Blastomycosis of the Central Nervous System

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ABSTRACT

The reported incidence of blastomycosis is increasing in certain regions of the United States. The diagnosis is primarily made via urine antigen testing, culture, or cytology smear. The differential diagnosis for blastomycosis includes pneumonia, tuberculosis, and non-infectious pulmonary disease. Clinical context and epidemiologic exposure play a crucial role in diagnosis. However, the differential can expand significantly if there is disseminated central nervous system involvement, especially if pulmonary manifestations are not seen. Imaging begins to play a vital role when differentiating disseminated blastomycosis from other etiologies such as malignancy. Herein we present a case of a 58-year-old male who presented with seizures and right sided gaze preference found to have disseminated central nervous system blastomycosis. In this article, we will discuss symptoms and imaging findings of disseminated blastomycosis to help guide diagnosis and management.

CASE REPORT

CASE REPORT

A 57-year-old male from Illinois with no significant past medical history presented with dyspnea and chest discomfort. Given his background as a middle aged, homeless individual with a history of intravenous drug use and tobacco smoking history, he had potential risk factors for blastomycosis. Physical exam findings were significant for crackles in the left lower lobe. Chest X-ray demonstrated a left lower lobe consolidation. The consolidation was biopsied by interventional radiology with Grocott's Methenamine Silver stain highlighting broad-based, budding yeast forms consistent with Blastomyces spp., and this diagnosis was further corroborated by a positive Blastomyces urine antigen test (Value: 5.9 ng/mL). Fungal blood cultures yielded negative results. The patient was discharged on a prescribed regimen of itraconazole oral solution 10 milligrams per milliliter, 20 milliliters twice daily with a recommended duration of 12 months as advised by consultation with infectious disease specialists. Subsequent monitoring of itraconazole levels revealed subtherapeutic concentrations across three separate occasions during the period leading up to the diagnosis of central nervous system blastomycosis. Despite challenges in ensuring consistent follow-up, a Blastomyces urine antigen test conducted five months post-initial treatment showed no detectable antigen, suggesting a response to the therapy.

Eight months after initiation of treatment, the patient

presented to the emergency department after being found unresponsive at his home. Paramedics reported no medication bottles, household cleaners, or other chemicals near his body at that time. He was given intranasal Narcan en route to the hospital and had a one-minute seizure while in the ambulance. On physical exam, the patient was in acute distress. He was tachycardic with regular rhythm. On pulmonary exam, he was tachypneic without accessory muscle use, with rhonchi throughout the bilateral lung fields. In the emergency department, he experienced multiple seizures characterized by tonic-clonic activity and right sided gaze deviation. The patient was intubated and received 2mg Ativan with seizures concluding after 1.5 minutes. The patient underwent a noncontrast CT head and CT head and neck angiogram and was found to have suspected left frontal ischemic infarct with possible hemorrhagic conversion versus left frontal mass with vasogenic edema and left lateral ventricle effacement (Figures 1,2). Laboratory values were within normal limits. Chest radiograph confirmed proper endotracheal tube placement and ruled out pneumothorax, pleural effusion, or any consolidations suspicious for blastomycosis (Figure 3).

Upon admission, neurology and neurosurgery specialists were consulted. Initial neurologic exam demonstrated disconjugate gaze, right eye slight exotropia, midline not tracking, with all other cranial nerves intact. Sensation was intact, withdrawing from pain in all 4 extremities, but unable to localize pain. Due to light sedation, gait and cerebellar function could not be assessed. Extensive laboratory testing was done.

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The patient was extubated the following day and was found to be alert and oriented only to name and year, but not location. Physical exam was remarkable for left lower extremity reflexes 3+.

MRI of the head with and without contrast was then performed (Figures 4 and 5). Findings were significant for multiple T1 isointense and T2/FLAIR isointense enhancing lesions with T2/FLAIR hyperintensity compatible with vasogenic edema. The largest lesion identified was $2.3 \times 1.9 \times 2.1$ cm with a localized to the left frontal lobe resulting in sulcal effacement, mass effect on the frontal horn of the left lateral ventricle, and a 5mm rightward midline shift. Lesions were also found in the superior left frontal gyrus, left occipital lobe, left parietal lobe, and left inferior cerebellar region. These concerning findings resulted in consultation with infectious disease, suggesting potential malignancy versus intracerebral abscess.

Left frontal stereotactic biopsy was performed by neurosurgery, with pathological identification of blastomycosis (Figure 6). At the time of diagnosis, the patient had a positive Blastomyces urine antigen test (value: 0.85 ng/mL). The patient underwent a treatment course with intravenous amphotericin B, receiving a total of 17 treatments over a five week period, followed by a transition to oral voriconazole. The intermittent schedule was tailored to the patient's tolerance to therapy as there were concerns for hypertensive urgency and Kaliuresis, as well as convenience due to transportation. Upon completion of the amphotericin B regimen, the Blastomyces urine antigen test yielded negative results. The patient was then prescribed oral voriconazole capsules 300 milligrams once daily for a one-year treatment period. However, challenges with treatment compliance necessitated an extension of the expected treatment period. During the first three months of voriconazole treatment, therapeutic drug monitoring revealed consistently subtherapeutic drug levels. Consequently, the dosage was adjusted to 400 milligrams daily. Subsequent consultation with infectious disease specialists raised concerns of voriconazole hyper metabolization. As a result, the patient was transitioned to 400 milligrams of itraconazole via capsule form for 12 months. As of the most recent follow up, the patient reports no acute symptoms related to central nervous system blastomycosis. He is continuing his antifungal regimen and has not experienced any recent seizures, focal neurological deficits, fever, or chills.

DISCUSSION

Blastomycosis is an uncommon fungal infection in the United States caused by *Blastomyces dermatitidis* or *B. gilchristii*. In addition to the commonly identified species, *Blastomyces helicus*, a dimorphic fungus predominantly affecting immunocompromised individuals in Western regions of the United States and Canada, has also been recognized as a causative agent of blastomycosis [1]. Incidence rates are reported to be <1/100,000 [2]. *Blastomyces spp.* are endemic to the soils of the Ohio and Mississippi River Valleys, southeastern US, and the Great Lakes region [3]. Endemic states, such as Illinois, have seen about 500 cases per 10 years [4].

Hospitalization rates are 2-3 times higher for Hispanic whites, Asian, and American Indian patients when compared to non-Hispanic whites. Ninety percent of Blastomyces dermatitidis infections have been found to occur in non-Hispanic whites [5]. Since 2015, endemic states such as Minnesota have seen a notable rise in Blastomycosis infection rates, with cases nearly tripling and mortality rates rising from 9% to as high as 23% by 2021 [6]. Pulmonary infection is most reported, with 79% of patients documenting symptoms of nonproductive cough, shortness of breath, and chest pain [7]. Evidence of disseminated Blastomycosis occurs in 25-50% of patients, with cutaneous findings such as papulopustular, verrucous, or crusted lesions being the most common form of dissemination (40-80%) [8]. Other extrapulmonary findings include osseous blastomycosis (5-25%), genitourinary blastomycosis (<10%), and CNS blastomycosis being the least common (5-10% of immunocompetent patients) [7].

Blastomyces spp. are thermally dimorphic fungi that grow as a mold in the environment (22-25 degrees Celsius) and produce infectious spores. After disruption of the soil, spores become aerosolized and inhaled into the lungs of a human host. Once these spores are inhaled into the lungs of the host (37 degrees Celsius), they convert to a pathogenic yeast capable of evading host immune responses. The dissemination of *Blastomyces* yeast is thought to be lymphohematogenous [21]. However, it has also been postulated that the mechanism is like other fungal infections, such as H. capsulatum and C. neoformans, in which survival in macrophages allow for extrapulmonary spread [9].

In the ever-evolving landscape of medicine, it remains crucial for physicians to recognize both the typical and atypical manifestations of numerous diseases. Interestingly, a meticulous review of the patient's medical record revealed a prior admission for pulmonary blastomycosis 8 months earlier. This case underscores the significance of detailed review of medical records, especially in cases with rare presentations. This report described a rare case of a patient who, in the absence of pulmonary symptoms, presented to the emergency department with seizures due to a central nervous system mass, eventually diagnosed as disseminated CNS blastomycosis. If the patient had presented with pulmonary findings consistent with blastomycosis, it likely would have altered his treatment plan and potentially avoid a stereotactic brain biopsy.

Clinical & Imaging Findings

Blastomycosis can present with a variety of symptoms derived from previously mentioned pulmonary and extrapulmonary manifestations. Pulmonary manifestations can range from asymptomatic to acute respiratory distress syndrome. Common symptoms include fever, non-productive cough, weight loss, hemoptysis, and lethargy. Plain radiographs may describe nodular opacities most commonly seen in the upper lobes of the lungs. Cutaneous findings can include verrucous, ulcerative, or crusted lesions [9]. Osseous lesions may present with painful soft tissue abscesses or sinus tracts

associated with lytic destruction of long bones, the skull, and ribs [10]. Genitourinary symptoms can include dysuria and urinary obstruction. In women, genitourinary infection can cause infection of the endometrium or salpinx [11,12]. CNS infection can ultimately present with neurologic symptoms such as headache, seizures, and visual disturbances, which this patient here experienced. One single institution study identified headache as the most common presentation of disseminated CNS blastomycosis (86.3%), followed by focal neurologic deficit (54.5%), altered mental status (45.5%), vision changes (22.7%), and seizures (13.6%) [13].

Diagnosis is made by direct visualization of Blastomyces. This can be performed using sputum cultures or tissue cultures stained with 10% KOH. In addition, Calcofluor-white stain is commonly used as a sensitive test to Blastomycosis infection as it binds the chitin component of fungal cell walls. Finally, Grocott's Methenamine Silver stain and Period Acid-Schiff Stain can bind the polysaccharides of fungal walls for direct visualization from tissue specimens. Radiographic findings are nonspecific but can be helpful within the proper clinical context [3].

The imaging findings of disseminated CNS blastomycosis are variable. Many patients with CNS dissemination are often initially identified via screening CT, but contrast enhanced MRI is the imaging modality of choice for the purpose of soft tissue resolution. The most common finding is basilar leptomeningitis, followed by intraparenchymal masses [14]. Parenchymal abscesses can be identified via an enhancing peripheral rim and reduced diffusion centrally. One study identified that parenchymal lesions could be hypo-, iso-, or even hyperdense. Studies have also shown lesions in ring configuration or mass-like enhancement [15]. It is difficult to differentiate these abscess etiologies from other fungal etiologies such as histoplasma or coccidiomycosis; however, complications specific to blastomycosis may include adjacent osteomyelitis if there is intracranial extension into the epidural space [13]. The patient here presented with multiple lobulated enhancing lesions with surrounding T2/FLAIR vasogenic edema.

Treatment & Prognosis

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All symptomatic patients diagnosed with Blastomycosis should receive antifungal treatment consisting of either amphotericin B or an azole such as voriconazole or itraconazole [16]. Current guidelines recommend 4-6 weeks of IV amphotericin B followed by at least one year of an oral azole [17]. Surgery has been recommended for CNS blastomycosis in the presence of mass lesions and osteomyelitis refractory to drug therapy [18]. Due to its rarity, the prognosis is unknown; however, mortality rates are reported to be between 4-22% [17]. Risk factors for a worse prognosis include immunocompromised state, multilobar pulmonary disease, obesity, and diabetes [19].

Differential Diagnoses

As stated in the table below (Table 1), there are a few other considerations in the differential for CNS blastomycosis.

Metastasis, intraparenchymal hemorrhage, and other pyogenic abscess are the primary conditions one should rule out when considering this diagnosis.

QUESTIONS

Question 1

What is the most common location of extrapulmonary manifestation in disseminated blastomycosis?

- Genitourinary 1.
- 2. Central Nervous System
- 3. Cutaneous (applies)
- 4. Osseous blastomycosis
- 5. Muscle

Explanation

2.

Genitourinary manifestations of blastomycosis occur 1 in as many as 20-30% of patients, with prostate involvement in less than 10% of males [Other extrapulmonary findings include osseous blastomycosis (5-25%), genitourinary blastomycosis (20-30%), and CNS blastomycosis being the least common (5-10% of immunocompetent patients)]

Central nervous system blastomycosis is a very rare form of disseminated blastomycosis, occurring in only about 5-10% of cases [Other extrapulmonary findings include osseous blastomycosis (5-25%), genitourinary blastomycosis (20-30%), and CNS blastomycosis being the least common (5-10% of immunocompetent patients)]

3. Cutaneous blastomycosis is the most common form, seen in up to 80% of patients [Evidence of disseminated Blastomycosis occurs in 25-50% of patients, with cutaneous findings such as papulopustular, vertucous, or crusted lesions being the most common form of dissemination (40-80%)]

4 Osseous blastomycosis affects up to 25% of patients [Other extrapulmonary findings include osseous blastomycosis (5-25%), genitourinary blastomycosis (20-30%), and CNS blastomycosis being the least common (5-10% of immunocompetent patients)]

5. There is no muscle involvement with blastomycosis infection [Pulmonary infection is most reported, with 79% of patients documenting symptoms of nonproductive cough, shortness of breath, and chest pain. Evidence of disseminated Blastomycosis occurs in 25-50% of patients, with cutaneous findings such as papulopustular, verrucous, or crusted lesions being the most common form of dissemination (40-80%). Other extrapulmonary findings include osseous blastomycosis (5-25%), genitourinary blastomycosis (20-30%), and CNS blastomycosis being the least common (5-10% of immunocompetent patients)]

Ouestion 2

Which of the following is true regarding blastomycosis infection?

1. It is endemic in pacific regions such as California and Arizona

2. It more commonly affects males than females (applies)

3. Incidence rates of blastomycosis are 1 in 100 people per year

- 4. Treatment regimen involves 4-6 weeks of penicillin
- 5. Infections only occur in adults

Explanation

Infection is not commonly seen in areas like California and Arizona. [Inhalation of *B. dermatitidis* or *B. gilchristii* from disrupted soil in Ohio and Mississippi River Valleys, Southeastern U.S. or Great Lakes regions]

1. Blastomycosis more commonly affects males than females [It is postulated that this difference in incidence is likely due to males being more likely to participate in activities that increase exposure to *Blastomyces spp.* such as fishing, hiking, and camping]

2. Incidence rates for blastomycosis are much lower than 1 in 100 people per year. [Incidence rates are reported to be <1/100,000]

3. Treatment for blastomycosis does not involve penicillin [Current guidelines recommend 4-6 weeks of IV amphotericin B followed by at least one year of an oral azole]

4. Infections can occur in patients of any age [Males aged 41-50 years old have the highest incidence, however cases have been reported anywhere between 2 years old to 93 years old]

Question 3

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Which of the following is true in regards to imaging findings in disseminated CNS Blastomycosis?

1. Noncontrast head CT will demonstrate a hypodense mass with sulcal effacement

2. T1 weighted MRI will demonstrate a hyperintense lesion

3. T2 Weighted imaging will demonstrate a hypointense lesion

4. MRI with DWI will demonstrate centrally localized restricted diffusion (Applies)

5. Disseminated CNS blastomycosis is FDG avid

Explanation

1. Noncontrast head CT will show a hyperdense mass with sulcal effacement [Hyperdense mass with potential sulcal effacement, midline shift, and vasogenic edema. Osseous erosion or sclerosis.]

2. T1 weighted MRI will demonstrate hypo- or isointense lesions [Hypo- or isointense lesions]

3. T2 weighted MRI will not demonstrate hypointense lesions, but rather hyperintense lesions [Hyperintense lesions, per table 1]

4. Due to presence of a necrotizing granulomatous response, there will likely be restricted diffusion localized centrally in the lesion [Centrally localized restricted diffusion]

5. Disseminated blastomycosis does not display FDG avidity on imaging [Not FDG Avid]

Question 4

Which of the following characteristics on imaging may help differentiate CNS blastomycosis from any other pyogenic intraparenchymal abscess?

- 1. Adjacent osteomyelitis (applies)
- 2. Centrally restricted diffusion on DWI
- 3. Peripheral rim enhancement
- 4. FDG Avidity
- 5. Sulcal effacement

Explanation

1. Osteomyelitis is more specific for blastomycosis compared to other pyogenic abscesses [It is difficult to differentiate these abscess etiologies from other fungal etiologies such as histoplasma or coccidiomycosis; however, complications specific to blastomycosis may include adjacent osteomyelitis if there is intracranial extension into the epidural space]

2. Centrally restricted diffusion is nonspecific and can be seen in both CNS blastomycosis and pyogenic abscesses. [Parenchymal abscesses can be identified via an enhancing peripheral rim and reduced diffusion centrally]

3. Peripheral rim enhancement is nonspecific and can be seen in both CNS blastomycosis and pyogenic abscesses. [Parenchymal abscesses can be identified via an enhancing peripheral rim and reduced diffusion centrally]

4. FDG Avidity is not seen in any form of CNS blastomycosis or pyogenic abscess, but can be seen in metastases [Table 1]

5. Sulcal effacement can be seen in any kind of mass that is large enough to cause intraparenchymal compression [Table 1]

<u>Question 5</u>

Which of the following is true?

1. The prognosis of CNS blastomycosis is well defined

2. Indications for surgical resection of CNS blastomycosis includes cutaneous manifestations

3. Risk factors for a worse prognosis include obesity and diabetes (applies)

4. Blastomycosis is a clinical diagnosis, utilizing a combination of pulmonary symptoms and recent travel

5. The etiology of blastomycosis is water sources

Explanation

1. The prognosis of CNS blastomycosis is not well defined due to the limited number of cases. [Due to its rarity, the prognosis is unknown; however, mortality rates are reported to be between 4-22%]

2. Associated cutaneous manifestations are not an indication for surgical resection of blastomycosis [Surgery has been recommended for CNS blastomycosis in the presence of mass lesions and osteomyelitis refractory to drug therapy]

3. Diabetes and obesity are risk factors for a worse prognosis in blastomycosis [Risk factors for a worse prognosis include immunocompromised state, multilobar pulmonary disease, obesity, and diabetes] 4. Blastomycosis is not a clinical diagnosis [Diagnosis is made by direct visualization of *Blastomyces*. This can be performed using sputum cultures or tissue cultures stained with 10% KOH. In addition, Calcofluor-white stain is commonly used as a sensitive test to Blastomycosis infection as it binds the chitin component of fungal cell walls. Finally, Grocott's Methenamine Silver stain and Period Acid-Schiff Stain can bind the polysaccharides of fungal walls for direct visualization from tissue specimens.]

5. Blastomycosis does not come from water sources [After disruption of the soil, spores become aerosolized and inhaled into the lungs of a human host]

TEACHING POINT

Disseminated CNS Blastomycosis should be suspected in patients with rim-enhancing lesions with potential centrally localized restricted diffusion, especially in those from or traveling to endemic regions. Although rare, isolated intraparenchymal lesions can be seen, and lack of pulmonary manifestation should not exclude the diagnosis. One epidemiologic study of blastomycosis cases in Minnesota identified about a 3:1 male to female incidence ratio [6]. It is postulated that this difference in incidence is likely due to males being more likely to participate in activities that increase exposure to *Blastomyces spp.* such as fishing, hiking, and camping.

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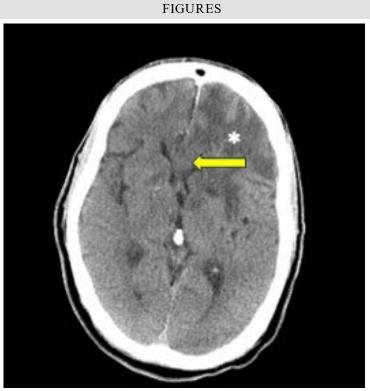


Figure 1: 57-year-old male diagnosed with Central Nervous System Blastomycosis

Findings: Axial noncontrast CT of the head demonstrates subtle hyperdensity within the left frontal lobe with surrounding vasogenic edema (asterisk) causing effacement of the left lateral recess and approximately 4mm of rightward midline shift (arrow)

Technique: Axial CT head without contrast, CTDIvol: 65.8 mGy, DLP: 1294 mGy-cm, 5-mm slice thickness

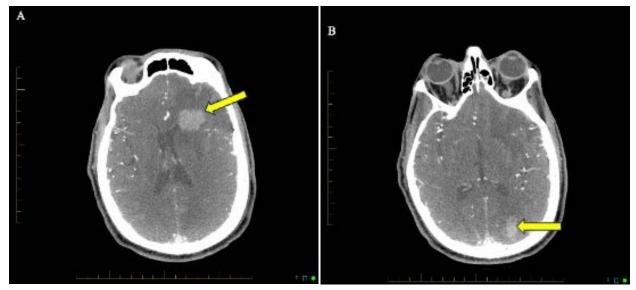


Figure 2: 57-year-old male diagnosed with Central Nervous System Blastomycosis

Findings: 2A) Axial contrast enhanced CT head and neck angiogram in the arterial phase; homogenously enhancing left frontal lobe lesion measuring 2.4cm x 1.9 cm with surrounding vasogenic edema (arrow). 2B) Axial contrast enhanced CT head and neck angiogram in the arterial phase; additional smaller enhancing left occipital lobe lesion measuring 1.6cm x 1.0 cm with surrounding vasogenic edema (arrow).

Technique: Axial CT head and neck angiogram, arterial phase, 5-mm slice thickness, Radiation (DLP): 844 mGy-cm, CTDIvol: 21.9 mGy, iopamidol (ISOVUE-370) 76%, 150 mL IV contrast given

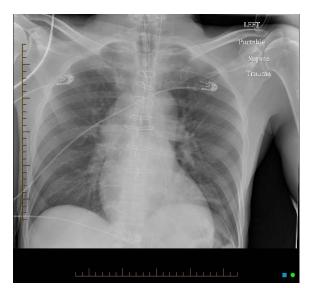


Figure 3: 57-year-old male diagnosed with Central Nervous System Blastomycosis

Findings: Median sternotomy wires present. Endotracheal tube seen terminating above the carina. Enteric tube seen coursing below the diaphragm. Cardiac silhouette is mildly enlarged. No focal pulmonary consolidations. No pleural effusion or pneumothorax.

Technique: Frontal chest radiograph, supine

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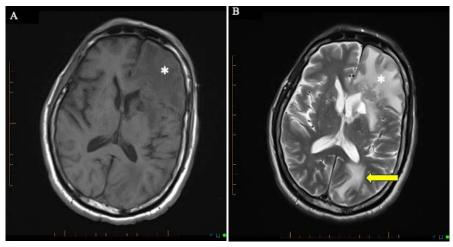


Figure 4: 57-year-old male diagnosed with Central Nervous System Blastomycosis

Findings: 4A) Axial MRI head pre-contrast, T1 sequence; isointense left frontal lobe lesion (asterisk). 4B) Axial MRI head pre-contrast, T2; signal hyperintensity in the left frontal lobe (asterisk) and left occipital lobe (arrow) with maintained gray-white matter differentiation consistent with vasogenic edema. Mass effect with effacement of the left lateral ventricle and 5mm of rightward midline shift.

Technique: Siemens Magnetom Aera XQ48, 1.5T, Gadoterate meglumine (DOTAREM) injection, 12 mL Intravenous given.

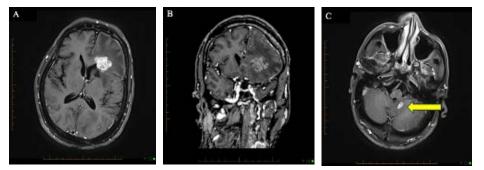


Figure 5: 57-year-old male diagnosed with Central Nervous System Blastomycosis

Findings: 5A) and 5B) MRI head post-contrast, T1 sequence; axial and coronal images demonstrate avidly enhancing left frontal lobe lesion which measures 2.3 x 1.9 x 2.1cm. 5C) MRI head post contrast axial image demonstrate an additional smaller enhancing left inferior cerebellar lesion (arrow). Technique: Siemens Magnetom Aera XQ48, 1.5T, Gadoterate meglumine (DOTAREM) injection 12 mL Intravenous given.

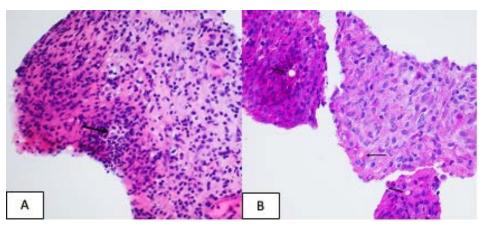


Figure 6: 57-year-old male diagnosed with Central Nervous System Blastomycosis

Findings: Microscopic examination of the brain tissue demonstrating acute and chronic inflammation with graunlohistiocytic response and rare fungal forms. These consisted of round to oval yeasts with thick refractile walls (**Figure A**). Periodic Acid-Schiff (PAS) stain highlighted the organisms (**Figure B**). The morphologic features were suggestive of *Blastomyces*.

6A) A round yeast with a thick wall (arrow) was identified amidst acute and chronic inflammation with granulomatous features. 6B) The yeasts (arrows) were positive for Periodic Acid Schiff (PAS) stain)

Technique: 6A) [Hematoxylin and Eosin (H&E), magnification 400x]. 6B) [Periodic Acid Schiff (PAS), magnification 400x].

Disease	СТ	MRI-T1	MRI-T2	MRI-DWI	Enhancement	PET
Disseminated CNS Blastomycosis	Hyperdense mass with potential sulcal effacement, midline shift, and vasogenic edema. Osseous erosion or sclerosis.	Hypo- or isointense lesions	Hyperintense lesions	Centrally localized restricted diffusion	Peripheral	Not FDG Avid
Metastasis	Hypodense	Hypointense	Hyperintense	No restricted diffusion	Homogenous	FDG Avid
Intracerebral hemorrhage	Hyperdense collection of blood surrounded by hypodense edema	Dependent on age of blood products	Dependent on age of blood products	Dependent on age of blood products	Homogenous	Not FDG Avid
Diffuse Large B Cell Lymphoma	Hyperdense, enhancing mass localized supratentorial	Hypointense	Iso- or hypointense	Restricted diffusion	Homogenous	FDG Avid

Table 1: Differential diagnosis table for disseminated CNS Blastomycosis based on imaging findings

Etiology	Inhalation of <i>B. dermatitidis</i> or <i>B. gilchristii</i> from disrupted soil in Ohio and Mississippi River Valleys, Southeastern U.S. or Great Lakes regions			
Incidence	<1/100,000 Blastomycosis cases, with 5-10% of cases representing disseminated CNS Blastomycosis			
Gender	3:1 male to female ratio [6]			
Age	Males aged 41-50 years old have the highest incidence, however cases have been reported anywhere between 2 years old to 93 years old [6]			
Risk Factors	Contact with infected soil, outdoor activities in endemic regions, immunocompromised state			
Treatment	4-6 weeks of intravenous amphotericin B, followed by oral azole therapy for 12 months			
Prognosis	Mortality rates have been reported to be between 4-23% [4,6,20]			

Table 2: Summary table of CNS blastomycosis

KEYWORDS

Blastomycosis, MRI, Central Nervous System, Brain, fungal

ABBREVIATIONS

HTN = Hypertension

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AUTHORS' CONTRIBUTIONS

Alexander Kazmer: Manuscript write-up, collection of patient data, literature review Rami El-Baba: Collection of patient data, interpretation, and annotation of figures Andreas Kontosis: Pathology figures and explanations Ewa Borys: Faculty sponsor for pathology slides

Mariah Siddiqui: Faculty sponsor, identified proper case for report

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