CASE REPORT

Primary cutaneous cryptococcosis in an immunocompetent man: A case report

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A R T I C L E   I N F O

Article history:
Received: Jan 18, 2012
Revised: May 2, 2012
Accepted: Jul 20, 2012

Keywords:
Cryptococcus neoformans
immunocompetent
primary cutaneous cryptococcosis

A B S T R A C T

Cutaneous cryptococcosis usually develops secondary to hematogenous spread in immunocompromised hosts. Primary cutaneous cryptococcosis (PCC) is a rare condition characterized by localized skin eruptions and positive culture for Cryptococcus neoformans but without dissemination to the internal organs. Herein, we describe a typical case of PCC in an immunocompetent male who presented with a 1-month history of scattered erythematous indurated papules and plaques on his arm and without fever. The histology of his skin, tissue culture, and multiplex polymerase chain reaction (PCR) confirmed cutaneous cryptococcal infection by C neoformans var. neoformans. After extensive work-ups showed no evidence of systemic dissemination or underlying cellular-immunity deficiency, the diagnosis of primary cutaneous cryptococcosis was made. Treatment with fluconazole 400 mg daily for 14 days followed by 200 mg daily for another 14 days led to complete resolution of the skin lesions, and subsequent follow-up showed no signs of relapse.

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Introduction

Cryptococcus neoformans is an opportunistic encapsulated yeast that infects immunocompromised human hosts.1 Four serotypes have been identified: C neoformans var. grubii (serotype A); C neoformans var. gattii (serotypes B and C); and C neoformans var. neoformans (serotype D).2,3 Serotype D is most common in cutaneous cryptococcosis.4,5 However, recent further subspeciation of Cryptococcus has concluded that other serotypes can also cause cutaneous cryptococcal infections.6,7 Cutaneous cryptococcosis is extremely rare in immunocompetent hosts. In immunocompromised hosts, it usually disseminates from a distant site and is characterized by a poor outcome.8 Primary cutaneous cryptococcosis (PCC) is a rare entity with a favorable prognosis.9 This case report describes an immunocompetent and otherwise healthy nonfebrile elderly male with scattered erythematous indurated papules and plaques on the arm. PCC was caused by C neoformans var. neoformans as evidenced by skin culture and multiplex polymerase chain reaction (PCR). There were no signs of systemic dissemination and the lesions completely resolved after 4 weeks of fluconazole treatment.

Case report

An 87-year-old retired male living in a rural area presented with a 1-month history of scattered asymptomatic erythematous indurated papules and plaques on the right arm (Figure 1). The patient was otherwise healthy and showed no lymphadenopathy, fever, night sweating, malaise, weight loss, headaches, or other constitutional symptoms. Before the eruption, he had no history of contact with pigeons and no trauma or other medical conditions requiring long-term medication other than intermittent pruritus due to eczema. He occasionally used topical corticosteroid agents during flare-up of eczema. A skin biopsy was performed under the impression of atypical infection or cutaneous lymphoma. Skin histology showed dermal granulomatous infiltrates composed of histiocytes, multinucleated giant cells, and necrosis (Figure 2A). Numerous variable-sized yeasts surrounded by clear halos and sporadic narrow-based budding were identified by periodic acid-Schiff stain (Figure 2B) and mucicarmine stain (Figure 2C). A tissue culture showed growth of Cryptococcus species, which was confirmed by a multiplex PCR preferable to C neoformans var. neoformans (Figure 3) (primers 5′- GGAACAGCAACCACACTACTG; 5′-CATATTGGGTGGCATCTTACTGAGG; 5′-CATATTGGGTGGCATCTTACTGAGG GA; 5′-CCAGGAAACATGGTTTGAG; 5′-GGTTGTGGAAGGCAAAGAAAC, based on the report of Ito-Kuwa et al10). Both human immunodeficiency virus serology and serum cryptococcal antigen test were negative. A lumbar puncture was not performed because the patient showed no symptoms or signs of meningeal involvement.

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http://dx.doi.org/10.1016/j.dsi.2012.07.001

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Hemogram, biochemical panel including serum glucose level, plasma cortisol, and adrenocorticotropic hormone level, T-cell subset analysis, lymphocyte mitogen stimulation test, serum protein electrophoresis, chest radiograph, and cranial computed tomography were normal. Blood, urine, and sputum cultures showed negative results. Based on the clinical and laboratory results indicating an immunocompetent status without dissemination, the diagnosis of PCC was made. After intravenous administration of 400 mg fluconazole daily for 7 days, the patient was discharged with a prescription for oral fluconazole 400 mg daily for another 7 days followed by 200 mg daily for 14 days. The 1-month treatment completely resolved the skin lesions (Figure 4), and the lesions showed no recurrence after 2 months of follow-up.

Discussion

Cryptococcosis is an opportunistic infection caused by encapsulated yeast, C neoformans. This pathogen is found in soil, fruit, vegetables, decaying wood, and the feces of many birds, especially pigeons. It usually emerges in immunocompromised patients, such as those with a history of underlying malignancy, organ transplant, acquired immunodeficiency syndrome, or corticosteroid therapy, although occasionally it may occur in immunocompetent hosts.

Cutaneous cryptococcosis usually results from hematogenous dissemination from other distant organs in immunocompromised hosts, referred to as secondary cutaneous cryptococcosis (SCC). The airway is believed be the main entry portal. Cutaneous involvement occurs in 10-20% of cases of disseminated cryptococcosis. However, direct inoculation is a possible route, which causes primary cutaneous cryptococcosis (PCC). A history of trauma is the most frequently reported risk factor to provide a portal of entry, and foreign body puncture and animal-related trauma are the most common related causes. Patients with hobbies or occupations that put them at risk of injuries with exposure to soil, dust, wood sticks or debris, or bird droppings are at the greatest risk of PCC. The mean duration between inoculation and clinical manifestation is usually 8 days. In addition, C neoformans var. neoformans has a lower thermotolerance compared with the other serotypes, which may explain its dermatotrophism.

The diverse clinical manifestations of PCC include papules, pustules, nodules, plaques, vesicles, ulcers, eczymosis, cellulitis, subcutaneous lesions resembling erythema nodosum, herpetiform or molluscum contagiosum-like lesions, and polymorphic lesions. Therefore, cutaneous cryptococcosis should be suspected if the skin eruptions respond poorly to standard treatment, and a diagnostic skin biopsy should be performed.

The rare cases of PCC usually have favorable outcomes, even in immunocompromised patients. Compared with patients with SCC, patients with PCC tend to be older and are characterized by

Figure 1 Scattered erythematous indurated papules and plaques on the right arm.

Figure 2 (A) Results of histopathologic examination depicting dermal granulomatous infiltrate (40×) (hematoxylin and eosin stain). (B) Periodic acid-Schiff stain in high power view (400×) showing numerous spherical encapsulated yeasts. (C) Mucicarmine staining results (400×).
also lead to infection in immunocompetent hosts. In immunocompetent hosts, the most common sites of lesions are the facial area and upper extremities. Immunocompromised hosts are characterized by multiple lesions, typically in the trunk or lower extremities. A diagnosis of PCC should be considered a diagnosis of exclusion, because cutaneous lesions are a symptom of systemic cryptococcosis. Extensive work-ups including a detailed history, physical examination, and laboratory examination are essential to exclude dissemination. A lumbar puncture is indicated when symptoms of central nervous system (CNS) involvement are present; however, its usefulness is debatable in the absence of localizing signs. Underlying immunodeficiency should also be evaluated. 

Because the optimal treatment regimen for cutaneous cryptococcosis is not well established, treatment usually varies according to the extent of disease and host immunocompetence. In immunocompetent patients, the Infectious Disease Society of America guidelines recommend treating cryptococcal CNS infection or dissemination with amphotericin B (0.7–1 mg/kg/day) plus flucytosine (100 mg/kg/day) for at least 4 weeks, followed by consolidation therapy with fluconazole (400–800 mg/day) for a minimum of 8 weeks and maintenance therapy with fluconazole (200 mg/day) for 6–12 months. As for pulmonary disease fluconazole 400 mg daily for 6–12 months is recommended in mild to moderate disease. The regimen differs in severe or progressive disease, which is the same as treating CNS involvement. Secondary cutaneous cryptococcosis is treated in a manner similar to that of CNS infection, whereas fluconazole 400 mg daily for 6–12 months is recommended to treat PCC in an immunocompetent host. However, a short-term (2 weeks) course of fluconazole treatment (200 mg daily) has also proven to be effective in PCC.

The clinical manifestations in the current study included a circumscribed skin lesion in an unclothed area without evidence of dissemination or cellular immunity deficiency. A tissue culture of C neoformans var. neoformans and a good response after 1 month of treatment were consistent with a diagnosis of PCC. Although no clear source of infection was identified, chronic scratching was a plausible portal of entry. Even in immunocompetent patients, a chronic course of indolent but unprotected scratching wounds should always raise the suspicion of atypical infections, including PCC.

**References**


**Figure 3** Molecular characterization of Cryptococcus spp. Identification of this fragment preferably corresponding to C neoformans var. neoformans. Products from primer Cap64 showed a band at around 400 base pairs. Products from primer Lac1 showed a single broad band at around 1 kilo base pairs. Products from all primers Cap64 showed the broad band of 800 base pairs comprising the broad band of several bands at around 200 base pairs. Products from primer Lac1 showed a single broad band at around 400 base pairs in our polymerase chain reaction product may be used to distinguish the var. neoformans and serotypes A/B/C. There may be two bands comprising the broad band of 800–1000 base pairs seen in our result. The existence of a band at around 400 base pairs under Cap64 confirms the species of Cryptococcus. Thus, the infection of the skin tissue caused by C neoformans var. neoformans (serotype D) is preferable.

**Figure 4** Complete recovery with minor eczematous scaling after 1 month of treatment.


