Skeletal Radiology (2019) 48:2021–2027
https://doi.org/10.1007/s00256-019-03234-9

CASE REPORT

Spinal blastomycosis: unusual musculoskeletal presentation with literature review

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Received: 23 February 2019 / Revised: 24 April 2019 / Accepted: 30 April 2019 / Published online: 28 May 2019

Abstract

We report a case of a 41-year-old male who presented to our institution with a large groin mass. CT, MRI and PET imaging was performed and was concerning for a soft tissue abscess likely originating in the lumbar spine. Differential considerations included infection, with atypical infections such as tuberculosis strongly considered. Biopsy revealed fungal elements preliminarily reported as consistent with *Cryptococcus neoformans* but later revealed to be *Blastomyces dermatitidis*. The patient responded positively following the introduction of appropriate treatment. This case illustrates the imaging similarities between spinal blastomycosis, spinal tuberculosis, and other fungal infections as well as the need for biopsy to differentiate.

Keywords Blastomycosis · Fungal · Infection · MRI · Tuberculosis · Vertebrae · Spinal · Abscess

Introduction

Blastomyces dermatitidis is endemic to the upper Midwest United States and southeast Canada to include the Great Lakes, Ohio and Mississippi river valleys. Individuals infected with *B. dermatitidis* may or may not become symptomatic. However, when symptomatic, the lung is the most commonly involved organ followed by the skin and bones. In disseminated infections, the genitourinary and central nervous systems may be involved [1]. Since imaging findings of spinal blastomycosis may mimic tuberculosis, other fungal infections or malignancy, biopsy is required to differentiate.

Case report

A 41-year-old male patient initially presented to an outside institution in a neighboring state with a cough and low-grade fever. Chest radiograph preformed at that outside institution revealed a band-like right upper lobe (RUL) opacity with a subsequent chest computed tomography (CT) exam demonstrating RUL peribronchovascular opacity and mediastinal lymphadenopathy (Fig. 1a). A positron emission tomography (PET) CT demonstrated slightly increased metabolism in the mediastinal lymphadenopathy, but no significant uptake in the lung opacity. Additional hypermetabolic, mildly destructive

This material was previously presented at the American Society of Neuroradiology (ASNR) meeting. A release was obtained to submit this case report for publication from the ASNR.

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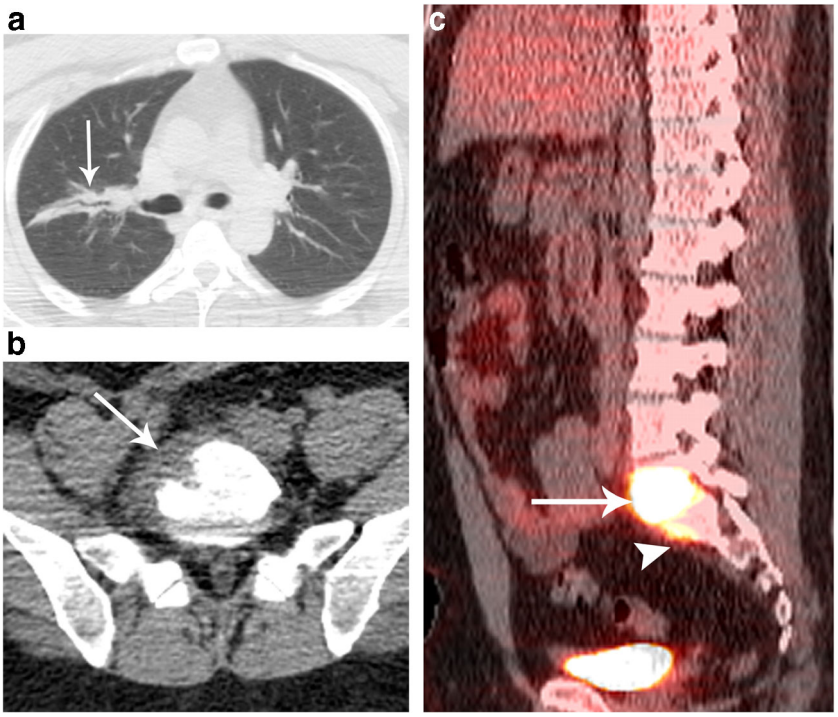


Fig. 1 41-year-old man with fever and cough. PET-CT performed at an outside institution. **a** CT axial image (lung window) demonstrates band-like peribronchovascular opacity with associated bronchiectasis (arrow). **b** Axial CT image (soft tissue window) shows destruction of the right L5 anterior vertebral body with an associated soft tissue component (arrow). **c** Sagittal PET-CT fused image demonstrates increased uptake within the L5 lesion (arrow) and along the S1 superior endplate (arrowhead)

osseous lesions with soft tissue components were identified in the right L5 and S1 vertebrae (Fig. 1b,c). The patient was told that the lung findings were suspicious for malignancy and that the vertebral lesions were concerning for metastases. A lumbar spine (L-spine) magnetic resonance imaging (MRI) exam was recommended; however, the MRI was not performed, possibly since the patient was not experiencing any back-related symptoms. The patient was subsequently lost to follow-up.

The patient later developed generalized low back pain which he initially attributed to his occupation, since his job

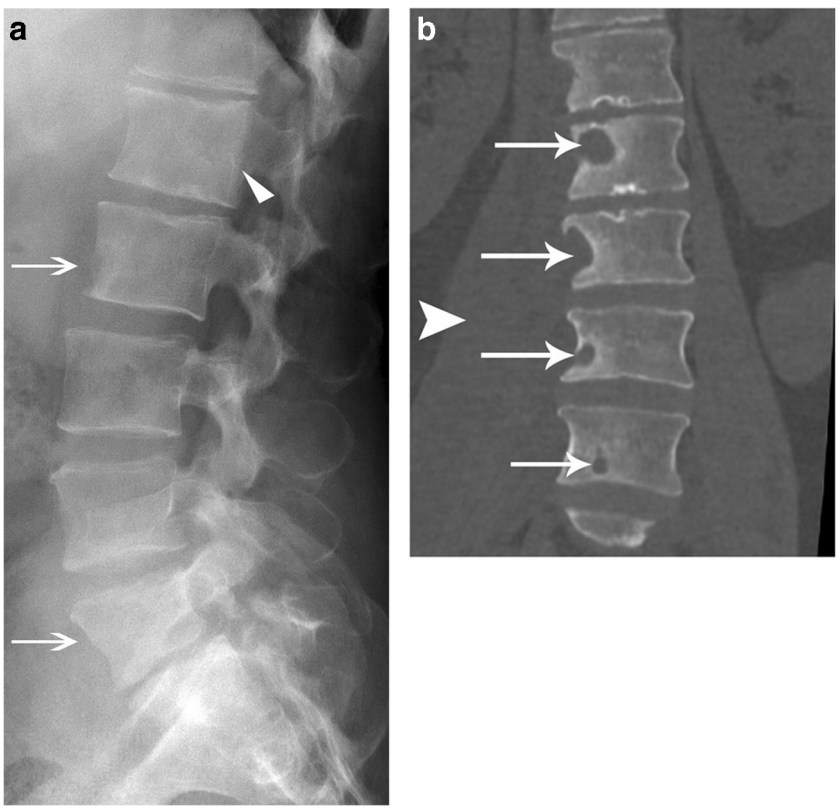


Fig. 2 Imaging obtained when patient presented to our institution 14 months later with back pain and a right groin mass. **a** Lateral lumbar spine radiograph demonstrates destructive foci in the anterior L2 and L5 vertebral bodies with subtle surrounding sclerosis (arrows), and a lytic area in the posterior L1 vertebral body with pedicle extension (arrowhead). **b** Lumbar spine CT with coronal reconstruction shows multiple right-sided lytic vertebral body lesions (arrows) with asymmetric enlargement of the right psoas muscle (arrowhead) and relative preservation of the disk spaces

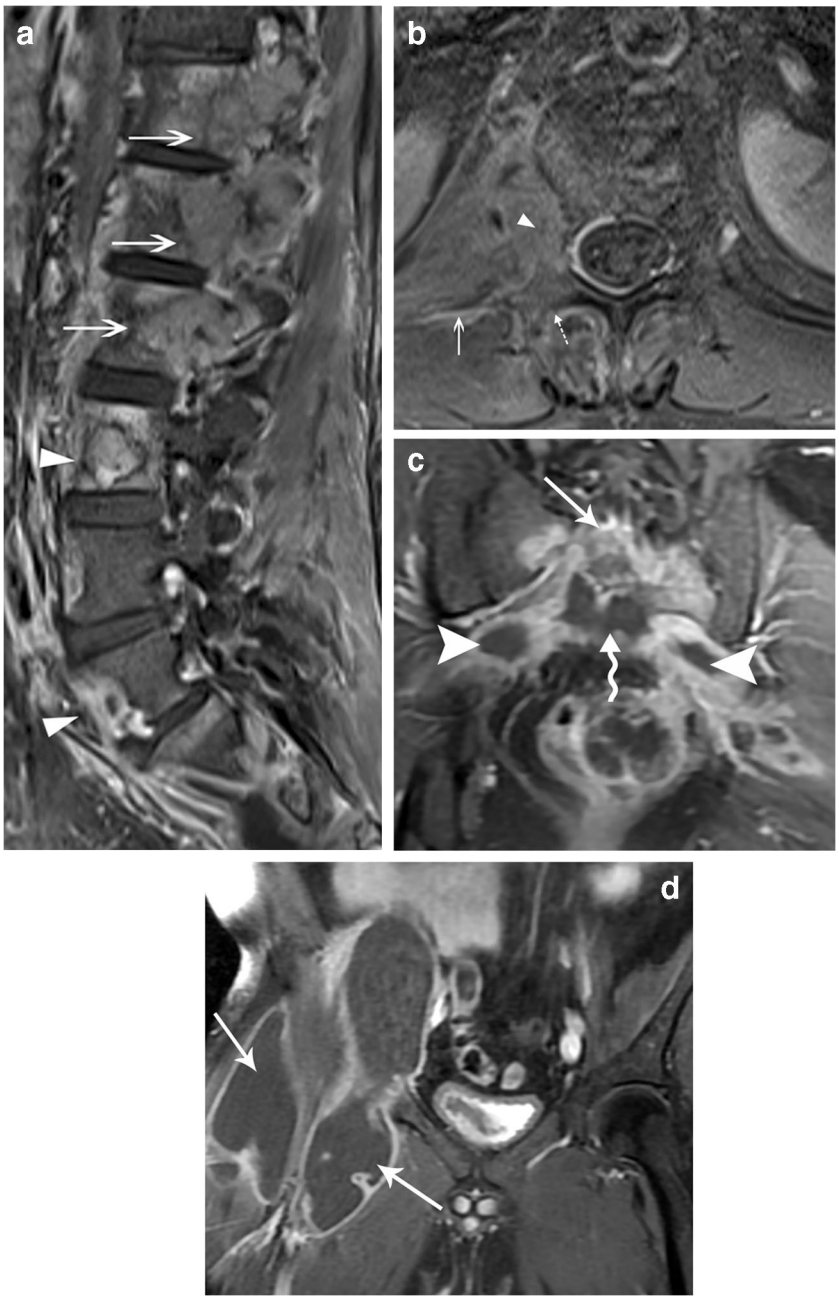


Fig. 3 **a**–**d** MRI obtained when patient presented to our institution 14 months later with back pain and a right groin mass. **a** Sagittal T1-weighted post-gadolinium fat-saturated image demonstrates extensive destruction of the right posterior T12–L2 vertebral bodies with pedicle extension and involvement of multiple neural foramina (arrows). Additional osseous lesions in the L3 and L5 vertebrae with sparing of the disk spaces (arrowheads). **b** Axial T1-weighted fat-saturated image at the L1-L2 level demonstrates right psoas enhancement with enhancing soft tissue extending into the neural foramen and epidural space (arrowhead). Extension into the right 12th rib (straight arrow) and the posterior elements (dotted arrow) is a feature that suggests blastomycosis over tuberculosis. **c** T1-weighted coronal post-gadolinium fat-saturated image demonstrates sacral osseous involvement (straight arrow) with adjacent presacral fluid collections (wavy arrow) that track into and along both piriformis muscles (arrowheads). **d** More caudal, T1-weighted coronal post-gadolinium fat-saturated image demonstrates a large, multiloculated, peripherally enhancing fluid collection with internal septations extending along the right iliopsoas muscle into the right groin (arrows)

required strenuous physical labor. The patient initially sought relief from a chiropractor; however, the symptoms worsened with the back pain eventually localizing to the right lower lumbar region. He also developed fevers, chills, night sweats, anorexia and unintentionally lost 25 pounds. A right inguinal mass later developed and gradually increased in size over 2–3 months. This mass prompted his presentation to our institution 14 months after he initially sought medical care at the outside institution.

At our institution, L-spine radiographs, L-spine CT, L-spine and pelvis MRIs were performed to evaluate the patient's back pain and groin mass. The radiographs and CT demonstrated sclerotic bordered areas of osseous destruction which favored a more long-standing process (Fig. 2a,b). The L-spine MRI demonstrated multiple osseous lesions with involvement of both the anterior and posterior vertebral bodies, relative sparing of the intervertebral disc spaces, and extensive involvement of the posterior elements and neuroforamen (Fig. 3a). Soft tissue enhancement extended into the surrounding paraspinal structures to include the psoas musculature and right posterior 12th rib with minimal involvement of the epidural space (Fig. 3b). Peripherally enhancing abscesses extended inferiorly along the psoas musculature to involve both piriformis muscles, the sacrum and subcutaneous soft tissues of the right proximal thigh (Fig. 3c,d). Ultrasound of the right groin depicted a large mildly complex fluid collection with

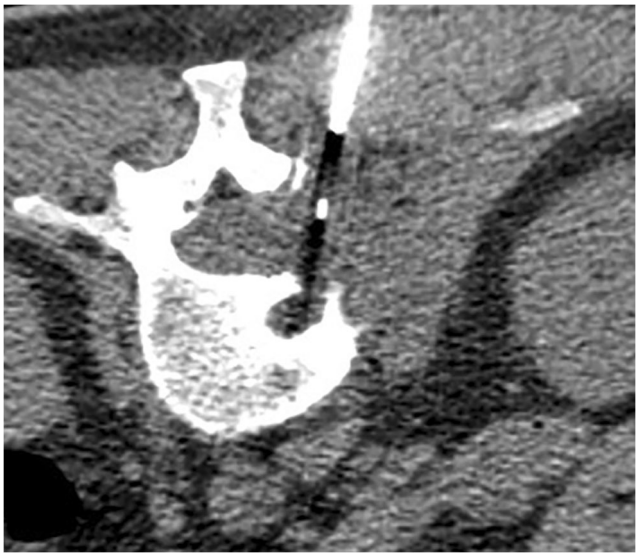


Fig. 4 CT-guided biopsy of the right L1 vertebrae

internal debris and incomplete septations. Of note, the patient denied incontinence or lower extremity paresthesias.

Further history was elicited which revealed that the patient lived in a mountainous part of the eastern United States. He denied caving, hiking, or other significant outdoor activity, and his only known animal exposure was contact with dogs. He was not aware of prior tuberculosis exposure. He denied being incarcerated and was not immunocompromised. Nevertheless, an atypical infection, to include *Mycobacterium tuberculosis*, was considered likely based on the imaging findings, and a CT-guided percutaneous biopsy of the right L1 vertebral body was performed (Fig. 4). The immediate preliminary pathology interpretation based on fine-needle aspiration morphology was fungal elements suspicious for *Cryptococcus neoformans*. Following application of special stains the following day, a final diagnosis of *B. dermatitidis* was reported. H&E stained slides of the bone biopsy demonstrated non-necrotizing granulomatous inflammation. A GMS stain revealed numerous yeast forms measuring 10–12 μm in diameter, located within histiocytes. The intracellular yeast forms lacked a capsule on mucicarmine stain consistent with a diagnosis of *B. dermatitidis* (Fig. 5a–c). Five days after the biopsy, polymerase chain reaction (PCR) test confirmed *B. dermatitidis* with hyphal forms diagnostic of *B. dermatitidis* identified 3 weeks later on the fungal culture.

Ultrasound-guided aspiration of the right inguinal mildly complex cystic mass returned approximately 1 L of purulent fluid. Intravenous liposomal amphotericin was administered for 6 weeks followed by an additional 12 months of oral itraconazole therapy. One and 3 month follow-up MRI examinations demonstrated progressive decrease in the size of the cystic masses and gradual resolution of the lumbosacral osteomyelitis (Fig. 6a,b). After 3 months, the majority of the patient's symptoms had resolved with the exception of mild intermittent back pain.

Discussion

Blastomycosis is caused by *B. dermatitidis,* and it is one of the endemic North American mycoses. Blastomycosis has an incidence according to the Centers for Disease Control of 1–2 cases per 100,000 population, but levels as high as 10–40 cases per 100,000 people are present in endemic areas [2]. Other synonyms previously used for this disease include Gilchrist's disease, North American Blastomycosis and Chicago disease [3]. Blastomycosis can also rarely occur in areas of Africa and southwest Asia [4].

B. dermatitidis is a thermally dimorphic fungus that can reproduce in either a mycelial or a yeast-like state depending on the temperature. Wet soil containing animal droppings or decaying vegetable matter is the main source of human exposure to the fungus, usually effecting middle-aged males due to their increased outdoor occupational or recreational activities

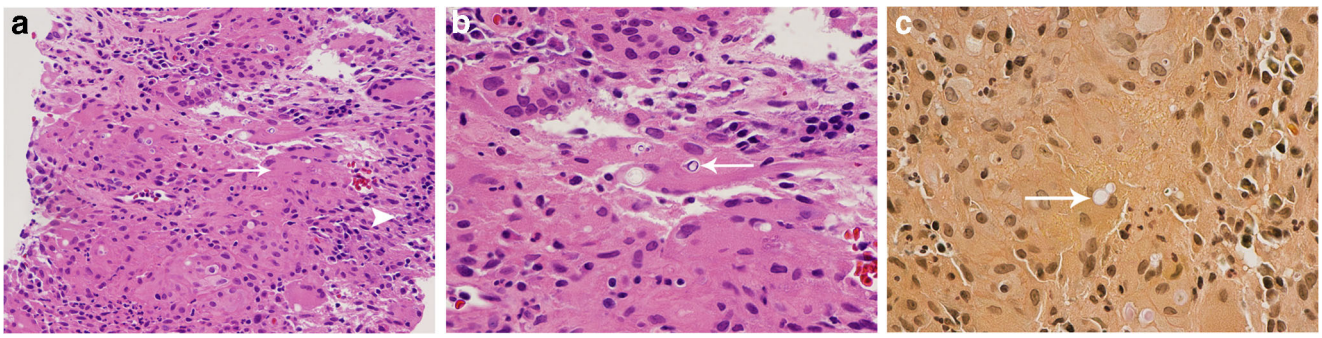
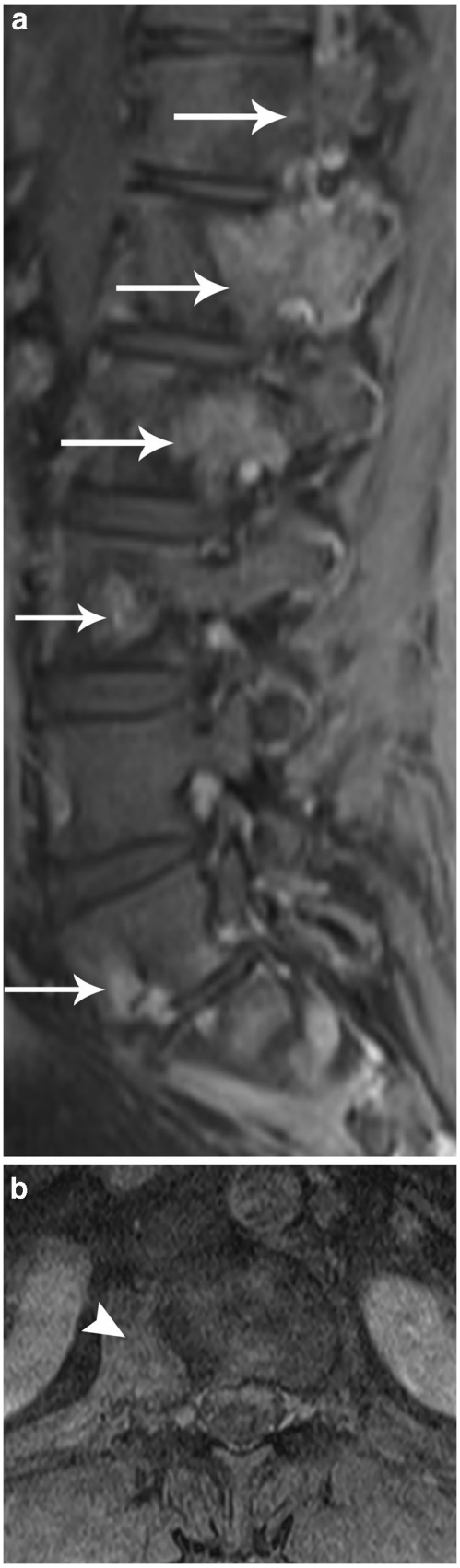


Fig. 5 Photomicrographs of the patient's bone biopsy specimen. **a** Hematoxylin and eosin (H&E) staining at 200x magnification demonstrates non-necrotizing granulomatous inflammation characterized by multinucleated giant cells (arrow) and a peripheral rim of lymphocytes (arrowhead). **b** Further magnification to 400x reveals small, round yeast forms (arrow) that measure approximately 10–12 μm in diameter. **c** Mucicarmine stain viewed at 400x magnification shows no magenta staining around the yeast form (arrow) demonstrating an absence of the mucinous capsule that would be present with *Cryptococcus neoformans*. The diagnosis of *B. dermatitidis* was supported by the size of the yeast form and the lack of a thick, mucinous capsule was later confirmed with culture results



◀ **Fig. 6** MRI 3 months after antifungal therapy. **a** T1-weighted post contrast fat-saturated image similar in location to pretreatment. Figure 3a image, demonstrates decreased soft tissue, foraminal, and osseous enhancement (arrows), particularly at T12. **b** Axial T1-weighted post contrast fat-saturated image at L1-L2, similar to pretreatment. Figure 3b, demonstrates decreased right psoas and foraminal enhancing soft tissue and mass effect on the right lateral epidural space (arrowhead)

[3]. Since *B. dermatitidis* is not transmitted from person to person, it is generally not considered contagious.

Blastomycosis can be asymptomatic, or it may present with disseminated involvement that is potentially fatal. The most commonly involved organ, by far, is the lung. Blastomycosis can present acutely with influenza-like symptoms including fever, cough, myalgia, arthralgia, and pleurisy. The phagocytic actions of macrophages and white blood cells usually prevent proliferation of *B. dermatitidis*; however, pneumonia and dissemination to other organs can occur [3]. The pulmonary symptoms may resolve spontaneously, but in disseminated infection, the prognosis is poor unless proper treatment is initiated in a timely manner. Since blastomycosis can resemble malignancy and other atypical infections, including tuberculosis, an accurate diagnosis is often delayed [5].

The second and third most commonly involved organ systems are the integumentary and musculoskeletal (MSK), respectively. Spread from the pulmonary system to these systems most often occurs hematogenously but on occasion may occur by direct inoculation. Musculoskeletal manifestations of blastomycosis vary and include case reports of patients developing osteomyelitis and soft tissue or muscle abscesses. The central nervous and genitourinary organ systems are less commonly involved [6].

Our patient had MSK findings that included destruction and collapse of multiple thoracic and lumbar vertebral bodies, relative preservation of the disc space, and non-contiguous vertebral involvement with spread likely along the anterior longitudinal ligament [7–13]. These findings are often identified in blastomycosis, but they can also occur in other fungal infections involving the spine to include coccidioidomycosis and tuberculosis [12, 14–17]. While there is no foolproof way to differentiate between blastomycoses, cryptococcus, coccidioidomycosis and tuberculosis on imaging, the location of the lesions and the development of soft tissue abscesses can be helpful. Both blastomycosis and tuberculosis have a predilection for the thoracolumbar junction; whereas, coccidioidomycosis most commonly involves the thoracic spine with cryptococcus typically involving the lumbar spine [7, 8, 13, 18]. In addition, both blastomycosis and tuberculosis can form large paraspinal abscesses that occasionally extend into the groin and upper thigh with fistula formation more commonly noted in blastomycosis [7, 14, 19–21]. In contrast, even though cryptococcus often involves the pedicles and lamina, fistula formation is unusual [12]. Given that the vertebral lesions in

this patient involved the thoracolumbar, lumbar and sacral areas, coccidioidomycosis was considered unlikely. Cryptococcus was also considered unlikely due to the presence of large paraspinal abscesses. To help differentiate between blastomycosis and tuberculosis, which both can involve the thoracolumbar and lumbar regions and form paraspinal abscesses, the presence of posterior element involvement and extension into the posterior ribs is highly suggestive of blastomycosis with the latter rare in tuberculosis [12, 15]. In fact, extension into the posterior ribs has been reported in as many as 50% of patients with blastomycosis and <5% of patients with tuberculosis [8, 22].

Effective treatment of blastomycosis requires rapid consideration of an atypical infection in order to obtain a timely diagnosis and quickly begin appropriate therapy. *B. dermatitidis*, *Cryptococcus neoformans* and *Histoplasma capsulatum* may all present histologically as yeast forms within the cytoplasm of histiocytes on biopsy or fine-needle aspirate sampling. However, the yeast form of *H. capsulatum* can often be morphologically differentiated due to the smaller size of the yeast, while the yeast forms of *Cryptococcus* and *B. dermatitidis* are larger and can be difficult to distinguish on morphologic exam only. Preliminary diagnosis from either surgical pathology or cytopathology such as in the setting of intra-operative frozen section consultation, can be challenging with less than 80% of fungal organisms correctly identified at the time of immediate interpretation using only morphologic features [23]. Nevertheless, distinction is generally possible with the aid of special stains and by evaluating better quality slides with permanent material compared to frozen section or uncover slipped smears based on the morphologic assessment. Morphologic features that can be used to suggest a diagnosis include yeast size, budding patterns and the presence of a capsule, which can be assessed on formalin-fixed paraffin-embedded tissue with the use of special stains. In the minority of cases in which morphology and special stains are indeterminate, PCR testing of culture material and formalin-fixed paraffin-embedded tissue is available. Additionally, antigen testing for blastomycosis antigens can be performed with urine and serum using an enzyme immunoassay (EIA). The most sensitive test, and therefore the gold-standard for diagnosis remains the fungal culture which may take several days or weeks.

With respect to size, *H. capsulatum* is smaller (2–4 μm) than *Cryptococcus neoformans* (4–10 μm) or *B. dermatitidis* (8–15 μm) and *Coccidioides immitis* is usually much larger (20–200 μm) [23]. The mucicarmine stain can help differentiate between these three fungi with *Cryptococcus neoformans* staining magenta due to a thick, mucinous capsule whereas *B. dermatitidis* and *Coccidioides immitis* do not stain magenta due to lack of a mucinous capsule [24]. Perhaps more useful is that *B. dermatitidis* can be strongly suggested when broad-based buds are identified as both *Cryptococcus neoformans* and *H. capsulatum* have narrow-based budding [3, 23].

Initial therapy for blastomycosis is usually pharmacological with non–life threatening and non-CNS infections usually treated with azoles to include ketoconazole, itraconazole, and fluconazole with up to 36% of patients successfully treated entirely with medicine [18]. Amphotericin B remains the drug of choice for patients with severe life-threatening or CNS disease, pregnant and immune compromised patients, transplant recipients, and patients on chronic glucocorticosteroids [25]. Even in patients with vertebral osteomyelitis and the absence of neurologic deficits or a major spinal deformity, the use of non-operative treatment has been recommended [26]. In patients with a delay in diagnosis or spinal canal compromise, surgery may be indicated [20]. Fortunately, current medical regimens are usually successful in treating blastomycosis, unlike prior to the availability of specific antifungal therapy when mortality rates of up to 60% were reported [27].

In conclusion, even though there are some distinguishing imaging features, spinal blastomycosis has many imaging similarities to other fungal infections as well as spinal tuberculosis. Therefore, early biopsy is required for a definitive diagnosis in order to initiate an appropriate therapeutic regimen in a timely manner.

Acknowledgements Dr. Kristin Atkins of the University of Virginia Department of Pathology helped with the pathology images for this report.

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

References

1. Smith JA, Kauffman CA. Blastomycosis. Proc Am Thorac Soc. 2010;7(3):173–80 Review.
2. CDC (2018) Blastomycosis statistics; [cited 2009 May 19]. https://www.cdc.gov/fungal/diseases/blastomycosis/statistics.html
3. Saccente M, Woods GL. Clinical and laboratory update on blastomycosis. Clin Microbiol Rev. 2010;23(2):367–81 Review.
4. Frean JA, Carman WF, Crewe-Brown HH, Culligan GA, Young CN. Blastomycoses dermatitidis infections in the RSA. S Afr Med J. 1989;76(1):13–6.
5. Fang W, Washington L, Kumar N. Imaging manifestations of blastomycosis: a pulmonary infection with potential dissemination. Radiographics. 2007;27(3):641–55 Review.
6. Lemos LB, Guo M, Baliga M. Blastomycosis: organ involvement and etiologic diagnosis—a review of 123 patients from Mississippi. Ann Diagn Pathol. 2000;4(6):391–406 Review.
7. Rasouli MR, Mirkoohi M, Vaccaro AR, et al. Spinal tuberculosis: diagnosis and management. Asian Spine J. 2012;6(4):294–308.
8. Gehweiler JA, Capp MP, Chick EW. Observations on the roentgen patterns in blastomycosis of bone: a review of cases from the Blastomycosis Cooperative Study of the Veterans Administration and Duke University Med Center. Am J Roentenol Radium Ther Nucl Med. 1970;108:497–510.

9. Bassett FH, Tindall JP. Blastomycosis of bone. South Med J. 1972;65:547–55.
10. Williams RL, Fukui MB, Meltzer CC, et al. Fungal spinal osteomyelitis in the immunocompromised patient: MR findings in 3 cases. Am J Neuroradiol. 1999;20:381–5.
11. Moorthy S, Prabhu NK. Spectrum of MR imaging findings in spinal tuberculosis. AJR. 2002;179(4):979–83.
12. Kim CW, Perry A, Currier B, Yaszemski M, Garfin SR. Fungal infections of the spine. Clin Orthop Relat Res. 2006;444:92–9.
13. Hadjipavlou AG, Mader JT, Nauta HJ, Necessary JT, Chaljub G, Adesokan A. Blastomycosis of the lumbar spine: case report and review of the literature, with emphasis on diagnostic laboratory tools and management. Eur Spine J. 1998;7(5):416–21.
14. Saccente M, Abernathy RS, Pappas PG, et al. Vertebral blastomycosis with paravertebral abscess: report of 8 cases and review of the literature. Clin Infectious Dis. 1998;26(2):413–8.
15. Dalinka MK, Dinnenberg S, Greendyk WH, Hopkins R. Roentgenographic features of osseous coccidioidomycosis and differential diagnosis. J Bone Joint Surg Am. 1971;53:1157–64.
16. Mahiquez M, Bunton KL, Carney G, Weinstein MA, Small JM. Nonsurgical treatment of lumbosacral blastomycosis involving L2-S1. Spine. 2008;33:E442–6.
17. Güler N, Palanduz A, Ones U, al e. Progressive vertebral blastomycosis mimicking tuberculosis. Pediatr Infect Dis J. 1995;14(9):816–8.
18. Rammaert B, Gamaletsou MN, Zeller V, et al. Dimorphic fungal osteoarticular infections. Eur J Clin Microbiol Infect Dis. 2014;33(12):2131–40.
19. Goldman AB, Freiberger RH. Localized infectious and neuropathic diseases. Semin Roentgenol. 1979;14:19–32.
20. Sivalingham J, Kumar A. Spinal tuberculosis resembling neoplastic lesions on MRI. J Clin Diagn Res. 2015 Nov; 9(11):TC01–TC03
21. Dimar JR 2nd, Puno RM, Nowacki MR, Carreon LY. Surgery for blastomycosis of the spine. Am J Orthop (Belle Mead NJ). 2014;43(11):E266–E271.
22. Johansen IS, Nielsen SL, Hove M, et al. Characteristics and clinical outcome of bone and joint tuberculosis from 1994–2011: a retrospective register-based study in Denmark. Clin Infect Dis. 2015;61(4):554–62.
23. McClain CM, Van Horn GT, Chappell JD, Stratton CW. Coccidioides, cryptococcus, or blastomyces? A diagnostic dilemma encountered during frozen section evaluation. Pediatr Dev Pathol. 2012;15(1):71–5.
24. Larone DH. Medically important fungi. 5th ed. Washington, DC: ASM; 2011.
25. Bradsher RW, Chapman SW, Pappas PG. Blastomycosis. Infect Dis Clin N Am. 2003;17(1):21–40 vii. Review.
26. Gottlieb JR, Eismont FJ. Nonoperative treatment of vertebral blastomycosis osteomyelitis associated with paraspinal abscess and cord compression: a case report. J Bone Joint Surg Am. 2006;88(4):854–6.
27. Chapman SW. Blastomyces dermatitidis. In: Mandell GL, Bennett JE, Dolin R, editors. Principles and practice of infectious diseases. New York: Churchill Livingstone; 2000. p. 2733–46.