BRIEF ARTICLE

An Unusual Case of Blastomycosis Presenting as "Punched Out" Ulcerations

Adrian T. Azar, BA[1], Robert A. Quiring, MD[1], Poonam C. Sharma, MD, PhD[2], Robert T. Brodell, MD[1,2]

[1] Department of Dermatology, University of Mississippi Medical Center, Jackson, MS, USA
[2] Department of Pathology, University of Mississippi Medical Center, Jackson, MS, USA

ABSTRACT

Background: Cutaneous blastomycosis commonly presents as verrucous, hyperkeratotic nodules or plaques. Less commonly, it presents as ulcerations with accompanying scale crusting or verrucous features.
Case Report: A healthy 34-year-old incarcerated male with a history of drug abuse presented with several, well-defined (punched out), deep ulcerating cutaneous lesions with undermined borders. There was no crusting, or verrucous features. The clinical differential diagnoses included pyoderma, vasculitic ulcers, and pyoderma gangrenosum. The histopathology from a gluteal ulceration demonstrated pseudoepitheliomatous hyperplasia with acute, chronic, and granulomatous inflammation. GMS stain of the specimen exhibited thick-walled yeast demonstrating broad-based budding typical of blastomycosis and tissue cultures grew *Blastomyces dermatitidis* after one month.
Conclusion: Ulceration without verrucous features can portend cutaneous blastomycosis. Many dermatologists may be unaware of this atypical, non-verrucous presentation. Diagnosis using fungal culture of the wound or tissue takes weeks to result. A prompt biopsy and histopathologic examination or broad-range PCR testing of a wound swab, tissue or urine specimen can lead to an early diagnosis.

INTRODUCTION

Blastomycosis is an infectious disease caused by Blastomyces, mainly *B. dermatitidis* and *B. gilchristii*. These dimorphic fungi infect both immunocompetent and immunocompromised individuals.[1] Blastomycosis is endemic to North America found in natural water sources, soil and rotten wood along the Great Lakes and Ohio and Mississippi River valleys. Inhaled airborne conidia initially infect the lungs before disseminating to other organs including skin, bone, and the central nervous system.[2] While 50% of cases remain asymptomatic, serious infections can be fatal in up to 4% of cases.[1] Cutaneous blastomycosis (CB) is the most common extrapulmonary presentation of blastomycosis, occurring in 40-80% of patients with disseminated disease.[2] CB commonly presents with hyperkeratotic, crusted wart-like plaques or nodules demonstrating irregular borders that overlie subcutaneous abscesses that can mimic keratinocytic skin cancers.[3] Alternatively, focal crusted ulcerations with heaped-up

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borders can appear adjacent to verrucous plaques.[2] However, there are only few reports of patients presenting with well-defined, clean, bright red ulcers without scale crust or significant verrucous changes.

CASE REPORT

An incarcerated 34-year-old African American male from Mississippi with a history of prior substance abuse presented with a two-month history of progressing painful "punched-out" ulcers with undermined edges and hyperpigmented borders on the right forearm **(Figure 1a)** and left buttock **(Figure 1b)**. A 30-pound weight loss, fevers, chills, night sweats and hemoptysis were reported. The patient was hemodynamically stable with slight leukocytosis and an elevated erythrocyte sedimentation rate (ESR) of 88 mm/hr and C-reactive protein (CRP) of 17 mg/L. Deep and superficial abscess formation on the proximal forearm, left scrotum were noted on CT imaging. A bacterial cellulitis was suspected. Following debridement of the forearm ulcer, empiric vancomycin 1g BID and cefepime 1g TID were administered intravenously. Bacterial, anaerobic, and mycobacterium blood and tissue cultures were negative at one week, while fungal cultures were pending. New nodular, slightly crusted lesions appeared on the chest and back one week later. Histopathology from a 6 mm punch biopsy of a left gluteal ulcer demonstrated pseudoepitheliomatous hyperplasia with acute, chronic, and granulomatous inflammation **(Figure 2a).** H&E **(Figure 2b)** and GMS **(Figure 2c)** staining demonstrated thick-walled yeast forms demonstrating broad-based budding. The I&D fluid from the right forearm was inoculated onto three types of slants for fungal cultures: Sabouraud dextrose agar (SDA) without antibiotics, SDA supplemented with 0.05g/L chloramphenicol, and SDA supplemented with 0.4g/L cycloheximide. After incubation at room temperature, beige feathery colonies with yellow reverse were observed on the plain SDA on Day 14. These colonies were identified as Blastomyces species complex using Matrix-Assisted Laser Desorption/Ionization Time-of-Flight (MALDI-TOF) mass spectrometry. Chest x-ray demonstrated bilateral opacities in a miliary pattern, consistent with pulmonary blastomycosis. Treatment with amphotericin B 5mg/kg daily for 7 days was started, and the patient was transitioned to itraconazole 200mg BID for 12 months leading to healing of all skin lesions and pulmonary disease.

DISCUSSION

This patient presented with clean-appearing ulcerations not associated with the hyperkeratotic, verrucous nodules or plaques typical of CB.[1,4,5,6] There are very few reports of CB with this unusual presentation.[4,7,8] Fungal cultures are the gold standard for diagnosing blastomycosis but can take weeks to grow.[2] The initial diagnosis in this case rested upon a biopsy that demonstrated the thick-walled yeasts with broad-based budding. Thus, a biopsy is recommended in patients with suspected bacterial pyoderma and ulcerations not responding to empiric antibiotics, negative bacterial cultures, and when other risk factors for CB are present including residence along the Mississippi river, incarceration, and a history of drug abuse.

Finally, broad-range PCR testing to detect fungal DNA can be performed to identify the Blastomyces species. This test may play a crucial role when the specimens do not reveal the presence of a fungal pathogen

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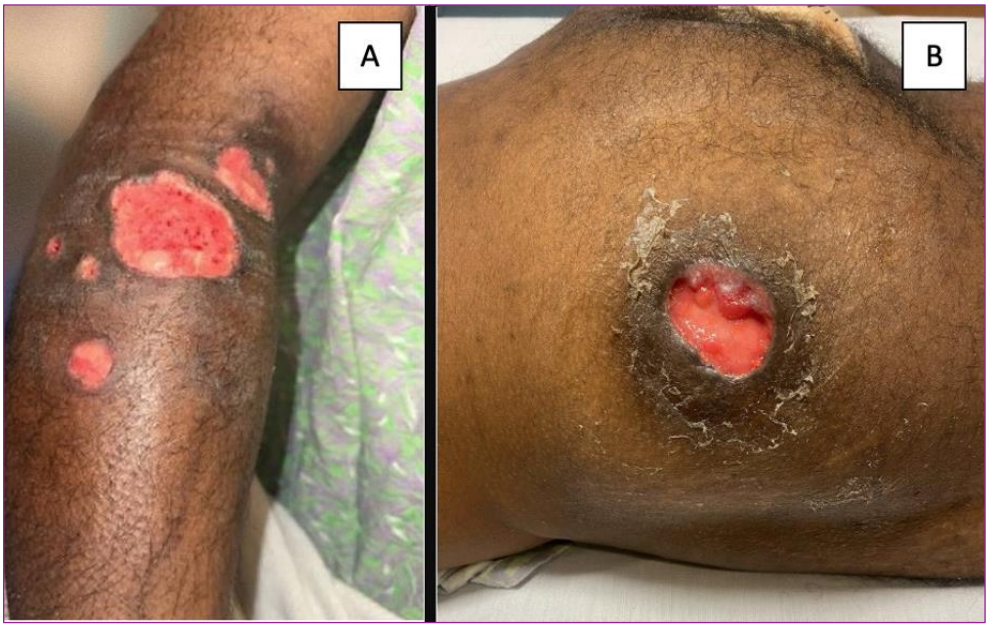

Figure 1. Large, painful punched-out, ulcerations with undermined edges, hyperpigmented borders were present on the right forearm **(A)** and left buttocks **(B).** There were no verrucous changes and no scale or crusting of these lesions.

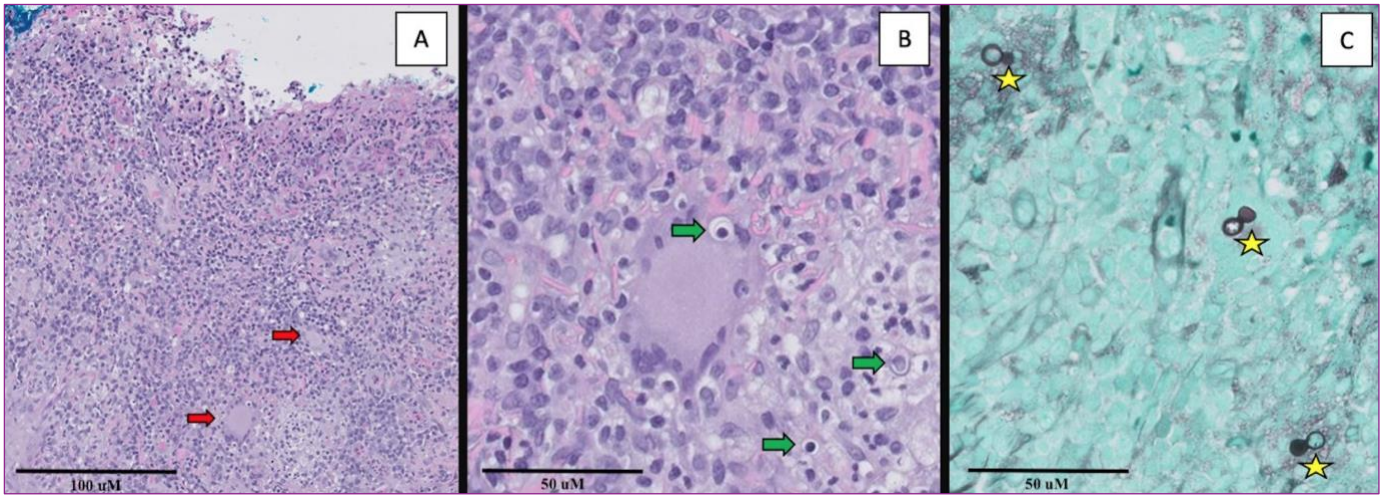

Figure 2. (A) H&E x10: Pseudoepitheliomatous hyperplasia with a prominent underlying inflammatory infiltrate and several multinucleated giant cells (red arrows). **(B)** H&E x20: Thick-walled yeast forms (green arrows) present within the multinucleated giant cell. **(C)** GMS x20 Uniform shaped yeast forms with thick refractile walls and broad-based budding (yellow stars).

because of low numbers of organisms or lack of viability. Even when a fresh tissue specimen is no longer available, it can be performed on paraffin-embedded tissue. Both fungal 28S and Internal Transcribed Spacer sequence (ITS) rDNA can be used as targets for the PCR assays. Results are available in 2-3 days while certain real-time PCRs can provide identification within approximately five hours.[9,10] CDC recommends ordering an enzyme immunoassay urine antigen test initially for blastomycosis diagnosis. This is a non-invasive approach and may have the highest

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sensitivity and the quickest turnaround time.[10] The molecular as well as antigen-antibody detection tests have quicker turnaround times as compared to the culture methods.[11] The sensitivity and specificity of testing option tests are reviewed in **Table 1.**[11]

Table 1: Diagnostic efficiency parameters for different tests for Blastomyces.

Tests	EIA Urine Ag	EIA Serum Ag	CF Ab	ID Ab	PCR	Histopathology	Cytology
Sensitivity	76-93%	56-82%	9-57%	28-56%	86%	81%	38-97%
Specificity	High (Cross reacts with Histoplasma Ag)	High (Cross reacts with Histoplasma Ag)	30-100%	100%	99.4%	100%	100%

Ag: Antigen; Ab: Antibody; EIA: Enzyme immunoassay; CF: Complement fixation; ID: Immunodiffusion; PCR: Polymerase chain reaction.

Early diagnosis and intervention are critical to preventing further dissemination of blastomycosis to other organ systems sometimes even death. Once the diagnosis of blastomycosis is made, recommended treatment involves azole antifungals for mild pulmonary or disseminated disease while amphotericin B is reserved for moderate to severe disseminated disease involving extensive pneumonia, multiorgan disease, hemodynamic instability or those requiring hospitalizations. The lipid formulation of amphotericin B of 3-5mg/kg daily is recommended for 1-2 weeks.[2] This patient was then transitioned from 5mg/kg amphotericin B to itraconazole 200mg BID. Because of the renal toxicity of amphotericin B, transitioning to azoles is recommended after improvement is demonstrated while monitoring of levels to ensure appropriate drug adsorption and adherence.[2,12] Primarily cutaneous symptoms can be treated with 200mg itraconazole TID for three days, followed by once or twice daily dosing for 6-12 months.

CONCLUSION

CB can present with deep ulcers absent the verrucous surface features, crust, and scale more typical of this condition. Clinicians and dermatologists should be aware of this possibility, as delays in treatment can significantly impact morbidity and mortality. Maintaining a high index of suspicion for the possibility of a deep fungal infection led to the special stains and fungal tissue cultures that confirmed the diagnosis permitting the initiation of effective treatment. PCR is an evolving technique that can lead to a more rapid diagnosis for nonspecific lesions with unclear etiology while fungal cultures are pending. We hope this case stimulates reports of other similar cases demonstrating atypical presentations of CB so that the true prevalence can be determined.

Conflict of Interest Disclosures: Robert T. Brodell is a principal investigator for clinical trials (Novartis and Sanofi), the Corevitas psoriasis biologic registry and owns stock in Veradermics, Inc. These potential conflicts of interest are not believed to be relevant to the content of this article. Adrian Azar and Robert Quiring have no conflicts of interest to disclose.

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Corresponding Author:
Robert T. Brodell, MD
2500 North State Street Jackson, Mississippi 39216
Phone: 601-984-1540
Email: rbrodell@umc.edu

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References:

1. McBride JA, Gauthier GM, Klein BS. Clinical Manifestations and Treatment of Blastomycosis. *Clin Chest Med*. 2017;38(3):435-449. doi:10.1016/j.ccm.2017.04.006
2. 2Saccente M, Woods GL. Clinical and laboratory update on blastomycosis. *Clin Microbiol Rev*. 2010;23(2):367-381. doi:10.1128/CMR.00056-09
3. Johnson E, Martin M, Sharma R, Meyer C, Kanne J. Blastomycosis. *Journal of Thoracic Imaging.* 2022; 37 (1): W5-W11. doi: 10.1097/RTI.0000000000000562.
4. Owen WR, Thurs K, Kim DL. Blastomycosis Presenting as a Nonhealing Wound. *Advances in Skin & Wound Care.* 2012; 25 (7): 321-323. doi: 10.1097/01.ASW.0000416005.78089.b0.
5. Elmas ÖF, Uyar B, Kilitçi A. A 25-Year History of Leg Ulceration: Cutaneous Blastomycosis. *Dermatol Pract Concept*. 2020;10(3):e2020054. Published 2020 Jun 29. doi:10.5826/dpc.1003a54
6. Melton M, Baquerizo Nole K. Primary Cutaneous Blastomycosis: An Ulcerated Wound in an Immunocompetent Patient. *Cureus*. 2023;15(9):e45786. Published 2023 Sep 22. doi:10.7759/cureus.45786
7. Balasaraswathy P, Theerthanath. Cutaneous blastomycosis presenting as non-healing ulcer and responding to oral ketoconazole. *Dermatol Online J*. 2003;9(5):19.
8. Zhao TM, Gao J, She DY, Chen LA. Blastomycosis in China: a case report and literature review. *Chin Med J (Engl)*. 2011;124(24):4368-4371.
9. Lieberman JA, Bryan A, Mays JA, Stephens K, Kurosawa K, Mathias PC, SenGupta D, Bourassa L, Salipante SJ, Cookson BT. 2021. High Clinical Impact of Broad-Range Fungal PCR in Suspected Fungal Sinusitis. J Clin Microbiol 59:10.1128/jcm.00955-21. https://doi.org/10.1128/jcm.00955-21
10. Sidamonidze K, Peck MK, Perez M, Baumgardner D, Smith G, Chaturvedi V, Chaturvedi S. Real-time PCR assay for identification of Blastomyces dermatitidis in culture and in tissue. J Clin Microbiol. 2012 May;50(5):1783-6. doi: 10.1128/JCM.00310-12. Epub 2012 Mar 7. PMID: 22403418; PMCID: PMC3347106.
11. Centers for Disease Control Algorithms for identifying Deep Fungal Infections. https://emergency.cdc.gov/coca/calls/2023/callinfo_092123.asp
12. Caldito EG, Antia C, Petronic-Rosic V. Cutaneous blastomycosis. *Jama dermatology*. 2022;158(9):1064-1064. doi:10.1001/jamadermatol.2022.3151

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