

Molluscum contagiosum-like lesions: a telltale sign of disseminated cryptococcosis

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Introduction: Cryptococcosis is an opportunistic fungal infection caused by *Cryptococcus neoformans*. This systemic fungal infection affects 6 to 13% of patients with acquired immunodeficiency syndrome (AIDS). Only 10% of patients with this condition develop cutaneous manifestations.

Case Summary: A 20-year-old male, newly diagnosed case of HIV (Human Immunodeficiency Virus), presented with multiple skin-colored molluscum contagiosum-like umbilicated papules on the face, neck and both arms. Lesions increased in number rapidly and were associated with respiratory distress. Histopathologic examination revealed findings of opportunistic fungal infection suggestive of cryptococcosis. Serum Cryptococcal Antigen Latex Agglutination System (CALAS) test was also positive. Patient was then diagnosed as a case of cryptococcosis and was a candidate for intravenous amphotericin B. However, before the planned medication was given, the patient experienced severe respiratory distress and expired several hours later.

Conclusion: Molluscum-like skin lesions may be a telltale sign of a disseminated opportunistic fungal infection, including Cryptococcosis. Early diagnosis followed by prompt and aggressive treatment would improve outcome and survival of the patient.

Key words: Cryptococcosis, AIDS, HIV

INTRODUCTION

Cryptococcosis is an opportunistic infection caused by a ubiquitous encapsulated yeast, *Cryptococcus neoformans*, present in soil, dust and pigeon excreta. It occurs in 6 to 13% of patients with acquired immunodeficiency syndrome (AIDS) with low CD4

lymphocyte counts.^{1,2} The incidence of cryptococcosis has increased together with the occurrence of life threatening infection among HIV infected individuals with profound immune suppression.³

The main route of infection is inhalation of small yeast forms which are aerosolized. Pulmonary infection is usually the primary infection, most frequently self-limited and may be asymptomatic.^{1,2} After the primary infection in the lungs, the disease can disseminate via hematogenous route to various organs, including the central nervous system and skin.⁴

Cutaneous sign may be the first indication of infection, preceding the diagnosis of disseminated disease, making its recognition important to early treatment. Cutaneous cryptococcal infection should be presumed to be disseminated until proven otherwise.⁴

CASE

A 20-year-old male presented with multiple asymptomatic flesh-colored umbilicated papules with some excoriations over the face and upper extremities since 2 weeks prior to consult. No lesions were seen over the palms, soles, oral mucosa and genital area. He was also newly diagnosed with HIV, with a CD4 count of 15cells/ μ L, since 5 days prior to consult. The past medical

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history was positive for pulmonary tuberculosis (TB) category I. Patient started his TB medications since 6 months prior to consult, but he was not compliant. Family medical history was noncontributory. Patient denied illicit drug use but admitted having multiple sexual partners, all of whom were of the same sex. Review of the systems was unremarkable. There were no signs of meningeal irritation or neck stiffness. The deep tendon reflexes were normal. Dermatological examination showed multiple flesh-colored molluscum contagiosum-like umbilicated papules, some topped with erosions and crusts, on the face, neck and both arms (Fig. 1A-C).

A 4-mm punch biopsy of the skin lesion revealed parakeratosis of the stratum corneum and mild thinning of the epidermis. The dermis revealed edema and a granulomatous inflammatory infiltrate consisting of yeast-like structures within macrophages. There was a mild superficial perivascular infiltrate of lymphocytes (Fig. 2). Periodic Acid Schiff (PAS) stain showed presence of encapsulated yeast cells within macrophages (Fig. 3A). Mucicarmine highlighted the cell wall of the yeast cells (Fig. 3B). Gomori's Ammoniacal Silver (GAS) stain positively stained the yeast cells (Fig. 3C). Histopathologic diagnosis was opportunistic fungal infection suggestive of cryptococcosis.

Two days after his initial consult, patient was admitted due to difficulty of breathing. Chest X-ray showed development of pneumonic densities in the right lung, and infiltrations in the upper left lobe. Serum Cryptococcal Antigen Latex Agglutination System (CALAS) test was positive with 1:4096 dilution. Blood fungal culture and blood aerobic culture and susceptibility test showed presence of encapsulated yeast cells (*Cryptococcus neoformans*) after 10 hours and 3 days of incubation respectively. Patient was put on IV amphotericin B, however, several hours after admission the patient experienced rapid deterioration of respiratory function and decrease in oxygen saturation, leading to his demise.

DISCUSSION

Cryptococcosis is the infection caused by the encapsulated yeast *C. neoformans*. The yeast was previously subclassified into three varieties based on biochemical differences, and into four non-hybrid serotypes according to capsular agglutination reactions namely *C. neoformans* var. *grubii* (serotype A), *C. neoformans* var. *neoformans* (serotype D), and *C. neoformans* var. *gattii* (serotype B and C). The *neoformans* and *grubii* varieties can be isolated from pigeon excreta and are more common in AIDS patients. *C. neoformans* var. *neoformans* (serotype D) is more

likely to be found in skin lesions.⁵

Patients with impaired cell-mediated immunity, such as those infected with HIV, solid-organ transplant recipients, and those on chronic corticosteroid therapy, are most vulnerable to cryptococcal infections. Clinical manifestations of the disease depends on the host response, inoculum size and innate virulence of the organism.⁴

Although the main portal of entry is through inhalation into the lungs, the disease usually presents with signs of extrapulmonary dissemination such as meningitis and cutaneous manifestation. Disseminated cryptococcus is more commonly seen in individuals with a CD4 T cell count of <50/ μ L.^{1,2}

The most commonly recognized site of disseminated cryptococcosis is the central nervous system. This present with classic signs of meningismus, change in consciousness, mental changes, and nerve palsies. Cutaneous cryptococcosis is rare (10 to 20%). The lesions may vary greatly in morphology, are seldom pathognomonic, and most commonly mimic molluscum contagiosum. Other presentations include acneiform papules or pustules, tumors, plaques, abscess, cellulitis, purpura, draining sinus, ulcers, bullae, subcutaneous swelling, herpetiform lesions, violaceous lichenoid lesions, nodular eruption on chin, a warty tumor on foot, a pseudofolliculitis and cryptococcosis mimicking Kaposi sarcoma.⁶

Systemic diagnosis is established with the aid of serology, blood culture and lumbar puncture, cerebrospinal fluid (CSF) serology, culture and India ink staining. Cutaneous diagnosis is best accomplished and confirmed by skin biopsy and culture. On biopsy, the cell wall will stain with either methenamine silver or periodic acid-Schiff, and the capsule will stain with mucicarmine or Alcian blue preparation.⁷

While fungal culture remains the gold standard for establishing a diagnosis, it is cumbersome and time-intensive. Serologic testing for cryptococcal antigen such as latex agglutination, is important since it can confirm the diagnosis immediately and has prognostic indications. This test is rapid and specific to blood and CSF, based upon the principle that anti-cryptococcal antibody-coated latex particles will agglutinate with antigens from the polysaccharide capsule. A CSF antigen titer of >1:1024 is associated with a higher risk of mortality.^{8,9}

The Infectious Disease Society of America practice guidelines state that disseminated cryptococcosis, defined as involvement of at least two noncontiguous sites or evidence of high fungal burden on cryptococcal antigen titer, should be treated as if the patient has meningoencephalitis. Treatment for central nervous

system-related cryptococcal infection is divided into three phases: induction, consolidation, and maintenance. Induction therapy should last a total of 14 days and consist of intravenous amphotericin B (0.7-1.0 mg/kg per day) plus oral flucytosine (100 mg/kg per day) divided into four doses, followed by oral fluconazole (400 mg/day) for eight weeks during the consolidation phase. Since amphotericin is nephrotoxic, renal function must be monitored during treatment. In patients who are predisposed to renal dysfunction or are not tolerant of conventional amphotericin B, alternate lipid formulations are available. Thereafter, maintenance therapy consists of oral fluconazole (200 mg/day) for a minimum of 12 months, but there are no set guidelines with regards to duration of treatment as it depends on the immune status of the individual.¹⁰

In disseminated disease, cutaneous lesions may precede or follow the signs of involvement of CNS and lungs. Skin findings in disseminated cryptococcosis indicate a poor prognosis especially in immunocompromised hosts. A timely diagnostic workup, including skin biopsy, blood cultures, and lumbar puncture, is crucial since skin lesions may mimic other infectious processes. Prompt, appropriate antifungal treatment should be initiated to decrease morbidity and mortality.

CONCLUSION

This case emphasizes the importance of cutaneous manifestations of cryptococcosis as the first hint for a disseminated infection. Early recognition, appropriate presumptive rapid diagnostic examination and prompt aggressive antifungal treatment can become life-saving.



Figure 1. Clinical findings of multiple flesh-colored umbilicated papules, some topped with erosions and crusts, on the face (A), neck (B) and both arms (C). Lesions were similar to molluscum contagiosum.

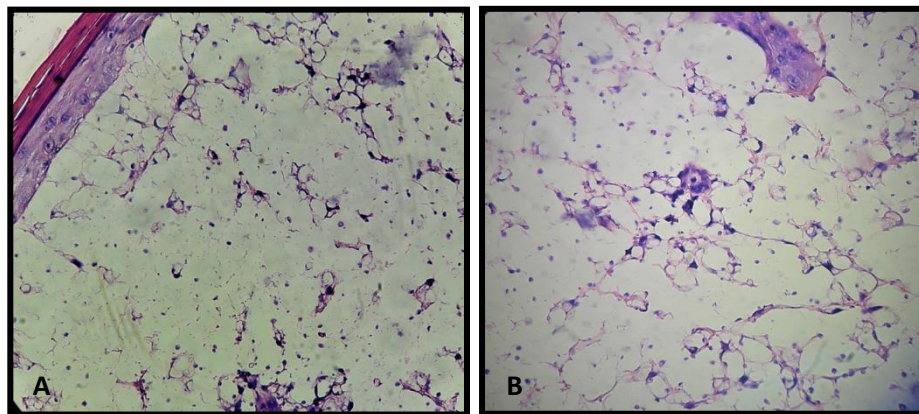


Figure 2. Histopathology of the skin lesion, H&E x400. The dermis reveals edema (A) and a granulomatous inflammatory infiltrate consisting of yeast-like structures within macrophages (B).

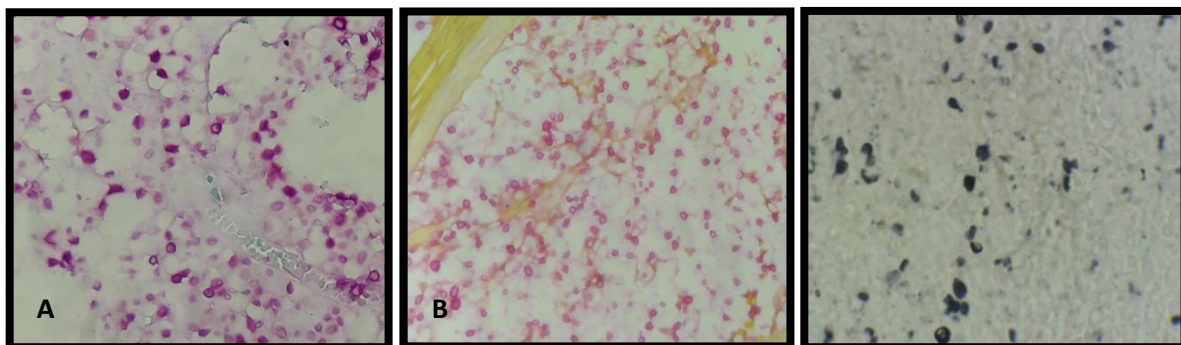


Figure 3. PAS stained positive for yeast cells (spherules with prominent capsules in a zone of clearance or “halo” around the cells), x400 magnification (A). Mucicarmine stained the cell wall of the yeast cell, x400 magnification (B). Numerous encapsulated fungal spores were stained by GAS stain, showing black color (C).

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