Abstract

We report a case of acute cryptococcal meningitis (CM) masquerading as normal pressure hydrocephalus (NPH) in an immune-competent female. An 85-year-old human immunodeficiency virus-negative female presented to the emergency room for altered mental status and difficulty walking. She was increasingly lethargic, with urinary incontinence and gait instability. A previous computed tomography was reported to have ventricular dilatation out of proportion to the degree of cortical atrophy. Magnetic resonance scan of the brain revealed ventricular dilatation and subtle debris layering the occipital horns of the lateral ventricles. A working diagnosis of NPH had been made considering the clinical symptoms and imaging. She became febrile to 103°F. Lumbar puncture was then performed which showed increased protein, decreased glucose, and mononuclear pleocytosis. India ink preparation of the cerebrospinal fluid was positive for Cryptococcus along with a positive cryptococcal antigen test. The patient was started on treatment for CM, but the patient continued to deteriorate further and died on the same day. Blood cultures subsequently grew Cryptococcus neoformans as well.

Keywords: Critical care, cryptococcosis, infectious diseases, meningitis

Introduction

Cryptococcus neoformans is an environmental saprophyte. The majority of disease burden is individuals with defective cell-mediated immunity. Cryptococcal meningitis (CM) is a common manifestation of cryptococcosis, although cutaneous as well as pulmonary presentations can occur.

Human immunodeficiency virus (HIV) infection is one of the main risk factors, responsible for about 80% of disease incidence. Individuals taking immunosuppressant drugs constitute a majority of the disease load in the HIV-negative population. Rarely, cryptococcosis has been reported in immune-competent hosts as well.

We report a case of acute CM masquerading as normal pressure hydrocephalus (NPH) in an immune-competent female.

Case Report

An 85-year-old female with a past medical history significant for type 2 diabetes mellitus presented to the emergency room for progressively altered mental status and difficulty walking. She was increasingly lethargic and was less interactive with family for 3 weeks before presentation. She also had urinary incontinence and gait instability. A previous computed tomography was reported to have ventricular dilatation out of proportion to the degree of cortical atrophy. Magnetic resonance scan of the brain revealed ventricular dilatation and subtle debris layering the occipital horns of the lateral ventricles. A working diagnosis of NPH had been made considering the clinical symptoms and imaging. She became febrile to 103°F. Lumbar puncture was then performed which showed increased protein, decreased glucose, and mononuclear pleocytosis. India ink preparation of the cerebrospinal fluid was positive for Cryptococcus along with a positive cryptococcal antigen test. The patient was started on treatment for CM, but the patient continued to deteriorate further and died on the same day. Blood cultures subsequently grew Cryptococcus neoformans as well.

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blood urea nitrogen - 21 mg/dL, and creatinine - 0.7 mg/dL. Magnetic resonance scan of the brain revealed subtle debris layering the occipital horns of the lateral ventricles without restricted diffusion, consistent with either intraventricular hemorrhage or pus [Figures 2 and 3].

She was febrile to 103°F. Blood and respiratory cultures were obtained and she was started on a broad-spectrum coverage for possible meningitis. She developed diabetic ketoacidosis, which was addressed. She had two episodes of seizure-like activity. A lumbar puncture was initially deferred, whereas NPH had remained the most probable diagnosis, and the patient had a high international normalized ratio (INR). It was performed emergently following clinical deterioration, with development of fever.

The cerebrospinal fluid (CSF) collected had increased protein, decreased glucose, and mononuclear pleocytosis. It was subjected to Gram-stain, which showed yeast and the species of the yeast were confirmed to be \textit{C. neoformans} on culture. India ink preparation of the CSF was positive for \textit{Cryptococcus} along with a positive cryptococcal antigen test. The patient was dosed with intravenous liposomal amphotericin B and oral flucytosine. HIV test was negative.

The patient continued to deteriorate further and had a cardiac arrest on the same day. She underwent cardiopulmonary resuscitation but could not be revived. Blood culture bottles subsequently grew \textit{C. neoformans} species. This finding although previously reported\cite{4} solidifies the fact that \textit{Neoforans} sp. can affect immune-competent hosts as well.

Clinical features of CM include subacute headache and confusion. Altered mental status has been associated with poorer prognosis. Intracranial pressure can be frequently elevated leading to cranial nerve palsy and seizures. Classical signs of meningitis are present in as few as 20% of the cases.\cite{7} The course of the disease can be complicated by an intracranial space-occupying lesion. These “cryptococcomas” can cause severe neurological manifestations such as blindness and hydrocephalus, requiring neurosurgical intervention.\cite{8,9} Very rarely, in the absence of a space-occupying lesion, the patient may develop cognitive impairment and gait ataxia in addition to an obstructive hydrocephalus with demonstrable ventricular dilatation.\cite{10}

NPH, on the other hand, is characterized by a wide-based “magnetic” or “shuffling” gait.\cite{11} Another pathognomonic feature is urinary incontinence secondary to detrusor overactivity.\cite{12} Memory loss with frontal and subcortical deficits can also be early signs of NPH. In our elderly patient, the triad of gait dysfunction with urinary incontinence and cognitive decline led to a clinical diagnosis of NPH. The absence of papilledema and confirmed CT findings of ventricular enlargement also favored the diagnosis of NPH.\cite{13} A need to reverse anticoagulation delayed a lumbar puncture in our patient, and the absence of fever and an immunocompetent state acted as confounding agents, pointing more toward NPH rather than CM.

Atypical presentations of CM are seen in HIV-seronegative patients. Some patients have symptoms for up to several months before presentation, whereas others present with acute illness of only a few days. Fever is seen in 50% of cases.\cite{5} A headache, lethargy, memory loss, and personality changes develop over few weeks. In patients with solid organ transplant, 2.8% of patients acquire cryptococcal infection.\cite{14} About 25% of transplant recipients with \textit{C. neoformans} infection develop fungemia.\cite{14}

\textbf{Discussion}

\textit{C. neoformans} is an encapsulated saprophyte. Two species, \textit{C. neoformans} and \textit{Cryptococcus gattii} are the principal organisms affecting humans.\cite{10} The mode of spread is inhalation, which causes subclinical pneumonitis. The organism reaches the CNS through hematogenous spread.\cite{4} \textit{C. neoformans} has been known to be primarily opportunistic, whereas \textit{C. gattii} primarily affects immunocompetent hosts in the tropical and subtropical regions.\cite{5} Our patient was immune-competent with an isolation of \textit{C. neoformans} species. This finding although...
Lumbar puncture remains the mainstay of diagnosis of CM. It should be noted that diagnosis is difficult in immunocompetent hosts as the culture and antigen tests can be frequently negative. The CSF white cells are elevated with a predominance of lymphocytes in HIV-negative individuals. CSF protein is usually elevated and glucose is low. India ink examination is positive in HIV-infected individuals but only positive in about 50% of non-HIV-infected cases. Culture is usually positive within 24–48 h on bacterial as well as fungal culture media.

*C. neoformans* forms mucoid colonies. Detection of cryptococcal polysaccharide antigen by latex agglutination or enzyme immunoassay has a sensitivity of >90% and a titer of >1:4 dilution is very specific. Histological tissue sections with Gomori’s methenamine silver and periodic acid–Schiff staining can be performed.

CM is uniformly fatal if left untreated. The course of disease is more acute in HIV-positive individuals. In our patient, the treatment was delayed due to high INR and the clinical features mimicked NPH. On diagnosis, the patient was started on a course of liposomal amphotericin B and fluconazole. This was in accordance with the Infectious Disease Society of America and World Health Organization guidelines. For any patient, the treatment comprises three phases, the induction phase, the consolidation phase, and the maintenance phase. As per these guidelines, a non-HIV and nontransplant patient should be started on 4–6 weeks of amphotericin B (0.7–1 mg/kg/day) and fluconazole (100 mg/kg/day) for initiation followed by 8 weeks of fluconazole 800 mg OD for consolidation and fluconazole 200 mg OD for maintenance thereafter.

**CONCLUSION**

We share our experience in dealing with an immunocompetent individual with CM was to make clinicians aware that the clinical findings can be less acute. It can cause an increase in intracranial pressure with classical findings of NPH as confounding agents. Timely initiation of therapy after a prompt lumbar puncture and CSF analysis can be lifesaving.

**Declaration of patient consent**

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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**Conflicts of interest**

There are no conflicts of interest.

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