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# Selected Topics: Psychiatric Emergencies

## CRYPTOCOCCAL MENINGOENCEPHALITIS PRESENTING AS A PSYCHIATRIC EMERGENCY

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☐ **Abstract—Background: Organic conditions can often mimic neuropsychiatric disorders, leading to delays in diagnosis and treatment for the most vulnerable populations presenting to the emergency department (ED). Case Report: Here we discuss a case of cryptococcal meningoencephalitis seemingly consistent with psychosis on initial evaluation, and present strategies to recognize and treat this condition. Why Should an Emergency Physician Be Aware of This?: Due to the indolent time course of this disease, initial symptoms of altered mental status and personality changes may be attributed to drug use or psychiatric illness before more overt evidence for increased intracranial pressure and neurologic infection develops. It is important for emergency clinicians to maintain a high level of suspicion for this condition in at-risk patients and reassess them frequently during their ED visit.** © 2019 Elsevier Inc. All rights reserved.

☐ **Keywords—meningitis; cryptococcal meningitis; agitation; psychiatric emergencies; infectious diseases**

### CASE REPORT

An approximately 45-year-old man with no identifying information was brought into the Emergency Department (ED) by Emergency Medical Services (EMS) for altered mental status. On arrival, he was disheveled and cachectic. Per report, EMS was called for "bizarre behavior" noted by the patient's roommates. In the field, the patient was yelling, combative, and not answering questions or following commands. Drug-related paraphernalia (including a crack pipe) was found on scene. Secondary to increasing agitation and combativeness, he was placed in four-point restraints when he arrived in the ambulance bay during the triage process. Vitals on presentation were: temperature of 35.9°C (96.6°F), heart rate of 108 beats/min, blood pressure 146/105 mm Hg, respiratory rate of 14 breaths/min, and oxygenation of 100% on room air. The patient was triaged to a hallway bed in the low-acuity section of the ED.

Upon physician evaluation, the patient was found unresponsive, restrained to the stretcher. His left eye was deviated laterally and the pupil of the left eye was fixed and dilated, nonreactive to light. All four extremities were extended and stiff, and there was no response to sternal rub. Respirations were agonal and intermittent. He was moved to the resuscitation area of the ED and intubated for airway protection.

After intubation, the patient was immediately taken for computed tomographic angiography (CTA). Concurrently he received a bolus of 1 g/kg of mannitol intravenously, with initial presumption that elevated intracranial pressure (ICP) was leading to herniation. The pupillary examination

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improved, as may be expected with an osmotic agent. The following CTA of the head/neck did not show any abnormalities to explain the etiology of the herniation, remarking that there were "no intracranial hemorrhage, mass, mass effect, or midline shift" to explain the blown pupil on presentation. After the CTA was performed and the patient was back in the resuscitation area, both pupils became fixed and dilated again on re-examination. Repeat vital signs revealed a temperature of 38.3°C (101°F) and heart rate of 180 beats/min. An infectious etiology was favored, prompting the performance of a diagnostic lumbar puncture (LP). The opening pressure was severely elevated to 55 mm Hg, and cerebrospinal fluid (CSF) tested positive for cryptococcal antigen, consistent with cryptococcal meningitis (CM) (1). Subsequent serum testing also revealed the patient to be human immunodeficiency virus (HIV) positive.

## DIFFERENTIAL DIAGNOSIS

Upon initial evaluation of the triage note and vitals, the clinical picture seemed consistent with psychosis, either secondary to acute decompensation of psychiatric illness or a sympathomimetic toxidrome from illicit drugs such as crack/cocaine, phencyclidine, or amphetamines. Other common considerations would include antipsychotic nonadherence, drug-induced psychosis, acute mania, excited delirium syndrome, and toxidromes that manifest with behavioral disturbances like serotonin syndrome and neuroleptic malignant syndrome. Of note, excited delirium syndrome has been associated with psychosis, tachycardia, and elevated temperature, but this diagnosis is not recognized by the *Diagnostic and Statistical Manual of Mental Disorders*, Fifth Edition (2).

However, upon examination of the patient, it was evident that a definite primary medical process was occurring, causing signs of increased ICP with a clinical syndrome consistent with herniation (posturing, blown pupil, agonal respirations, and coma). Concomitant use of sedatives-hypnotics or alcohol could cause decreased responsiveness, but the severely abnormal neurologic examination signaled that a herniation event was likely occurring. The CTA of the head/neck was performed after a hyperosmotic agent was given and during the period of temporary resolution of the clinical signs of herniation. It was presumed that the increased ICP was transiently alleviated during the scan, thus masking the underlying edema/herniation.

Given this age range and no knowledge of past medical history, it was important to consider neurologic crises that could cause these symptoms. This may be precipitated by a space-occupying lesion such as an intracranial hemorrhage (spontaneous or traumatic), parenchymal edema, or intracranial mass from toxoplasmosis, lymphoma, tuberculosis, or other etiologies causing obstruction of CSF flow.

Infectious causes were considered in the differential diagnosis, especially given the elevated temperature, including *Neisseria* and pneumococcal meningitis, herpes simplex virus encephalitis, as well as possible autoimmune and inflammatory disorders. Metabolic/endocrine emergencies may also be implicated. This would include illnesses such as myxedema coma, hyponatremia, and Wernicke encephalopathy.

## AN EMERGENCY PHYSICIAN'S APPROACH TO POSSIBLE CM MENINGOENCEPHALITIS

### *Identifying At-Risk Patients*

Although it is essential to be able to identify the patients most at risk for having central nervous system infections, this may often prove difficult in the ED setting. Given that presenting symptoms such as altered mental status can be vague, especially for more occult etiologies like CM, likelihood of central nervous system infection is increased in patients with HIV, patients with poor access to medical care or unknown past medical history, history of intravenous drug use, and solid-organ transplant patients, as well as other immunocompromised patients (3). Examples of known cases in non-HIV-infected patients include systemic lupus erythematosus, leukemia, lymphoma, and Cushing syndrome (4,5). Importantly, cases have also been noted in otherwise immunocompetent patients with common chronic conditions such as diabetes mellitus and chronic renal failure (6).

### *Physical Examination Findings*

The possibility of meningoencephalitis, including CM, is worth considering even in patients without overt meningeal signs. The most common symptoms include headache, fever, and malaise (7). However, subacute onset of personality change, psychosis, and altered mental status are not uncommon. Symptoms may be present for a period of several days to weeks, with fluctuating levels of acuity (the median time to diagnosis being 44 days) (8). Of note, nuchal rigidity occurs in only 25% of patients with CM (6,7,9).

There are some complications that are unique to CM that warrant discussion. There is a strong association of increased ICP with this type of fungal meningitis. As such, it will often present with sequelae of ophthalmologic findings and can progress to worsening mental status and eventually lead to obtundation or coma secondary to herniation. Vital signs may be useful with respect to identifying patients with elevated ICP. These include fever, increased diastolic blood pressure, and eventually, signs of Cushing reflex (hypertension, slow irregular respirations, bradycardia) (10).

Uniquely, ophthalmologic abnormalities are found in half of patients diagnosed with CM. Cranial nerve palsies, visual-field defects, and papilledema, as well as other ophthalmologic findings, have been described in multiple reports (11). It was shown that half of all infection-associated cranial nerve palsy cases (especially involving CN III and VI) were associated with CM (12,13).

It is also possible to have concurrent pulmonary and skin manifestations (14). However, there is no one identifiable skin lesion associated with the disease.

*Diagnostics*

Imaging is of limited definitive diagnostic value for CM, but can help narrow your differential and risk-stratify patients for LP. Computed tomography as well as magnetic resonance imaging often are unremarkable. On occasion there will be hydrocephalus, cerebral edema, leptomeningeal enhancement, or multiple ring-enhancing masses that can be mistaken for toxoplasmosis. Therefore, imaging is pursued to rule out other pathologies in an obtunded patient with evidence of increased ICP or with focal neurologic signs to stratify the risk of performing an LP.

In patients with fever and coma, the highest yield test is LP. Fungal meningitis tends to have pleocytosis, high protein, low glucose, lymphocyte predominance, and, in the case of CM, strong association with high opening pressures (> 20 cm $H_2O$) (15). Of note, cryptococcal antigen has been a validated marker of disease in the CSF, historically. However, point-of-care serum tests have been studied and found to be highly sensitive and specific when compared with CSF cryptococcal antigen (16). It has been proposed as a possible screening modality given its high sensitivity, especially in cases where LP is deemed high risk.

Additionally, CM has been shown in case studies to be a cause of syndrome of inappropriate antidiuretic hormone secretion (SIADH), and as a result, altered mental status may be secondary to hyponatremia (17). Often, there is the inclination to stop looking for a cause of altered mental status if there are large electrolyte abnormalities that could offer an explanation. However, in cases such as this, the underlying etiology of SIADH is critical to successfully treat the patient (18).

*Treatment*

Prognosis is highly dependent on initial management of this disease (19). Without treatment, this disease is universally fatal (20). Treatment should focus on airway management in cases of altered mental status, antifungal therapy, and aggressive reduction of ICP by CSF removal. Initial antifungal treatment in the ED includes amphotericin B and flucytosine (21). With respect to increased ICP, LP is both therapeutic and diagnostic (9). Experts recommend removal of enough CSF to decrease ICP below 20, as it has significant impact on morbidity and mortality (22). Of note, steroids are contraindicated.

## CONCLUSION

The patient in this case was triaged as a psychiatric complaint and placed in restraints. Given that drug intoxication and decompensation of mental illness commonly present in the ED, it may be an easy pitfall to consider illicit drug use or psychosis as the most likely diagnosis when a patient is altered. However, this case underscores the importance of psychiatric or non-life-threatening intoxication being diagnoses of exclusion, and to question the etiology of new-onset psychosis. It is possible that this patient had an abrupt change in status between triage and being placed in a hallway, when he was found to be exhibiting the stigmata of brain herniation. Patients who are not alert and oriented prompt more frequent reassessment. When a patient is unidentified without a known history of either psychiatric disease or drug use, it may be especially necessary to be more vigilant.

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