Primary Cutaneous Cryptococcosis Caused by Cryptococcus Neoformans in an Immunocompetent Patient

Olga Marushchak, DO1, Shane A. Meehan, MD2, Sue Ann Wee, MD3

1 Department of Internal Medicine, Mount Sinai Morningside-West, New York, NY
2 Department of Dermatology, New York University Grossman School of Medicine, New York, NY
3 The Art & Science of Dermatology, PC, New York, NY

Abstract
Cryptococcosis is a fungal infection caused by Cryptococcus species, most commonly affecting immunocompromised individuals, while very few cases of the infection in immunocompetent hosts are available in the literature. In this manuscript, we present a case of primary cutaneous cryptococcosis caused by Cryptococcus neoformans in an immunocompetent patient. While cutaneous manifestation is usually a secondary sign of the disseminated disease, our patient presented with primary cutaneous cryptococcosis. Additionally, reports on cryptococcosis cases suggest that immunocompetent hosts are typically infected by C. gattii. However, culture of the discharge from our immunocompetent patient showed heavy growth of C. neoformans. This case highlights the importance of considering cutaneous cryptococcosis as differential diagnosis of ulcerated skin lesions in patients with an exposure to bird droppings, regardless of their immune status and systemic manifestations.

Introduction
Cryptococcosis is a fungal infection caused by Cryptococcus species, most commonly in immunocompromised individuals, especially in patients with HIV, organ transplant, and cancer chemotherapy.1-4 The infection is relatively uncommon in immunocompetent patients in the absence of immunosuppression. Thus, cryptococcosis might be overlooked in immunocompetent individuals, which can lead to delayed diagnosis and treatment, and in some cases, fatal outcome.3

Cutaneous cryptococcosis can present with a variety of skin manifestations. The most common presentation of disseminated cutaneous cryptococcosis is umbilicated papules on the head or neck; other cutaneous manifestations include abscesses, cellulitis, pyoderma gangrenosum-like lesions, acneiform pustules, vegetating crusted plaques, whitlow, and a combination of polymorphic lesions.5-8 Primary cutaneous cryptococcosis typically presents with solitary skin lesions (often nodules that ulcerate) in exposed body areas.5

Case Report
A 67-year-old woman presented with a 6-month history of localized papules and...
plaques on her back. Upon review of systems, there was no fever, night sweats, pain, or cough. Her past medical history was unremarkable and she had no known history of malignancy, immunodeficiency, or immunosuppression. A more detailed history led to the revelation of exposure to pigeon droppings as she fed pigeons inside her New York home about one year prior to the onset of her skin lesions. In addition, a previous roommate several years prior had kept pet birds inside the patient’s home. The physical examination revealed four ulcerated papules and plaques, some of which drained a purulent discharge on her left lower back (Figure 1). No similar lesions were found on other parts of the body. No relevant underlying disease was noted during physical examination.

A shave biopsy of the ulcer margin was obtained and the histopathologic examination revealed variably-sized yeast-like organisms surrounded by clear capsules and granulomatous infiltrate (Figures 2 and 3). The organisms stained with PAS-D, GMS, Fontana-Masson, and a mucicarmine. Histologic findings were consistent with cryptococcosis. Culture of the discharge showed heavy growth of Cryptococcus neoformans.

Given an absence of systemic signs and symptoms and a negative chest X-ray, the diagnosis of primary cutaneous cryptococcosis was made. The patient was treated with oral fluconazole with complete resolution of her skin lesions. There was no recurrence of lesions or evidence of dissemination during the four months of follow-up.

**DISCUSSION**

Cryptococcosis most commonly affects pulmonary and central nervous systems, manifesting as pneumonia and meningoencephalitis.\(^3\) Patients generally become infected with pulmonary cryptococcosis after inhaling the yeast basidiospores, usually from contaminated soil, bird or bat droppings.\(^7\) Meningoencephalitis may occur with secondary spread of the infection to the central nervous system.\(^4\) Cutaneous lesions are typically a sign of the disseminated disease and can occur in about 5-20% of affected patients.\(^5\) Primary cutaneous infection may be caused by direct inoculation of the fungus into the skin by a contaminated object and is characterized by skin lesions with positive culture in the absence of systemic disease.\(^5\) In our case, the cutaneous manifestation of localized lesions, histopathological findings, positive culture...
Figure 2. Hematoxylin-eosin-stained biopsy specimen of ulcer margin showing variably sized yeast-like organisms surrounded by clear capsules and granulomatous infiltrate within the dermis.

Figure 3. Biopsy specimen stained with Grocott methenamine silver (GMS) stain.
results, absence of fever, negative systemic workup, and excellent response to antifungal therapy support the diagnosis of primary cutaneous cryptococcosis, which is a rare condition recognized as a distinct clinical entity.\textsuperscript{7,8}

Reports on cryptococcosis cases suggest that \textit{C. neoformans} commonly causes infection mainly in immunocompromised patients, while \textit{C. gattii} variant usually affects immunocompetent hosts.\textsuperscript{1,2,9,10} However, culture results from our immunocompetent patient was positive for \textit{C. neoformans}, further confirming the rarity of this clinical presentation.

The origin of our patient’s infection is likely exposure to \textit{C. neoformans} while having contact with pigeons. This case highlights an atypical clinical presentation of primary cutaneous cryptococcosis with ulcerated papules and plaques in an immunocompetent patient. Therefore, physicians should consider cutaneous cryptococcosis in their differential diagnosis of ulcerated skin lesions in patients with an exposure to bird droppings, regardless of their immune status.

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**Corresponding Author:**
Olga Marushchak, DO
Department of Internal Medicine, Mount Sinai Morningside-West, 1000 10th Ave, Ste 3A-08, New York, NY 10019
Phone: 212-259-6777
Email: omarushc2@student.touro.edu

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