Cryptococcal Meningitis Presenting as Normal Pressure Hydrocephalus in an Immunocompetent Patient

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Abstract

Background: Cryptococcus neoformans, an encapsulated saprophytic fungus, is an opportunistic pathogen that is more commonly encountered in immunocompromised individuals. Normal pressure hydrocephalus (NPH) is characterized by the classic clinical triad of gait disturbance, urinary incontinence and dementia in the presence of enlarged ventricles and with normal cerebrospinal fluid (CSF) pressure. Although cryptococcal meningitis (CM) has been reported in association with NPH, it is rarely on the differential diagnosis for hydrocephalus in immunocompetent patients, especially those without fever or meningeal signs.

Case presentation: We report a case of chronic cryptococcal meningitis disguised as normal pressure hydrocephalus in an immunocompetent elderly patient. The disease progressed in a 79-year-old man over one year of worsening cognition, gait disturbances and urinary incontinence. His presentation was complicated by developing parkinsonian features as well as weight loss. He had a presumed diagnosis of normal pressure hydrocephalus considering a computed tomography demonstrated hydrocephalus out of proportion to the amount of atrophy. He underwent a large volume lumbar puncture and his cerebrospinal fluid analysis was remarkable for pleocytosis and elevated protein which raised the concern for an infectious cause. Further investigations yielded a positive cryptococcal antigen in the cerebrospinal fluid and serum. The patient was treated with antifungal agents with favorable results.

Conclusion: This case report highlights the importance of sending cerebrospinal fluid for analysis as more similar cases are emerging in literature, it would be a critical step in ruling out treatable causes of dementia and spare the patient from unnecessary invasive procedures such as shunt placement to treat the hydrocephalus while overlooking the underlying cause.

Keywords: Cryptococcus neoformans; Cryptococcal meningitis; Normal pressure hydrocephalus

Introduction

Cryptococcus neoformans, an encapsulated saprophytic fungus, is an opportunistic pathogen. The majority of patients with cryptococcal meningitis have an identifiable immunodeficiency, such as advanced human immunodeficiency virus (HIV) infection or other conditions causing defective cell-mediated immunity [1,2]. Normal pressure hydrocephalus (NPH) is characterized by the classic clinical triad of gait disturbance, urinary incontinence and dementia in the presence of enlarged ventricles and without elevated cerebrospinal fluid (CSF) pressure. Although cryptococcal meningitis (CM) has been reported in association with NPH [3,4], it is rarely on the differential diagnosis for hydrocephalus in immunocompetent patients, especially those without fever or meningeal signs. Here we describe an immunocompetent man with CM who presented with findings compatible with NPH; he responded well to anti-fungal treatment.

Case Report

A 79-year-old man with past medical history of atrial fibrillation presented with one year of slowly-progressive cognitive decline, gait disturbance and urinary incontinence. Six months before presentation he developed a shuffling gait, frequent falls and slowing of movements. Urinary hesitancy, occasional incontinence as well as a twenty-pound weight loss were reported over the prior few months. On exam, he was a febrile. He had some parkinsonian features including bradykinesia, shuffling gait with some magnetic features and frequent freezing spells. The Montreal Cognitive Assessment score was 8/30 upon admission. Head computed tomography (CT scan) demonstrated mild to moderate hydrocephalus out of proportion to the amount of atrophy (Figure 1).

Figure 1: Axial view of brain CT scan without contrast. There is mild to moderate hydrocephalus out of proportion to the amount of cortical atrophy.

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Given the presence of the classic NPH triad and CT scan findings, a high-volume lumbar puncture was performed in preparation for a ventriculoperitoneal (VP) shunt. Opening pressure was normal at 15.5 cm H2O. CSF findings included: total protein 94 mg/dL; white blood cell count 108 cells/mm³ with 55% lymphocytes, 13% histiocytes and 31% neutrophils; glucose of 39 mg/dL. (concomitant serum glucose of 97 mg/dL). CSF cryptococcal antigen was positive with a titer of 1:40. Serum cryptococcal antigen was 1:320. Fungal cultures of the CSF and blood were negative. HIV antigen/antibody results were negative. Computed tomography of chest, abdomen and pelvis as well as total body PET scan did not reveal malignancy. The patient was treated with liposomal amphotericin B and flucytosine for four weeks and then transitioned to amphotericin B and flucytosine. On 12-week follow-up he had significant improvement in his gait and mental status.

Discussion

Cryptococcus neoformans is an encapsulated saprophytic fungus which is found worldwide in soil contaminated with bird droppings. The usual mode of acquisition of infection is inhalation, and subclinical pneumonitis can occur early in infection. The majority of illness occurs in patients with defective cell-mediated immunity. HIV infection is the main risk factor globally, accounting for 95% of cases in middle and low-income countries and 80% of cases in high-income countries [1]. In HIV-negative patients with cryptococcosis, common predisposing conditions include chronic steroid therapy, receipt of an organ transplant, chronic organ failure, malignancy and rheumatologic disease. Meningitis is the most common manifestation of cryptococcosis in immunocompromised patients. This organism reaches the central nervous system via hematogenous spread, and recent work suggests a secreted fungal metalloprotease targets brain endothelium, leading to the observed neurotropism of the organism [5]. Uncommonly, immunocompetent patients develop cryptococcal illness [2]. In this group, pulmonary disease is seen with greater frequency.

Cryptococcal meningitis can have a very insidious course in immunocompetent patients with recurrent episodes of variable headache, fever, nausea, vomiting, cranial nerve palsies and visual disturbance [6]. Nearly identical presentations for CM and NPH have been reported in the literature. Mangham et al., described three patients with cryptococcal meningitis who underwent VP shunt placement and later were found to have cryptococcal meningitis. All three presented with fever and meningeval signs [7]. Patel et al., presented two cases of CM in immunocompetent individuals mimicking NPH. In both, cognitive decline preceded the gait impairment and urinary incontinence which is different from the usual course for idiopathic NPH [4]. Raheja et al., described an 85-year-old man who developed acute cognitive decline, gait disturbance and urinary incontinence and fever. Brain MRI showed enlarged ventricles with layering debris in the occipital horns of the lateral ventricles. CSF analysis revealed infection with cryptococcus [3]. A newer case report from Thailand described a case of Cryptococcus gattii meningitis that was misdiagnosed as NPH leading to ventriculoperitoneal shunt placement with subsequent shunt suprainfection. Their patient’s presentation was even more insidious than ours, with symptoms that developed over 2 years. She continued to have recurrent communicating hydrocephalus even with in-place VP shunt, and eventually developed very large intraabdominal VP shunt pseudocyst which was found to be infected with Cryptococcus gattii. This organism was also found in the CSF. Patient had a favorable outcome after replacing the infected shunt and appropriate anti-fungal treatment [8].

Conclusion

The diagnosis of CM in our patient was challenging given the chronicity of symptoms, absence of immunocompromise (other than advanced age) and absence of fever. Abnormal routine CSF test results led to the accurate diagnosis of cryptococcal meningitis and the patient experienced marked improvement with antifungal treatment. This case illustrates the importance of CSF analysis to assess for cryptococcal infection in all immunocompetent patients who present with signs and symptoms of NPH and avoid submitting the patients for unnecessarily invasive procedures such as placement of a ventriculoperitoneal shunt without actual treatment of the root cause of the perceived hydrocephalus.

References