



# Primary cutaneous cryptococcal infection with subsequent erythema nodosum in a 10-year-old immunocompetent girl

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## INTRODUCTION

Members of the *Cryptococcus* genus are opportunistic encapsulated yeasts that cause significant morbidity and mortality most often in immunocompromised hosts. Clinically, cryptococcal infections manifest most commonly as meningitis or a respiratory infection. The cryptococcal species are *Cryptococcus neoformans*, *Cryptococcus gattii*, and *Cryptococcus laurentii*, which each have diverse antigenicity and serotypes.<sup>1</sup> Although *C gattii* infections occur commonly in immunocompetent patients in endemic areas, *C neoformans* infections in immunocompetent individuals remain an infrequent occurrence.<sup>2</sup> Endemic areas of *C gattii* include tropical regions and the pacific northwestern of North America after an outbreak in 1999.<sup>3</sup> Cutaneous cryptococcal infection is most often observed secondary to disseminated cryptococcosis.<sup>1,4</sup>

## CASE

A 10-year-old girl with a medical history significant for intermittent asthma presented to the emergency department with a 2-week-old ulcerated nodule on her right foot. She was living in rural central Texas with no known exposure to avian excretion, pigeons, soil, or wood debris. She also denied any recent cutaneous injury and is fully immunocompetent. Her asthma was classified as intermittent, and she had not taken oral steroids or daily medications before presentation. Her primary care physician had prescribed a 7-day course of cephalexin, 500 mg daily. Four days after completion of the antibiotic, a painful eruption developed on her extremities and buttocks. There was no oral, ocular,

### Abbreviations used:

EN: erythema nodosum  
PCC: primary cutaneous cryptococcal

or genital involvement and no fevers, chills, or cough. The patient was not taking any other medications, herbal supplements, or vitamins and denied recent vaccination. Her parents did report the use of guaifenesin as needed for occasional cough they identified to be allergy induced. She had no animal exposures other than her pet Chihuahua and denied recent travel or contact with people who traveled outside the United States.

Physical examination was remarkable for a 2-cm ulcerated nodule with elevated pink borders and hemorrhagic crust on the dorsal aspect of the right foot (Fig 1). Additionally, there were red, dusky tender patches and nodules on the bilateral lower and upper extremities and on the buttocks (Figs 1 and 2). The lower extremity lesions were more prevalent on the anterior aspect. There was no lymphadenopathy in the popliteal, inguinal, axillary, or cervical basins. Pulmonary auscultation did not find accessory sounds. Her vital signs were stable and she was afebrile. Antistreptolysin titer and urine and blood cultures were normal. There was no clinical or laboratory evidence for disseminated infection.

Punch biopsies were performed for hematoxylin-eosin and tissue culture. The sample acquired from the ulcerated lesion on the right foot was notable for transdermal chronic inflammation with vague granulomas and yeastlike organisms highlighted by

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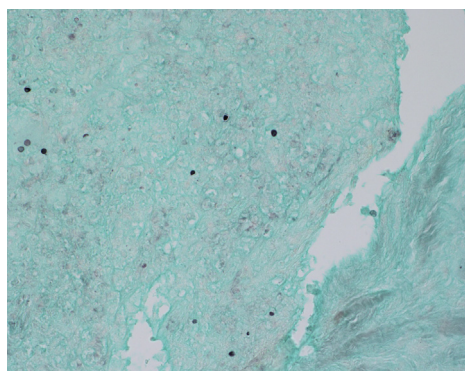
**Fig 1.** Ulcerated nodule on the dorsal aspect of the right foot.



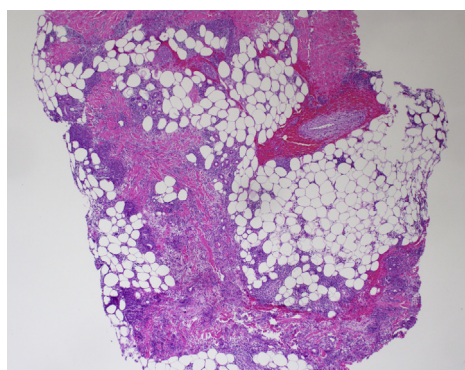
**Fig 2.** Red, dusky patches and nodules on bilateral lower and upper extremities.

the Gomori methenamine silver and Periodic acid–Schiff stains (Figs 3 and 4). The tissue culture from the ulcerated lesion grew *C neoformans* var. *neoformans*. Bacterial and mycobacterial cultures were negative. The sample taken from a red, dusky plaque on her left thigh showed granulomatous septal panniculitis with neutrophils consistent with erythema nodosum (EN) (Fig 4).

This patient's EN began to improve during her short hospital stay where she received supportive care. She was discharged before receiving a



**Fig 3.** Yeastlike organisms highlighted on Gomori methenamine silver stain.



**Fig 4.** Granulomatous septal panniculitis consistent with EN on Periodic acid-Schiff stains.

diagnosis for her ulcer and given a 2-week course of clindamycin. After leaving the hospital, the patient was lost to follow-up. She was not seen in clinic until 6 months after her hospitalization. At that point, her primary lesion and the EN had resolved without systemic antifungal treatment.

## DISCUSSION

Primary cutaneous cryptococcal (PCC) infection has no pathognomonic presentation but presents most frequently as an asymptomatic or moderately itchy and painful nodule, cellulitis, or ulceration in exposed domains of the skin.<sup>4,5</sup> There were only 35 cases reported of PCC infection in immunocompetent individuals since 1966.<sup>4,5</sup> The average age of affected patients is 57 years, and most patients presented with lesions on their hands or forearms and were engaged in work or hobbies that predisposed them to abrasions and exposure to wood debris, birds, or soil.<sup>4,5</sup> The location of our patient's primary lesion on the ankle is unprecedented, but it is often an exposed area, especially in children. The other 2 reports of children with PCC infection described lesions on the forearm and thumb.

Further, our patient had dusky plaques that were consistent with EN on histology. Although many infections are reported to trigger the development of EN, including other fungal organisms, there are no reports of *Cryptococcus*-induced EN to our knowledge. We also completed a literature review to rule out cephalixin and guaifenesin therapy as a potential cause and found no reports of such a reaction occurring.

Treatment options for PCC infection range from antifungal medications and surgical debridement to observation. The Infectious Disease Society of America recommends fluconazole, 400 mg orally every day for 6 to 12 months, for localized cutaneous infection in immunocompetent individuals.<sup>6</sup> Both Neuville et al<sup>4</sup> and Du et al<sup>5</sup> reported fluconazole to be an effective treatment option in most cases. Alternatives included itraconazole and amphotericin B. Itraconazole was an effective first-line therapy in clearing infection in 7 cases at doses of 100 to 400 mg/d for 3 to 6 months.<sup>5</sup> Surgical debridement with or without subsequent fluconazole treatment is another effective modality in achieving infection resolution.<sup>4,5,7</sup> Although most cases report the use of systemic antifungal agents, our patient cleared her infection without intervention. A similar case was reported on an 8-year-old boy with PCC infection who was treated with surgical incision and drainage without systemic antifungal therapy.<sup>2</sup> He experienced lesion resolution within 4 weeks without subsequent recurrence or dissemination at 4- and 6-month follow-up.<sup>2</sup> We suspect that a healthy immune system may have the potential to clear limited PCC infection without antifungal therapy. However, it is worth noting that there is one reported case of PCC infection of the toe untreated

for 5 months that developed into disseminated *Cryptococcus*.<sup>7</sup>

Our case broadens the spectrum of epidemiology and contributes to the growing understanding of PCC infection in immunocompetent individuals. Further, we report on the first documented case of EN induced by *Cryptococcus*. This finding is not surprising given the variety of causes of EN including other fungal infections such as coccidioidomycosis and histoplasmosis, and now *Cryptococcus* can be added to the list.

#### REFERENCES

1. Casadevall A. Cryptococcosis. In: *Harrison's Principles of Internal Medicine*. 19th ed. New York, NY: McGraw-Hill; 2015. Available from: URL: <http://accessmedicine.mhmedical.com/lib-ezproxy.tamu.edu:2048/content.aspx?sectionid=79739876&bookid=1130&jumpsectionID=98719368&ResultClick=2&q=cryptococcus>. Accessed January 10, 2015.
2. Lenz D, Held J, Goerke S, et al. Primary cutaneous cryptococcosis in an eight-year-old immunocompetent child: how to treat? *Klin Pädiatr* 2015;227(1):41-44.
3. Casadevall A. *Harrison's Principles of Internal Medicine*. 19th ed. New York, NY: McGraw-Hill; 2015.
4. Neuville S, Dromer F, Morin O, et al. Primary cutaneous cryptococcosis: a distinct clinical entity. *Clin Infect Dis Off Publ Infect Dis Soc Am*. 2003;36(3):337-347.
5. Du L, Yang Y, Gu J, Chen J, Liao W, Zhu Y. Systemic Review of Published Reports on Primary Cutaneous Cryptococcosis in Immunocompetent Patients. *Mycopathologia*. 2015;180(1-2): 19-25.
6. Perfect JR, Dismukes WE, Dromer F, et al. Clinical practice guidelines for the management of cryptococcal disease: 2010 update by the infectious diseases society of america. *Clin Infect Dis Off Publ Infect Dis Soc Am*. 2010;50(3): 291-322.
7. Spiliopoulou A, Anastassiou ED, Christofidou M. Primary cutaneous cryptococcosis in immunocompetent hosts. *Mycoses*. 2012;55(2):e45-e47.