Primary nasal cutaneous blastomycosis in an immunocompetent patient from a nonendemic area

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INTRODUCTION

Infection with *Blastomyces dermatitidis* can take many forms and has been called the great pretender or the endemic mimic.[1,2] Primary cutaneous blastomycosis can present as an exophytic, verrucous growth, a hyperkeratotic plaque, or an exudative ulcer. It has been misdiagnosed as pyoderma gangrenosum, verruca, squamous cell cancer, and keratoacanthoma.[1,2] We present a primary intranasal and cutaneous case of blastomycosis, with subtle clinical findings, from an area where *Blastomyces* sp. is not known to be endemic.

CASE REPORT

A 67-year-old woman presented with a 7-month history of a burning, stinging pain in the right nostril with erythema and edema. She had been using fluticasone propionate for many years for allergic rhinitis. Her history was significant for basal cell cancer of the face that was previously treated with Moh's micrographic surgery, papillary carcinoma of the thyroid, hypercholesterolemia, and hypertension. Despite treatment, there was progressively worsening erythema, edema, and rhinorrhea. On examination, in the right nasal vestibule, there was a mildly erythematous, hyperkeratotic verrucous plaque extending from the columella to just over the nasal verge (Fig 1). A punch biopsy was done for a presumptive diagnosis of squamous cell cancer or verruca. Histopathologic examination found pseudoepitheliomatous hyperplasia and granulomatous inflammation with round-to-oval budding yeast forms with refractile cell walls in the cytoplasm of giant cells, which was consistent with blastomycosis (Fig 2). Tissue culture grew a dematiaceous mold, which was considered a contaminant and was not further characterized. A sinus computed tomography scan and a chest radiograph were normal. A diagnosis of cutaneous and intranasal blastomycosis was made based on a typical clinical presentation and the consistent histopathology.

The patient, a physician, lived in San Francisco, was HIV negative, had no history of inoculation trauma, and had never traveled to endemic areas. Her only exposure to soil and damp foliage was gardening in San Francisco.

Voriconazole was begun at 400 mg orally twice a day for 2 days, then 200 mg orally twice a day. A plan was made for 3 to 6 months of treatment. Her nasal symptoms resolved at 2 weeks, and the nasal lesion resolved at 4 weeks. Because of side effects of nausea, numbness, refractory rosacea, and peripheral dysesthesia, the voriconazole was stopped at 6 weeks. Four weeks after the voriconazole was discontinued, the nasal lesion and nasal symptoms recurred. Treatment was then begun with itraconazole, 200 mg orally twice a day. It was continued for 3 more months and then stopped because of the mineralocorticoid side effects of refractory hypertension and edema with mild alanine transaminase elevation. Repeat biopsy was negative for fungal elements. There has been no recurrence of the nasal lesion in more than 1 year (Fig 3).

DISCUSSION

Blastomycosis is primarily a disease of North America and occurs in the states that border the

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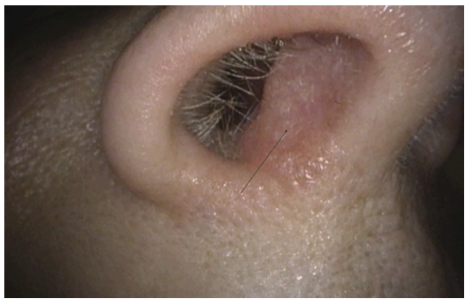

Fig 1. Exophytic verrucous lesion extending from nasal septa to just over the nasal columella.

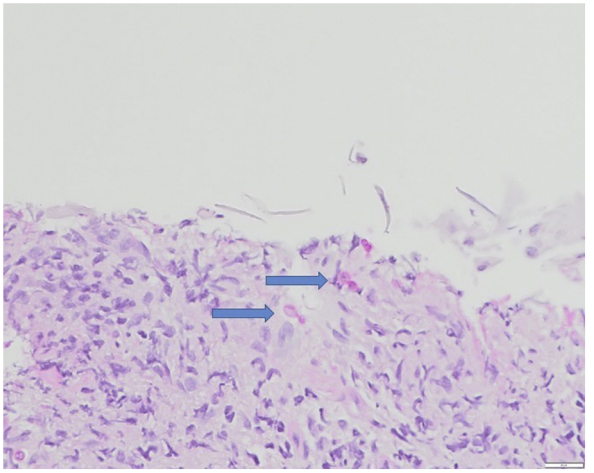

Fig 2. Granulomatous infiltrates. Arrows show scattered budding yeast forms 809 microns. (Hematoxylin-eosin stain; original magnification: ×60.)

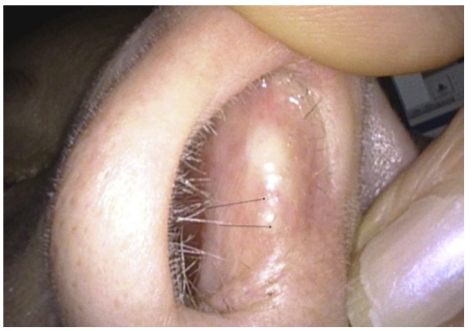

Fig 3. Lesion resolution posttreatment.

Great Lakes, the Ohio River, and the Mississippi River valleys. It is a thermally dimorphic fungus that grows as a mold in the environment and as a budding yeast in tissue.[1,2] It thrives in areas of wet earth enriched with decaying organic debris and animal droppings.[1-3] Sporadic cases from nonendemic areas are thought to occur from travel, endemic fomite transfer to nonendemic areas, or from latent infection in immunosuppressed hosts.[2,4] Most cases of blastomycosis are caused by 2 species of thermally dimorphic fungi—*B dermatitidis* and *Blastomyces gilchristii*.[2,3] Blastomycosis is not a reportable illness in California, and the last series in California was of 28 cases reported in 1967 with the caveat that "a careful study of history will reveal that a residence or visit to a known endemic area can be found."[5] Careful review in our patient, an excellent historian, could not find even a remote visit to an endemic area. The diagnosis of fungal infections without definitive culture is of course always challenging. Blastomycosis is a broad-based budding yeast; a few narrow-based buds were seen in this case. Blastomycosis species may appear narrow-based when they split or when buds are viewed tangentially. The appearance of narrow-based budding yeasts also raised the possibility of an Exophilia species. However, the size of the yeast forms and the clinical characteristics of this case made this seem less likely. A recent report considered the possible impact of climate change on the incidence and severity of endemic fungi through territorial expansion and inhalation of higher loads of fungal spores.[6] Benedict et al[3] suggest continued efforts to define true areas of endemicity and to carefully consider mycoses in other regions that are "not known to be endemic." If further studies find that *Blastomyces* are commonly found in areas of California, then this could help clinicians make more timely diagnoses. Our patient had also been using fluticasone for many years; fluticasone has been associated with increased risk of oropharyngeal candidiasis.[7] No cases of blastomycosis associated with inhaled steroids have been reported, but we suspect that local immunosuppression may have played a role in this case. Itraconazole, 200 to 400 mg/d is generally recommended for primary cutaneous blastomycosis. It often responds rapidly, within 2 weeks, but treatment may need to be continued for up to 6 months to clear and prevent relapse.[8,9] Newer triazoles, voriconazole, or posaconazole are options when concerns about drug resistance or absorption issues arise. Itraconazole may cause mineralocorticoid excess with pseudohyperaldosteronism by inhibition of the peripheral cortisol oxidizing enzyme, 11Beta-HSD2. Posaconazole may also cause mineralocorticoid excess by inhibiting steroidogenic oxidizing enzyme, CYP11B1.[10] Mineralocorticoid side effects are not seen with voriconazole. The absorption of voriconazole is not affected by the stomach's acidic pH and may be more bioavailable, whereas posaconazole has been used in refractory cases of pulmonary blastomycosis.[8,9] Regardless, careful assessment of all the patient's current

medications should be completed to assess drug interactions and effects on concomitant medical conditions. Itraconazole, voriconazole, and posaconazole can prolong the QT interval, exasperating existing QT interval conditions.[10] Itraconazole has negative inotropic effects that can worsen symptoms of heart failure.[10] Additionally, most azole antifungals have known drug-drug interactions with fairly common medications such as HMG-CoA reductase inhibitors, dihydropyridine calcium channel blockers, anticonvulsants, and sulfonylureas.[10] This report demonstrates a case of *Blastomycoses* infection without a known endemic fomite exposure. The demonstration of infection with *Blastomyces*, possibly from sources in areas in and around San Francisco, reminds us to consider "the great pretender" when evaluating similar cases. Further studies may be helpful in determining whether changes in the endemicity of *Blastomyces* species in California and other areas are occurring.[1,2,4,6]

REFERENCES

1. Saccente M, Woods GL. Clinical and laboratory update on blastomycosis. *Clin Microbiol Rev*. 2010;23(2):367-381.
2. DiSalvo AF. The ecology of blastomycosis dermatitidis. In: Al-Doory Y, DiSalvo AF, eds. *Blastomycosis*. New York, NY: Plenum Publishing Corporation; 1992:43-73.
3. Benedict K, Thompson GR III, Deresinski S, Chiller T. Mycotic infections acquired outside areas of known endemicity, United States. *Emerg Infect Dis*. 2015;21(11):1935-1941.
4. Casad DE, Waldmann WJ, Levan NE, Sorenson RH. North American blastomycosis in California—diagnosis of a case and a survey with 28 California observed cases. *Calif Med*. 1967; 106(1):20-27.
5. Carignan A, Valiquette L, Laupland KB. Impact of climate change on emerging infectious diseases: implications for Canada. *J Assoc Med Microbiol Infect Dis Canada*. 2019;4(2): 55-59.
6. Remien K, Bowman A. Fluticasone. StatPearls [internet]. January 2019. Updated May 10, 2019.
7. Proia L. How I treat blastomycosis. *Curr Fungal Infect Rep*. 2013; 7:21-28.
8. Proia L. Treatment of blastomycosis. *Curr Fungal Infect Rep*. 2010;4:23-29.
9. McBride JA, Gauthier GM, Klein BS. Clinical manifestations and treatment of Blastomycosis. *Clin Chest Med*. 2017;38(3): 435-449.
10. Beck KR, TelismanL, vanKoppen CJ, Thompsen GR III, Odermatt A. Molecular mechanisms of posaconazole- and itraconazole-induced pseudohyperaldosteronism and assessment of other systemically used azole antifungals. *J Steroid Biochem Mol Biol*. 2020;199:105605.