard palate of the posterior pharynx with mild anterior cervical lymphadenopathy prompted outpatient follow-up. An initial maxillofacial computed-tomography (CT) scan exhibited findings most consistent with chronic paranasitis with extensive opacification of the ethmoid and sphenoid sinuses. Chest radiology was noncontributory. Follow-up maxillofacial radiology revealed a malignant-appearing soft-tissue mass in the posterior aspect of the hard bony palate, with slight infiltration and destruction of the base of the paranasal sinuses (Fig. 1).

At the time of surgical intervention, differential diagnosis included squamous cell carcinoma, metastatic disease, and adenoid cystic carcinoma of the palate. A biopsy specimen excised from the hard palate (Fig. 2) revealed an abundance of granulation tissue, an abundance of inflammatory cells (primarily neutrophils), and rare multinucleated giant cells. Observation of innumerable broad-based budding yeast forms (Fig. 2), subsequently demonstrated to be Gomori methenamine silver stain positive and mucicarmine stain negative, narrowed the preliminary differential diagnosis to fungal disease caused by yeasts (including blastomycosis). This impression was supported by negative results for Cryptococcus neoformans serum antigen testing (1 day postbiopsy) and reactive complement fixation and Blastomyces dermatitidis-specific antigen results available 7 and 10 days postbiopsy, respectively, from reference laboratories. Antigen was quantitated at 12.49 ng/ml from urine (moderately positive reference range, 2.0 to 14.7 ng/ml; MiraVista Diagnostics, Indianapolis, IN). Laboratory diagnosis was confirmed by cultivation of characteristic B. dermatitidis mycelial growth from the biopsy specimen following 13 days of incubation on mycobiotic agar (Remel, Lenexa, KS) in 30°C ambient air and subsequent oligonucleotide hybridization with B. dermatitidis-specific rRNA (Accuprobe Blastomyces Dermatitidis Culture Identification Test; Gen-Probe, Incorporated, San Diego, CA). No fungal studies of respiratory secretions were undertaken.

The patient received intravenous liposomal amphotericin B at 5 mg/kg of body weight daily for 6 weeks; step-down fluconazole (1) was administered through a percutaneous gastrostomy tube (400 mg q24h), as additional lesions on her scalp and right foot were also culture positive for B. dermatitidis. Fluconazole was sub-
stituted for itraconazole within the step-down therapeutic component because the patient had poor oral intake and was less likely to tolerate and/or absorb itraconazole liquid formulation. Moreover, high-dose fluconazole regimens have been shown to be effective in the management of non-life-threatening blastomycosis (2, 3). The patient exhibited significant clinical resolution of palatal findings following approximately 4 weeks of amphotericin B therapy. However, final efficacy of the combination antifungal therapy for the palatal blastomycosis could not be determined, as the patient expired less than 3 months later due to myocardial infarction.

The dimorphic fungus *B. dermatitidis* typically exists in warm, moist soil of wooded areas that is rich in organic debris (4–7). While specific gender, season, age, race, or vocation is not typically predictive of the onset of blastomycosis, exposure to soil often provides a common link in reports of sporadic disease and outbreaks (8). Regions of Wisconsin and Tennessee have been classified as areas of high endemicity for blastomycosis (9).

Up to half of individuals infected with *B. dermatitidis* develop an asymptomatic illness. The organism has the potential to affect nearly every organ system during chronic disease (8). Studies of clinical blastomycosis published between 1956 and 1972 reported pulmonary, cutaneous, bone, and genitourinary involvement rates of 52% to 90%, 38% to 80%, 7% to 48%, and 10% to 33%, respectively (10–15). A paradigm shift toward mostly pulmonary disease has occurred in more-recent assessments. A total of 70% of blastomycosis cases in a Canadian survey revealed isolated pulmonary involvement (16). A total of 77% to 91% of single-manifestation blastomycosis in two United States regions of endemicity (17, 18) had pulmonary involvement, while between 0% to 3% and 4% to 6% had exclusive bone and cutaneous involvement, respectively. In their analysis of 326 blastomycosis cases, Chapman et al. (18) reported overall cutaneous and bone involvement rates of only 18% and 4%, respectively.

Blastomycosis has the potential to affect most bones, though skeletal disease is typically noted in long bones, vertebrae, and ribs (19). The organism preferentially infects metaphyseal and epiphyseal portions of the bone (20). An approximately 3-decade survey of skeletal blastomycosis at a United States medical center revealed 31 cases; of those cases, 7 (23%) showed skull and facial bone involvement. However, no specific mention was made of palatal involvement (20). With respect to the current case report, a PubMed (United States National Library of Medicine/National Institutes of Health) search utilizing permutations of the terms blastomycosis, *Blastomyces dermatitidis*, palatal, soft palate, and *B. dermatitidis* etiology. This search found two case series of oral South American blastomycosis (*Paracoccidioides brasiliensis* etiology) in the dental literature (21, 22).

The two papers shared the common theme of chronic, ulcerative *P. brasiliensis* lesions in Brazilian patients presenting as the first signs and symptoms of South American blastomycosis. de Almeida et al. (21) reported on the clinical course of a patient who presented with oral pain from the maxillary left quadrant and of a second patient with persistent mouth ulcers for several months. Oral ketoconazole therapy brought about disease regression and subsequent resolution within 2 to 4 months. Of 36 patients with
painful, chronic proliferative or ulcerative oral lesions in the series described by Sposto et al. (22), 17 (47%) exhibited disease in the palate and 23 (64%) had subsequent pulmonary involvement. Clinically apparent oral lesions were confirmed via histologic studies. Additional reports have described palatal paracoccidioidomycosis in United States residents at least 1 decade following residence in Venezuela or Brazil (23, 24).

Reder and Neel (25) reviewed 102 cases of blastomycosis at a United States referral hospital over a 10-year period that were confirmed by culture or histologic studies. Twenty-three cases had otolaryngologic manifestations; among these, nearly 70% had skin and mucosal involvement (primarily in the head and neck). Of the subset, 22% had laryngeal involvement. Histopathologic and gross features of laryngeal lesions resembled those of well-differentiated squamous cell carcinoma. However, no data regarding palatal \textit{B. dermatitidis} disease were described. Within the 23-patient subset, 17 (74%) had concomitant pulmonary involvement. A total of 83% of patients received either amphotericin (15 patients) or ketoconazole (4 patients) as a primary antifungal regimen. The male/female ratio for otolaryngeal blastomycosis was 2.8:1 in this series.

In conclusion, we present a case of erosive palatal blastomycosis in the context of disseminated disease without acute respiratory distress. This presentation is unusual for a number of reasons. First, extrapulmonary blastomycosis is typically observed with active pulmonary infection (8). Second, \textit{B. dermatitidis} currently has a lesser predilection for skeletal sites than has been described in past literature. Moreover, no specific reports of palatal blastomycosis have been documented. Finally, fungal etiologies of sinus tract disease in diabetic patients commonly include \textit{Aspergillus} spp. and those involved in rhinocerebral zygomycosis/mucormycosis (26, 27). Clinicians practicing in areas of \textit{B. dermatitidis} endemcity should include blastomycosis in the differential diagnosis of oral/palatal soft-tissue masses.

REFERENCES


