Candida parapsilosis intracerebral abscess and intralesional amphotericin B: a novel treatment approach to a rare infection. Illustrative case

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BACKGROUND Candida parapsilosis has been implicated in central nervous system (CNS) infections (i.e., meningitis or ventriculitis) but has not been previously reported to cause intracerebral abscesses. CNS infections secondary to C. parapsilosis are notoriously difficult to treat due to the poor CNS penetration of amphotericin B. Historically, intraventricular amphotericin B has been used to treat C. parapsilosis ventriculitis.

OBSERVATIONS A 15-year-old female with no comorbidities presented with nonresolving headaches, photophobia, fevers, and meningism. Computed tomography (CT) of the brain revealed a right frontal abscess. After multiple drainage surgeries, subsequent CT scans showed reaccumulation of her abscess. C. parapsilosis was cultured, and the patient was then taken to the operating room where an external ventricular drain catheter was successfully placed within the abscess cavity. Pus was repeatedly aspirated, followed by the instillation of intralesional amphotericin B twice a day for 2 weeks. The patient's clinical condition improved substantially with complete resolution of symptoms, improvement of infective markers, and resolution of radiological features of the abscess. Follow-up of the patient revealed the absence of symptoms and image characteristics of abscess on CT 3 months posttreatment.

LESSONS Intralesional amphotericin B is a novel but effective treatment of C. parapsilosis intracerebral abscess, an organism not previously described as a cause of intracerebral abscesses.

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KEYWORDS intracerebral abscess; Candida parapsilosis; intralesional amphotericin B
**Illustrative Case**

A 15-year-old female with no known comorbidities was referred from her local hospital with a 2-week history of headaches, photophobia, confusion, meningism, and fevers. Blood cultures cultured *Escherichia coli*, while her cerebrospinal fluid (CSF) analysis revealed bacterial meningitis (raised protein, polymorphs, and low CSF glucose) with no bacterial growth but with a meningitis screen multiple polymerase chain reaction positive for human herpes virus type 7. She received a course of IV acyclovir and ceftriaxone at the base hospital. While her confusion improved, her headaches, photophobia, and meningism persisted. She was referred to the supporting hospital where computed tomography (CT) imaging was done, revealing a partial ring-enhancing right frontal lobe lesion with the appearance of late cerebritis and early capsule formation with associated edema, mass effect, and early uncal herniation (Fig. 1). CT also revealed a superior sagittal sinus thrombosis and partial opacification of her left frontal, ethmoidal, and maxillary sinuses. It was deemed too early to intervene at this stage of abscess formation; therefore, the patient was initially treated with another course of IV antibiotics, therapeutic low-molecular-weight heparin, dexamethasone, and prophylactic antiepileptic drugs. Within a few days, she developed right pupillary dilatation, upward trend in inflammatory markers, and worsening headaches with vomiting. Repeat imaging showed a larger abscess with more definitive capsule formation, and then the decision was made to drain the abscess surgically. She was taken to the operating room for burr hole and abscess drainage by the neurosurgeons with subsequent front sinus washout and trephination by the otorhinolaryngologist. The cultures obtained from her abscess did not show any presence of organisms. However, cultures from her sinus washout yielded alpha-hemolytic *Streptococcus*, which exhibited sensitivity to ampicillin, prompting a change in her antibiotic treatment. The patient initially improved; however, 1 week after her first surgery, she developed signs and symptoms of raised intracranial pressure again (headaches, nausea, and vomiting), with increasing inflammatory markers on sequential testing. Repeat CT imaging revealed a re-collection of her abscess. She was then escalated to meropenem 2 g IV three times a day and taken back to the operating room for drainage through the same burr hole. The patient clinically improved after her second surgery. Cultures from her second drainage grew *C. parapsilosis*. The patient had micafungin 100 mg IV daily added to her antimicrobial regimen but deteriorated clinically, and the decision was made to intervene again.

Her abscess was drained, and an antibiotic-impregnated external ventricular drain catheter was placed within the abscess cavity. Postoperative imaging confirmed the successful placement of the catheter (Fig. 2).

Thereafter, 10 mL of fluid was aspirated from the abscess cavity twice a day with subsequent instillation of 25 mg of amphotericin B diluted in 3 mL of sterile 0.9% normal saline into the abscess cavity for 14 days. The other antibiotic courses were completed, and the micafungin was stopped.

After 14 days of intralesional amphotericin B and removal of the drain, imaging revealed complete resolution of her abscess. The patient’s symptoms and neurological deficit completely resolved, and her inflammatory markers decreased to within normal limits before discharge.

On follow-up, 3 months later, the patient complained of no symptoms, with imaging further confirming no recollection of any intracranial abscesses (Fig. 3).

**FIG. 1.** Contrast-enhanced CT scans of an intracerebral abscess caused by *C. parapsilosis*.

**FIG. 2.** Postoperative contrast-enhanced CT scans of the external ventricular drain catheter within the abscess cavity.

**Patient Informed Consent**

The necessary patient informed consent was obtained in this study.

**Discussion**

*C. parapsilosis* has a particular affinity for adhering to prosthetic materials and creating biofilms on plastic surfaces, making it an increasingly important cause of device and line/catheter-associated nosocomial infections. C. *parapsilosis* is a common skin commensal and is notoriously fastidious, which makes it difficult to culture and identify. It is also difficult to treat using conventional antifungal medication regimens and routes. The patient in this case most likely acquired the *C. parapsilosis* as a nosocomial infection from her prolonged hospital admission and multiple cycles of treatment, which used IV antibiotics via an invasive IV cannula, the most likely source of the infection. Traditionally, intracerebral abscesses, regardless of the underlying pathogen, are treated with a combination of surgical drainage, with or without capsulectomy, and systemic antimicrobial therapy. While many bactericidal antibiotics have good CSF penetration, the commonly used fungicidal agents such as amphotericin B and echinocandin antifungals do not. Higher doses increase systemic toxic side effects. To mitigate systemic toxicity and to increase target site concentration, some have advocated for intraventricular or intrathecal amphotericin B for severe fungal CNS infections. Intraventricular and intrathecal amphotericin B instillation has been associated with a host of neurotoxic side effects such as arachnoiditis, encephalopathy, headaches, and seizures, to name a few.

No sources could be found where amphotericin
B was directly instilled into the cavity of an abscess; however, in this case, the decision was made to use this technique as a way to increase the local site concentration of the drug. While the dosage of intrathecal amphotericin B is usually low to mitigate CNS toxicity, with the recommended maximum dosages of 2 mg, we opted to use higher doses (25 mg) due to the fastidious nature of the organism and the presence of a thick abscess wall. We hypothesized that the enclosed abscess cavity would mitigate the risk of CNS toxicity while allowing for maximum contact of the drug with the organism. The dosage we decided to use is similar to the dose of amphotericin B used for bladder instillation in patients with Candida cystitis.

This patient fortunately experienced no adverse side effects from this unconventional technique of administering this drug, and the abscess resolved completely with full neurological recovery.

Observations
This case is, to our knowledge, the first to describe C. parapsilosis implicated in an intracerebral abscess. It also describes how it was treated with a novel technique.

Lessons
Intralesional amphotericin B is a novel but seemingly effective treatment for an encapsulated C. parapsilosis intracerebral abscess, an organism not previously described to cause intracerebral abscesses. The safety is yet to be established; however, it may be an option in the treatment of difficult-to-treat, life-threatening intracerebral fungal abscesses where no other options are effective.

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References

Disclosures
The authors report no conflict of interest concerning the materials or methods used in this study or the findings specified in this paper.

Author Contributions
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Supplemental Information
Previous Presentations
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