

Non-shunt Management of Communicating Hydrocephalus in an Immunocompetent Host With Disseminated Central Nervous System Coccidioidomycosis

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Abstract

Disseminated coccidioidomycosis is associated with significant morbidity and mortality. Involvement of the meninges is often fatal if untreated, typically requiring lifelong antifungal therapy and neurosurgical intervention. We present the case of a young male without any known immunocompromising conditions who opted exclusively for medical management of newly diagnosed coccidioidomycosis meningitis with communicating hydrocephalus and discuss the controversy associated with this approach. This case highlights the importance of shared decision-making between patient and clinician, even if the plan diverges from available guidelines. Furthermore, we discuss clinical considerations in approaching the close outpatient monitoring of patients with central nervous system coccidioidomycosis with hydrocephalus.

Keywords

coccidioid meningitis, communicating hydrocephalus, ventriculoperitoneal shunt, IDSA, Coccidioidomycosis Study Group

Introduction

Over the last 25 years, there has been an increased incidence of disseminated coccidioidomycosis of varying manifestations in hosts without known immunocompromise, from tenosynovitis to meningitis with resultant hydrocephalus.^{1–4} Presenting symptoms of coccidioidomycosis meningitis include progressively worsening headaches, nausea, vomiting, visual deficits, and mental status changes with fewer traditional meningeal signs like nuchal rigidity.^{5,6} In addition to antifungal therapy, standard of care for coccidioidomycosis meningitis with symptomatic hydrocephalus includes neurosurgical intervention for definitive management of increased intracranial pressure (ICP). Current guidelines do not support the exclusive use of medical management.⁷ In this report, we describe a case of coccidioidomycosis meningitis-related hydrocephalus in an immunocompetent male, who declined recommended neurosurgical intervention and opted solely for medical management. Extending from this case, we discuss an approach for clinicians to closely monitor similar patients electing for non-shunt management of coccidioidomycosis

meningitis-related hydrocephalus. We present this case to highlight the importance of shared decision-making between patient and clinician, even if the therapeutic plan diverges from clinical guideline recommendations.

Case Report

A 29-year-old Canadian male of Indian descent without a significant past medical history presented to the emergency

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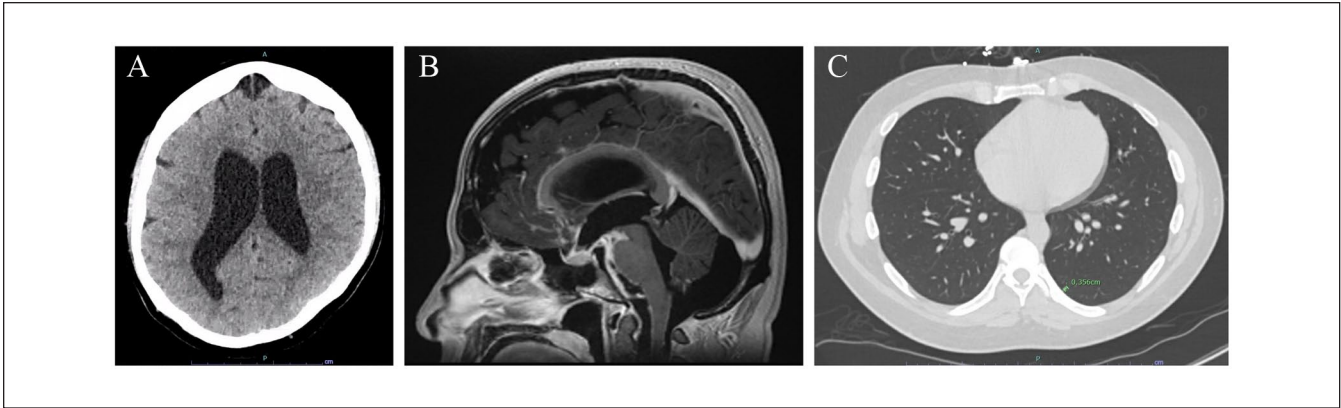


Figure 1. CT and MRI findings showing disseminated coccidioidomycosis basilar meningitis with communicating hydrocephalus and left lower lobe primary pulmonary nodule. (A) CT brain without contrast showing diffuse ventriculomegaly without trans-ependymal flow, consistent with hydrocephalus. (B) MRI brain sagittal view on T1 postcontrast sequence showing extensive basilar meningitis and communicating hydrocephalus. (C) CT thorax without contrast showing 3 mm left lower lobe pulmonary nodule. Abbreviations: CT, computerized tomography; MRI, magnetic resonance imaging.

department (ED) in Tucson, Arizona directly from a local optometry office after significant bilateral papilledema was noted on a routine exam required for an updated prescription for his corrective lenses. He denied nausea, vomiting, eye pain, and acute vision changes. However, he endorsed ongoing headaches for 6 months, initially starting in late spring following a job interview for a materials engineer position at a nearby mine and exploring other Sonoran Desert attractions in Arizona earlier in the year. He reported briefly living in India 4 years prior to presentation but was otherwise without notable travel history or high-risk social behaviors. He repeatedly presented to local EDs in Canada and underwent neuroimaging for his new-onset, severe headache postjob interview. Head computerized tomography (CT) and magnetic resonance imaging (MRI) during those visits revealed no acute abnormalities. At these ED visits, he was treated for migraines before discharging home. The patient also reported a 20-pound weight loss in the following months, but his weight stabilized and headache improved gradually after relocating to Arizona for his new job.

In our ED, a CT of the head showed ventriculomegaly with hydrocephalus (Figure 1A). Subsequently, an MRI of the brain confirmed extensive basilar meningeal enhancement with communicating hydrocephalus (Figure 1B). Neurosurgery was immediately consulted based on neuroimaging results. Following a successful lumbar puncture (LP), the patient was initially treated empirically for viral, fungal, bacterial, and mycobacterial meningitis, given his degree of hydrocephalus and hyperdense basilar meningeal enhancement on neuroimaging.

Initial cerebrospinal fluid (CSF) studies showed low glucose (19 mg/dL), elevated protein (279.8 mg/dL) with lymphocytic predominant leukocytosis (87% of 335 per μL), and an opening pressure of 33 cmH_2O . Empiric coverage was narrowed to cover *Mycobacterium tuberculosis* and *Coccidioides* spp. based on his international travel history and endemic exposure. Cerebrospinal fluid Gram stain did not visualize any organisms, spherules, molds, or yeasts. Bacterial and fungal cultures of CSF fluid did not yield any growth. Diagnosis of disseminated coccidioidomycosis meningitis was confirmed with positive *Coccidioides* enzyme immunoassay (EIA) IgG antibody, positive *Coccidioides* immunodiffusion (IMDF) IgM tube precipitin antibody, positive *Coccidioides* IMDF IgG complement fixation (CF) antibody, serum *Coccidioides* CF titer of 1:128, and CSF *Coccidioides* CF titer of 1:32. Computed tomography thorax imaging also identified a 3-mm left lower lobe pulmonary nodule without parenchymal consolidation, cavitory lesion, or pleural effusion (Figure 1C).

Our patient was treated with intravenous amphotericin B for 5 days with concurrent intravenous fluconazole until therapeutic azole levels reached blood-brain barrier penetration concentrations. Consistent with Infectious Diseases Society of America (IDSA) Clinical Practice Guidelines, our patient was advised to undergo ventriculoperitoneal (VP) shunt surgery with neurosurgery for definitive management of symptomatic hydrocephalus.⁷ However, he declined any invasive procedure due to his perception that his symptoms were not hindering his ability to perform his highly demanding occupational and daily activities. He

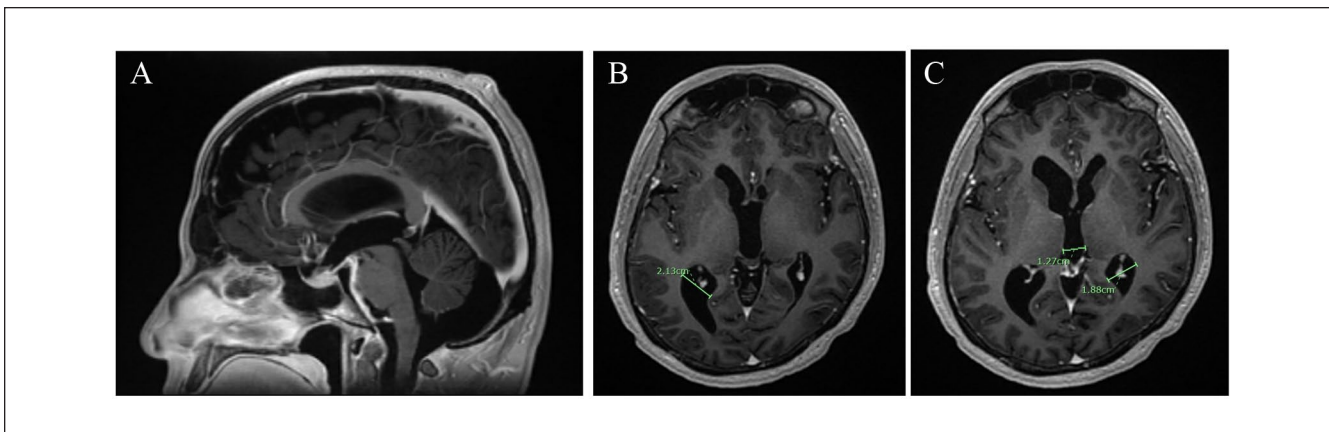


Figure 2. Repeat MRI brain after 4 months of exclusive medical management showing interval improvement of basilar meningitis with decreased communicating hydrocephalus. (A) MRI brain sagittal view in T1 postcontrast showing interval improvement in basilar meningitis. (B-C) MRI brain coronal view in T1 MP-RAGE postcontrast showing interval reduction in hydrocephalus. Abbreviations: MRI, magnetic resonance imaging; MP-RAGE, Magnetization Prepared - RApid Gradient Echo.

was transitioned to oral fluconazole before discharging home with close outpatient follow-up in subspecialty clinics while waiting to establish care with a primary-care physician. Prior to discharge, he was educated on warning signs and symptoms (including but not limited to visual changes, new neurological symptoms, urinary or bowel dysfunction, worsening headaches, refractory nausea, and vomiting) and given strict ED return precautions. He was also scheduled for a repeat outpatient brain MRI 3 months postdischarge.

Since discharge, he has been closely monitored for any progression of his intermittent headaches or further clinical signs of neurologic impairment and completed repeat brain MRI imaging (Figure 2A-C). Thus far, our patient endorses a positive response to and tolerance of oral fluconazole treatment with symptomatic and radiographic improvement.

Discussion

Coccidioidomycosis meningitis results in proteinaceous debris and arachnoid fibrosis that contribute to the development of hydrocephalus and increased ICP.⁸ In a recent Invited Commentary in *Clinical Infectious Diseases* authored by members of the IDSA Coccidioidomycosis Study Group, management of increased ICP and hydrocephalus in central nervous system (CNS) coccidioidomycosis was discussed.⁹ The experts recommended placement of an MRI-compatible VP shunt as the only permanent management approach, with other approaches like repeated CSF removal via LP or external ventricular drain (EVD) as temporary treatments.^{9,10} The experts also agreed that shunt placement should not be

delayed with concern that delays in shunting lead to worse patient outcomes.^{8,11}

However, published guidelines do not specify optimal timing for a shunt in the management of hydrocephalus with increased ICP for minimally symptomatic patients. Some studies question the necessity of shunt placement early in the disease process due to risks and complications associated with indwelling shunts.¹¹ VP shunt placement is a lifelong process associated with a high likelihood of shunt failure requiring revisions due to catheter obstruction, infection with catheter biofilm formation and abscess development, hemorrhage, and other postprocedural complications, such as seizures.^{8,12,13} Continued ventriculomegaly despite a properly functioning shunt and 9% mortality rate in patients who receive VP shunting are additional considerations.⁸

Our case emphasizes the importance of the general practitioner's basic understanding of outpatient management of disseminated coccidioidomycosis (Figure 3). In addition to outpatient management by a primary-care physician, patients with CNS coccidioidomycosis complicated by hydrocephalus should follow-up in the clinic with infectious disease experts in coccidioidomycosis and with neurologists. Medication management requires lifelong antifungal therapy (Table 1).^{7,14-17} Oral fluconazole remains the standard of care for coccidioidomycosis meningitis therapy, but intrathecal amphotericin B (AmBd) is recommended for pregnant patients in the first trimester due to teratogenicity of azoles.^{7,10,15} Table 1 provides a summary of adverse effects of anti-*Coccidioidal* agents and specific laboratory tests and studies to order for outpatient management of disseminated coccidioidomycosis.

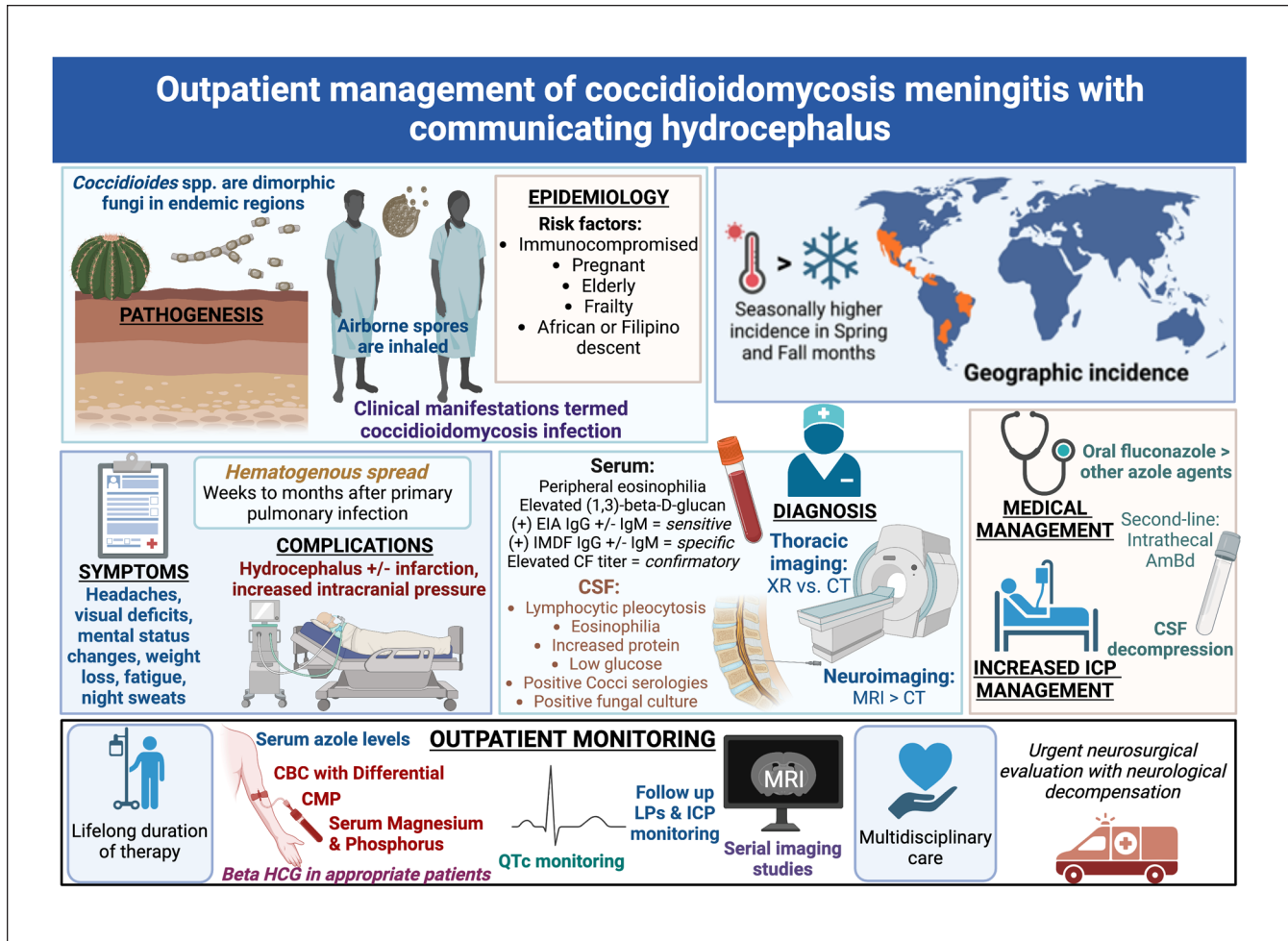


Figure 3. Central illustration: Outpatient management of coccidioidomycosis meningitis with communicating hydrocephalus. Abbreviations: EIA, enzyme immunoassay; IMDF, immunodiffusion; CSF, cerebrospinal fluid; ICP, intracranial pressure; LP, lumbar puncture; CBC, complete blood count; CMP, comprehensive metabolic panel; Beta HCG, Human Chorionic Gonadotropin, QTc, corrected QT interval.

For this case, we followed a patient-centered approach for non-shunt management of coccidioidomycosis meningitis-related hydrocephalus. As the patient presented with papilledema and hydrocephalus, immediate lowering of ICP early into his hospitalization was necessary to prevent long-term disability and death in the short term. After stabilization from immediate harm, we used shared decision-making with the patient, only proceeding with therapies for which he provided informed consent, which did not include repeat LP for further CSF removal or long-term shunt placement. Through very

close outpatient follow-up and repeat imaging, our patient's symptoms improved and ventriculomegaly diminished on oral fluconazole. Subsequent outpatient follow-up for the patient should include formal ophthalmological evaluation to assess for resolution of papilledema and repeat LP to assess for objective decrease in ICP. Even if the treatment plan decided upon differs from clinical practice guidelines, patient safety should remain the paramount concern in the management of coccidioidomycosis meningitis-related hydrocephalus during patient counseling and shared decision-making.

Table I. Summary of Coccidioidomycosis Meningitis Antifungal Management.

Antifungal Agent	Oral Bioavailability	Absorption affected by food consumption	CSF Penetration	Clearance	Recommended oral daily dose	Adverse effects	Routine Monitoring
Fluconazole	> 90%	Unaffected	Good-CSF concentration 80% that of serum concentration	Renal (80%); requires renal dose adjustment	400-1200 mg daily	Hepatotoxicity Teratogenicity	Liver function tests Regular monitoring of vitals and electrolytes Serum drug monitoring (can guide dose adjustments) Drug interaction monitoring (CYP450 inhibitor)
Itraconazole	55%	Enhanced by consumption of high fat meal and increased gastric acidity (e.g. consuming an acidic beverage; Coca Cola was specifically studied)	Poor-CSF concentration: 0.2-12% that of serum concentration	Hepatic (10%) Hepatic	Higher dosing is frequently used due to high rates of failure with lower dose 400-800 mg every 8 to 12 hours	Rarely, glucocorticoid suppression (i.e. Addison's disease) Aldosterone-like effects: hypokalemia, hypertension, peripheral edema *BLACK BOX WARNING* for heart failure patients due to negative inotropic effects Teratogenicity	Regular monitoring of vitals and electrolytes Baseline and routine echocardiograms with serum brain natriuretic peptide levels prior to initiation and whenever there is a clinical change, respectively. Serum drug monitoring Requires closer serum and clinical monitoring due to risk for toxicity and drug interactions
Voriconazole	> 90%	Decreases by 40-50% when taken with proton pump inhibitors or H2 blockers that reduce gastric acidity Decreased by >30% when taken with food	Less than fluconazole	Hepatic	4 mg/kg every 12 hours	Reversible visual deficits Severe photodermatitis Increased risk of skin cancer Potassium, calcium, and magnesium electrolyte abnormalities QTc prolongation Teratogenicity Increased risk for toxicity above 5.5 micrograms/mL	Counseling on sun safety: protective clothing, sunscreen, and avoiding direct sunlight Electrolyte monitoring before and during therapy to correct abnormalities as needed Regular ECG monitoring Serum drug monitoring
Posaconazole	> 50%	Enhanced by consumption of a high fat meal and acidic beverage	Poor-CSF concentration: 0.9% that of serum concentration	Hepatic (15%)	400 mg of oral suspension every 12 hours for cocci meningitis refractory to fluconazole	Reported in immunocompromised patients: Diarrhea, fever, nausea Electrolyte abnormalities QTc prolongation Teratogenicity	Electrolyte monitoring before and during therapy to correct abnormalities as needed Regular ECG monitoring Serum drug monitoring
Intrathecal Amphotericin B deoxycholate	N/A	N/A	Excellent- bypasses blood-brain barrier	Unknown (Urinary and biliary excretion account for <5% of dose)	Initial dose of 0.1 mg 3 times per week, gradually increasing the dose by 0.1 mg as tolerated Dose titrated to patient tolerability	Headache Nausea Vomiting Neurotoxicity: hearing loss, ophthalmoplegia, ataxia, paraplegia, neurogenic bladder, erectile dysfunction	Electrolyte monitoring Serum drug monitoring

Abbreviation: CSF, cerebrospinal fluid; QTc, corrected QT interval.

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Author Contributions

All authors contributed to the conception and design of the work; acquisition, analysis, or interpretation of the data for the work; drafting the work or revising it critically for important intellectual content; approval of the version to be published; and agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

Declaration of Conflicting Interests

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Ethics Approval

Our institution does not require ethical approval for reporting individual cases or case series.

Informed Consent

Written informed consent was obtained from the patient for their anonymized information to be published in this article.

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