**INTRODUCTION**

*Blastomyces dermatitidis* is a thermally dimorphic fungus endemic to North America. Human infections predominantly occur in states bordering the Ohio and Mississippi River valleys of the United States and Canadian provinces bordering the Great Lakes and the Saint Lawrence River.1 Usually, primary infection is through inhalation of conidia into the lungs, but the clinical spectrum of illness ranges from asymptomatic or chronic indolent disease to fulminant multisystem failure and is usually more severe in immunocompromised hosts. Here we describe a fatal case of disseminated blastomycosis in a young man with rapid progression to multiorgan failure after exposure to corticosteroids.

**CASE**

A 31-year-old man presented to his local hospital with a persistent productive cough, fever, and dyspnea, worsening over 3 weeks. He had been on medical leave from his work as a horticulturalist for 4 years before his presentation because of polyarthralgia but had never received a specific diagnosis. Four weeks before presentation, a diagnosis of inflammatory arthritis of his right knee was made by a rheumatologist, and a tapering regimen of prednisone was prescribed, starting at 50 mg/d. Over the following weeks, his right knee became dramatically more swollen and painful, and new fevers, a nonproductive cough, and progressive dyspnea at rest developed. He was sexually active with 1 long-term male partner and had no history of intravenous drug use. He was HIV seronegative, and previous medical evaluations found no known immune deficiency or underlying anti-inflammatory diseases.

One month after starting prednisone, he presented to his regional hospital and rapidly progressed to hypoxemic respiratory failure requiring positive pressure ventilation. A computed tomography scan of the chest showed innumerable diffuse small nodules at the end-bronchovascular bundles, with early cavitation of some lesions. His respiratory status continued to deteriorate despite empiric imipenem, vancomycin, azithromycin, and caspofungin, and he was transferred to our center on day 4 of admission.

On presentation to our center, the patient required high-pressure ventilatory support, and his empiric therapy was changed to liposomal amphotericin B, trimethoprim/sulfamethoxazole, meropenem, and vancomycin. A bronchoalveolar lavage was performed and yielded numerous large, broad-based budding yeast cells seen by direct calcofluor white staining (Fig 1). Culture of the bronchoalveolar lavage specimen confirmed *B dermatitidis*. Physiological examination found a 1- × 2.7-cm well-demarcated plaque with a hemorrhagic crust and an
erythematous border on his left forehead (Fig 2). Per the family history, this lesion began 10 days before hospitalization as an erythematous papule. A shave biopsy found an ulcerated specimen of skin with underlying loose granulomatous inflammation with frequent large round budding yeastlike organisms, also supporting the diagnosis of blastomycosis with dissemination to the skin (Fig 3). Culture of the lesion isolated \textit{B. dermatitidis}.

The patient could not be adequately oxygenated despite maximal ventilator support, and venovenous extracorporeal membrane oxygenation (ECMO) was initiated on day 3 after transfer. Voriconazole was added because of the possibility that liposomal amphotericin B could be adsorbed onto the ECMO membrane. Despite maximal support, the patient had refractory multiorgan failure, and ECMO was withdrawn after 28 days according to family wishes.

**DISCUSSION**

This patient presented with fulminant disseminated blastomycosis involving his lungs, skin, and presumptively his joints. Endogenous and exogenous immunosuppression are well-documented risk factors for disseminated disease. Infection is acquired through the environment, often associated with occupational exposure or with outdoor recreational activities.\cite{6} We believe our patient was initially infected through his work as a horticulturalist, and that his chronic ill-defined rheumatologic syndrome was an indolent rheumatologic manifestation of blastomycosis that was mistaken for fibromyalgia for an extended duration and eventually for an auto-inflammatory arthritis after it progressed. Blastomycotic arthritis is a chronic infection that usually manifests as monoarthritis or oligoarthritis, with the knee joint being the most commonly affected. The chronic indolent course of fungal arthritis can extend for months without signs of systemic disease, often leading to delays in diagnosis and initiation of inappropriate treatment such as intra-articular or systemic steroids.\cite{3} The prednisone course our patient received led to rapid dissemination of the infection, which manifested with worsening purulent knee arthritis that did not grow in bacterial culture, severe acute pulmonary disease, and a skin lesion.

The skin is the most common extrapulmonary site of infection and occurs in up to 80\% of patients with disseminated disease.\cite{4} Cutaneous disease often begins as papulopustular lesions that progress to the classically ulcerative or verrucous forms. The verrucous form exhibits centrifugal spread, resulting in a verrucous plaque up to many centimeters in diameter. The ulcerative form begins as erythematous nodules or pustules that ulcerate. These ulcers can have heaped-up borders with or without an exudative base. Like the verrucous form, the ulcerative form spreads but typically in a more asymmetric pattern, which may be from communication with miliary abscesses in the ulcer periphery, via sinuses.\cite{4,5} Atypical cutaneous blastomycoses lesions, such as pustular and pyoderma gangrenosum—like ulcerative lesions, have also been reported.\cite{6,7}
Histopathologically, cutaneous blastomycosis is characterized by pseudoepitheliomatous hyperplasia with intraepidermal microabscess formation and occasional intraepidermal blastomycetic cells. Presence in the dermis may also be a suppurating granulomatous reaction. Blastomycetic cells may be found in histiocytic giant cells or freely in the tissue. The yeast forms of the organisms are best demonstrated by periodic acid–Schiff and Grocott-Gomori methenamine silver nitrate stains.4

This case illustrates a severe presentation of disseminated blastomycosis in a young man, manifesting with pulmonary dysfunction, a cutaneous lesion, and arthritis in the knee. This illustrates the importance of keeping a high index of suspicion for fungal disease in the face of a plausible exposure history. It is likely that earlier diagnosis and subsequent earlier treatment of *B dermatitidis* infection may have prevented the fatal outcome in this case.

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