A man in his 40s was in his usual state of health until one year ago when he developed a progressively enlarging mass starting along his nasal septum and extending to the sidewall. He had no history of cancer, intravenous drug use, HIV, or other identifiable immunosuppression. He believed it began around the time he started inhaling brown heroin. Upon initial presentation the lesion was treated with a debridement. In addition to normal studies in relation to his immune system (HIV testing, CD4 counts, and flow cytometry), fungal complement fixation assays were negative, urine blastomycosis and histoplasmosis antigens were negative, and there was granulomatous inflammation with no organisms on the initial debridement and no growth on cultures. Without evidence of infection, he was initially given the diagnosis of sarcoidosis, which corresponded with bilateral hilar adenopathy on CT scan. He was treated with systemic steroids for presumed cutaneous sarcoidosis with some mild improvement. He was lost to follow-up for seven months when he then presented with progression with a new friable nodule at his medial canthus (Figure 1). One month later after another negative fungal culture, a repeat biopsy and tissue culture were performed (Figures 2, 3).

What is your diagnosis?
A. Cutaneous coccidiomycosis
B. Lupus pernio
C. Extranodal NK/T-cell lymphoma
D. Cutaneous blastomycosis

MICROSCOPIC FINDINGS & CLINICAL COURSE

Although the fungal complement fixation panel was negative on two separate occasions, GMS and PAS stains used on the final biopsy showed pseudopitheliotomatous hyperplasia (Figure 2) with extensive inflammation and granulomatous formation interspersed with large fungal yeasts with broad-based budding in the dermis and stratum corneum (Figure 3). These results confirmed the diagnosis of cutaneous blastomycosis. Itraconazole was started, and on his next follow-up appointment, there was significant improvement with resolution of the verrucous plaques with thin, dyspigmented scarring (Figure 4). The fungal culture eventually returned positive for B. dermatitidis. A CT scan of his chest after one month of treatment, demonstrated resolution of hilar adenopathy.

DISCUSSION

Blastomyces dermatitidis is a dimorphic fungus endemic to the Ohio and Mississippi River valleys. It is found in its mycelial form in the soil and infects patients via inhalation of spores. At body temperature it becomes a pathogenic yeast. Less than 800 infections due to B. dermatitidis are recorded annually in the US.1 B. dermatitidis causes systemic pyogranulomatous disease with pulmonary infection being the most common initial presentation. Dissemination can occur through the lymphatics or the blood; skin is the most common site of secondary infection. Skin infections usually involve the trunk and extremities and less commonly the head and neck.2 Even after HIV, CBC, and flow cytometry testing and age appropriate cancer screenings, no identifiable immunosuppression was found in this patient. Lesions of cutaneous blastomycosis vary and include verrucous papules or plaques, areas of purulence, subcutaneous
nodules, and ulcers with raised borders. Culture, histology, urine antigen, and complement fixation antibody testing can diagnose cutaneous blastomycosis. *B. dermatitidis* needs to be incubated at 30°C for 1-3 weeks, so cultures are often delayed. On microscopy, cutaneous blastomycosis typically shows extensive acute and granulomatous inflammation with pseudoepitheliomatous hyperplasia (PEH), potentially confusing the diagnosis with squamous cell carcinoma, especially if *B. dermatitidis* is not identified in the sample. Diagnosis of disseminated *B. dermatitidis* by an enzyme immunoassay (EIA) for urine antigen is 93% sensitive and 79% specific, and this test was negative in this patient. Serologies such as EIA, immunodiffusion (ID), and complement fixation (CF) are also used to identify blastomycosis antibodies. EIA is more sensitive and specific than ID and CF, but CF was used in this patient, which may account for delay in diagnosis. The sensitivity and specificity of CF for blastomycosis are reported to be 57% and 30% respectively.

The reported history of sarcoidosis dominated the differential diagnosis after the negative fungal complement fixation and urine antigen assays, culture, and debridement did not promptly uncover the correct diagnosis. Fortunately, PEH on biopsy and lack of improvement were clues towards blastomycosis. The patient attributed his disease onset to the time he began snorting brown heroin, a less pure and therefore less potent form of heroin. Snorting heroin can cause injury to the nasal tissue and also has been reported to cause a localized immunosuppression. This could predispose the patient to pulmonary and primary cutaneous blastomycosis. Brown tar heroin has been associated with other fungal infections, notably a systemic candida infection presenting with endophthalmitis, pustular dermatitis, and osteomyelitis. However, a potential association with blastomycosis appears to be speculative at this time.

The differential diagnosis for ulcerating, verrucous facial plaques as in this patient can be multiple. The possibilities include deep fungal infection, malignancy, lupus pernio, and lupus vulgaris among other rare granulomatous infections. Lupus pernio was the major contending diagnosis in this case due to the presumed history of sarcoidosis. Lupus pernio tends to appear in patients with chronic fibrotic disease and severe pulmonary involvement. It also more commonly appears as violaceous papules or plaques, but can become disfiguring leading to ulceration. The patient in this case did not respond to standard treatment for sarcoidosis further excluding this as the diagnosis. Once appropriately treated for blastomycosis with 200mg of itraconazole daily, the patient demonstrated resolution of hilar adenopathy within one month and substantial improvement in his facial plaques within two months.

This case report represents an advanced case of cutaneous blastomycosis and provides warning to the clinician to not be complacent with the diagnosis of sarcoidosis, even in the presence of negative fungal cultures, serologies, and urine antigen and complement fixation assays. The temporal course associated with starting to inhale brown tar

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heroin is uncorroborated scientifically, but the possibility of contamination is worth further investigation.

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