CLINICAL IMAGE

A CASE OF CUTANEOUS BLASTOMYCOSIS

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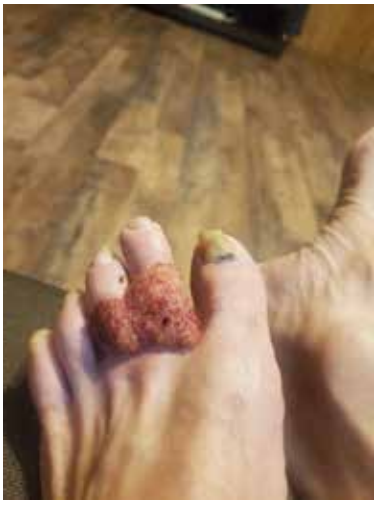
A 70-year-old Caucasian male presented complaining of growths on his left toes for 5 months. He reported that they were enlarging, tender, irritated and occasionally bled when they rubbed against his clothing. He denied any previous trauma to the foot.

FIGURE 1:

Verrucous plaques on dorsal aspect of the left toes with concomitant dermatophytosis of toenails



The patient previously had a renal transplant and has been taking antirejection medications, including tacrolimus, mycophenolate mofetil and prednisone. He also has a history of medication-controlled gastroesophageal reflux disease (GERD) and diabetes. His physical exam revealed raised lesions on the dorsal aspect of his second and third toes.

Initial biopsy of the lesion was conducted 3 months prior; the microscopic exam reading and diagnosis at that time was a pyogenic granuloma. The diagnosis was reconsidered when the patient failed to improve. Repeat punch biopsy of the left second toe demonstrated histological findings of epidermal acanthosis, hyperkeratosis and a mixed acute and chronic dermal inflammatory infiltrate. Grocott methenamine silver (GMS) stain revealed scattered yeast forms and possible hyphae in the dermis, consistent with deep fungal infection.

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Pathological examination of the specimen revealed round yeast-like cells up to 20 micrometers (0.000787402 inches) in diameter with thick non-pigmented walls, single broad-based buds and multiple nuclei. The patient was referred to an infectious disease specialist and started on treatment.

FIGURE 2:

GMS stain showing presence of fungal organisms GMS stain showing presence of fungal organisms

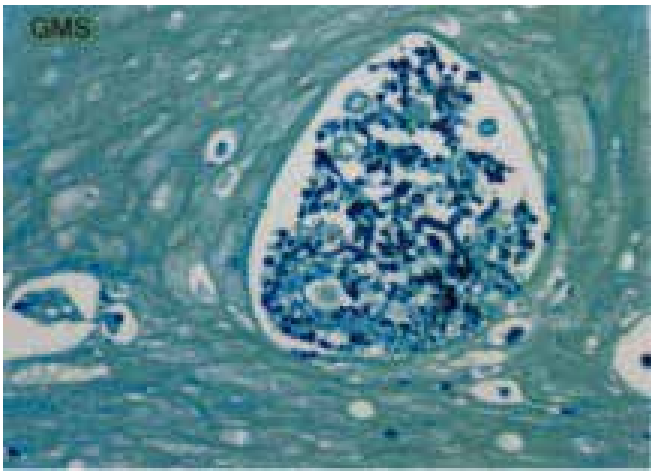
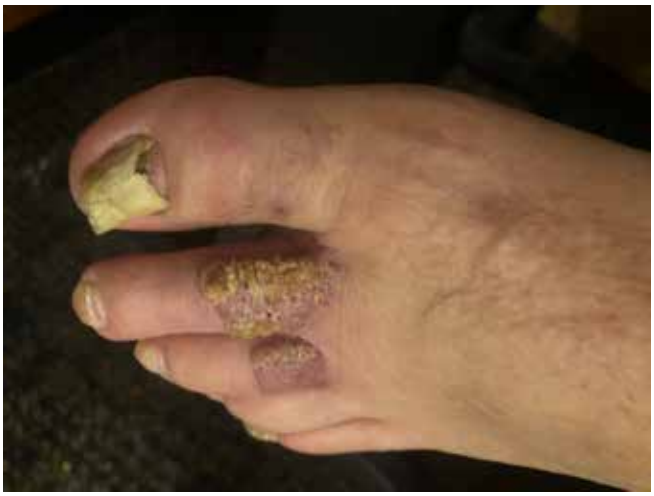


FIGURE 3:

Photograph of patient's foot 5 weeks after initiation of treatment



QUESTIONS:

1.This histological finding of broad-based budding yeast is consistent with which infection?

a. Histoplasmosis

b. North American blastomycosis

c. Coccidiosis

d. Cryptococcosis

e. South American blastomycosis

2. This fungus is endemic to which area?

a. Eastern and central United States

b. Southwestern United States and California

c. Central and South America

ANSWERS:

1. This histological finding showing broad-based budding yeast is consistent with which infection?

Correct answer:
B. North American blastomycosis

When visualized, *Blastomyces dermatitis* is differentiated from other yeast cells because of its size (8–15 µm in diameter), refractile cell wall and single, broad-based buds.[1] *Paracoccidioides brasiliensis*, which causes South American blastomycosis, is distinguished from North American blastomycosis by the presence of multiple, narrow-based buds arranged around the periphery of the mother cell.[1] Coccidioides pathologically is a spherule filled with endospores that resemble single yeast cells. However, they can be distinguished from blastomycosis in that they do not have broad based buds1 Pathologically, cryptococcus is 5–10 µm with narrow budding, heavily encapsulated yeast and not dimorphic. The possibility of cryptococcus was considered by the pathologists examining the specimen; however, the multiple nuclei goes against that diagnosis. Cryptococcus is an opportunistic fungal infection found primarily in immunocompromised. Histoplasma capsulatum hides within macrophages.

1. This fungus is endemic to which area?

Correct answer:
A. Eastern and central United States

Blastomycosis is endemic in southeastern and southcentral states bordering the Mississippi and Ohio River basins, the midwestern states and Canadian provinces bordering the Great Lakes, and a small area in New York and Canada along the St. Lawrence River and the Nelson River. Coccidioidomycosis is endemic to the southwestern United States and California. Paracoccidioides has a geographic distribution limited to Central and South America.

DISCUSSION:

Differential diagnosis for verrucous plaques includes warts, benign tumors, cancer and infections. When blastomycosis disseminates to the skin it can cause verrucous skin lesions that mimic squamous cell carcinoma. Although blastomycosis has been reported to involve almost every organ, the lungs are the most common site of infection, followed by the skin, bones, and genitourinary system. The characteristic cutaneous finding is a verrucous lesion, with irregular borders.[1] This tissue is often friable and bleeds easily.

Blastomycosis is typically acquired via inhalation of airborne conidia. Primary cutaneous blastomycosis is uncommon but can result from traumatic inoculation.[2] It is unknown whether this patient's infection was from direct cutaneous inoculation or hematogenous spread from a pulmonary blastomycosis, as he denied both pulmonary symptoms and foot trauma.

Infection may be acquired through the environment, and blastomycosis infection is often associated with occupational exposure or with outdoor recreational activities. This patient reported that he frequently performed yard work at his home in South Carolina. He was at risk because he was immunocompromised from immunosuppressive therapy for his renal transplant. Endogenous and exogenous immunosuppression are well-documented risk factors for disseminated blastomycosis.[3] Blastomyces can behave as an opportunistic pathogen, especially in patients with advanced acquired immunodeficiency syndrome, transplant recipients, those who are prescribed TNF-alpha inhibitors and other immunocompromised patients.[1] Infection with blastomycosis in renal transplant patients receiving antirejection medications has been documented in several previous case reports.[4,5]

TREATMENT:

Patients with extrapulmonary blastomycosis require therapy. Treatment options for patients include amphotericin B or an azole drug. Itraconazole is preferred for patients with mild-to-moderate disease not involving the central nervous system. Absorption of the capsule formulation is highly variable, requires gastric acidity and is enhanced when the agent is taken with food. Thus, in patients who receive concomitant medications that decrease gastric acidity, blood levels are reduced.[6] This patient takes pantoprazole 40 mg daily to control his GERD, which would have decreased the efficacy of itraconazole.

All immunocompromised patients with blastomycosis should be treated due to the potential for dissemination.[6] Amphotericin B is usually the treatment option for blastomycosis in immunocompromised patients, but it has adverse effects on the kidney and was deemed unsafe in this patient who was a kidney transplant recipient. Of note, case studies of kidney transplant patients infected with blastomycosis have reported treatment with either amphotericin B or itraconazole.[4,5] It is not known exactly how long immunosuppressed patients should receive treatment. Serody *et al* described a heart transplant patient with recurrence of fungal infection after ketoconazole and amphotericin B therapy and suggested lifelong antifungal treatment in that case.[4,5,7]

Our patient was referred to an infectious disease specialist and was prescribed terbinafine HCl 250 mg twice a day. Terbinafine is also used as a first-line oral agent for mild-to-moderate dermatophyte onychomycosis. It is used to treat onychomycosis in immunocompromised individuals and has fewer drug-drug interactions than itraconazole. However, patients taking terbinafine should be monitored for liver enzyme elevations. This medication is contraindicated in chronic or active hepatic disease.[8] A thorough literature review did not reveal any prior case reports documenting terbinafine as the treatment of blastomycosis in a kidney transplant recipient; however, as evidenced by the pre-treatment and mid-treatment pictures, it appears that terbinafine was efficacious in treating our patient's cutaneous blastomycosis.

CONCLUSION:

In immunocompromised patients with verrucous skin lesions, the clinician must consider the possibility of fungal infections, including blastomycosis. Several cases of blastomycosis in patients receiving antirejection medications for organ transplants have been previously documented.[5] Given the patient's immunocompromised state, a further delay in diagnosis and treatment could have led to a poor outcome, like the fatal case of disseminated blastomycosis in a young man with rapid progression to multiorgan failure after exposure to corticosteroids described by Lu J *et al*.[3] Blastomycosis may be initially misdiagnosed. This patient was initially diagnosed with pyogenic granuloma and the referring surgeon had considered amputation. Various case reports have cited incidents of cutaneous blastomycosis being initially misdiagnosed as pyoderma gangrenosum.[9] Thus, a high index of suspicion for deep fungal infection and collection of multiple samples for microbiology and histological evaluation should be performed when the diagnosis is uncertain and patients live in or have traveled to areas endemic for blastomycosis.[1]

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