Cryptococcal Meningoencephalitis with Meningomyelitis: A Case Report

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ABSTRACT
Cryptococcus is a very invasive fungal pathogen that usually involves the central nervous system. Cryptococcal meningomyelitis is very rare, even in patients with AIDS. Cryptococcus infection presenting as a spinal cord syndrome has been reported, but all of these cases were vertebral osteomyelitis. We report on an immunocompetent 49-year-old man with cryptococcal meningoencephalitis associated with thoracic-meningomyelitis and cranial nerve (CN) VI, VII, and VIII involvement. He visited the emergency department with a 10-day history of bilateral temporal headache and fever with chills with paraplegia the previous 2 days. The diagnosis of cryptococcal meningoencephalitis was confirmed by CSF study and brain/cervical spine MRI findings. Thoracic meningomyelitis was suspected because thoracic-lumbar spine MRI showed abnormal enhancement around the conus medullaris and at the spinal nerve roots. This patient also had CN VI and VII palsy and bilateral CN VIII involvement with acute hearing impairment.

Keywords: Cryptococcus, meningoencephalitis, meningomyelitis, CNS infection

INTRODUCTION

The lungs can be infected with cryptococcus through the respiratory tract, although central nervous system (CNS) involvement is more prominent. Cryptococcal pneumonia is often subclinical and transient.1 It can affect any organ through a hematogenous route, but has an unexplained preference for the CNS. Meningoencephalitis is the most common clinical manifestation of cryptococcus neoformans infection. Although cryptococcosis is considered an opportunistic infection as it affects mainly immunosuppressed individuals, it does rarely affect patients without immune deficiency. Most AIDS patients with this infection present with meningoencephalitis or septicemia (disseminated cryptococcosis), although localization to the bone marrow or an organ (e.g., the lungs, liver, spleen, kidney, myocardium, skin and prostate) is relatively common. Cases of cryptococcosis presenting as a spinal cord syndrome have previously been reported, but all these cases were vertebral osteomyelitis. We report on a 49-year-old man without HIV infection who presented with cryptococcal meningoencephalitis associated with thoracic-meningomyelitis and cranial nerve (CN) VI, VII, and VIII involvement.

CASE REPORT

A previously healthy 49-year-old man, who had an operation for L5-S1 herniation of an intervertebral disc (HIVD) 10 years previously, presented to our emergency department (ED) with a 10-day history of bilateral temporal headache and fever with chills. He complained of progressive bilateral leg weakness and urine retention for 4 days. His lower limbs had become totally paralyzed 2 days before admission. Initial vital signs were normal except for a mildly elevated BP (159/96 mmHg). The Glasgow Coma Scale score was E3V5M6. He had significant weakness in the bilateral lower extremities (muscle power scored as 1/5), hypotonia, hyporeflexia, and positive Babinski’s signs on physical examination. Pinprick and light touch sensations were...
lost up to the level of the tenth thoracic (T10) dermatome. Laboratory examination showed an abnormal white cell count (14500/mL) (84% segments, 4% basophils, 12% lymphocytes) and hyponatremia. Initial thoraco-lumbar spine radiography and brain-computed tomography (CT) showed no significant findings. A lumbar puncture revealed a cerebrospinal fluid (CSF) white cell count of 32 cells/mL, which were mainly mononuclear cells (neutrophils:lymphocytes:monocytes = 4:7:21); red cell count of 5 cells/mL; a glucose level of <5 Mmol/L (serum glucose level of 7.659 Mmol/L); lactate level of 65.5 mg/dL (10.8-19.9 mg/dL); protein level of 174.2 mg/dL (15-45 mg/dL); and an opening pressure of 600 mm H2O. Both Gram stain and acid-fast stain of the CSF were negative. Cryptococcus was found on India ink stain, and was later confirmed as Cryptococcus neoformans on culture. He was then admitted to the neurological intensive care unit (ICU) and intravenous Amphotericin B (2 mg/day initially, total dose 3516 mg) and oral fluconazole (400 mg/day initially) were given. Brain and cervical spine MRI findings were consistent with meningoencephalitis. Thoracic-lumbar spine MRI showed abnormal enhancement around the conus medullaris and at spinal nerve roots (Figure 1). The patient’s condition improved and he was transferred to the ward after 4 days in ICU. However, bilateral blurred vision and double vision developed after admission, which were confirmed as bilateral 6th cranial nerve palsy due to increased intracranial pressure. Other sequelae included bilateral vestibular nerve involvement with acute hearing impairment and right peripheral facial nerve palsy. HIV antibody was negative on two different occasions. Other immunological and endocrinological laboratory studies including antinuclear antibody, rheumatoid factor, C3, C4, thyroid stimulating hormone, T3, and free T4 were all within the normal ranges. He was discharged uneventfully after 5 months of hospitalization.

DISCUSSION

Cryptococcosis in the immunocompromised host has a high morbidity and mortality. Approximately 90% of cryptococcosis occurs in AIDS patients. The typical clinical manifestations are meningoencephalitis and pneumonia. Cryptococcomyelitis is very rare, even in patients with AIDS.

Cryptococcus infection is more common in men, possibly because of occupational exposure or a lack of estrogens. Children are less commonly affected (less than 100 reported cases). The number of children with cryptococcosis will probably increase with more prevalent HIV infection in the future. Presentation of the disease includes asymptomatic pneumonia, meningoencephalitis, or a wide systemic dissemination. The CNS is especially prone to infection. It is essential that severely immunosuppressed patients be screened for occult cryptococcus meningitis in suspected cases. Involvement of the parenchyma of the brain as well as the meninges occurs in 40-86% of patients as the organism has an unexplained predisposition for these sites. The infection can be acute or chronic.

Nonmeningeal or nonparenchymal brain involvement is uncommon. An acute onset (<7 days) or chronic (>30 days) onset of headache, fever and nuchal pain suggesting meningeal irritation are the presenting symptoms. However, neither headache nor fever is present in HIV-infected patients. Instead, they can present with lethargy, obtundation, stupor, coma, or even dementia. Clinical signs lack precision in predicting the etiology in meningitis. Papilledema due to increased intracranial pressure is a common complication of cryptococcal infection, but focal neurological signs such as cranial nerve palsies are rare. Intracerebral, cerebellar, and spinal cord lesions, although rare, have been noted. Complications of CNS involvement include internal hydrocephalus, focal motor deficits, changes in mentality, and symptoms of increased intracranial pressure. Cases of vertebral osteomyelitis in immunocompetent patients have been reported, mainly in Zimbabe and South Africa, although they are exceedingly rare.

A few points can be learned from this case. CSF India ink stains, cryptococcal antigen assay, and culture should be done in all patients presenting with myelitis, irrespective of immunological status. The typical CSF study findings in fungal meningitis include elevated opening pressure, a WBC count of 200-500 (variable, dependent upon fungus), neutrophils usually <50%, elevated protein, an elevated lactate level and a glucose level usually < 40 mg/dL. The above tests are less expensive than tests for organisms such as cytomegalovirus and varicella-zoster virus, which can cause radiculomyelitis in HIV-infected patients. The scarcity of reports may be due to low suspicion and under-diag-

Figure 1. Dural sac and spinal nerve root enhancement (Arrow).
nosis by clinicians.

Early and aggressive medical treatment of Cryptococcus neoformans myelitis with Amphotericin B and fluconazole in nonimmunocompromised patients may be life-saving, as in the present case. Su et al. described a patient who had both operative treatment and antifungal therapy.14

Emergency physicians should have suspicions of cryptococcosis in immunocompetent patients with spinal myelopathy. Additionally, diplopia due to increased intracranial pressure with CN VI palsy may indicate cryptococcal infection. Treatment options include Amphotericin B, 5-fluorocytosine and fluconazole. Surgical intervention may be needed. The prognosis of patients with early and aggressive treatment is good. Astute physicians should always be alert to the possibility of a common infection with an uncommon presentation.

REFERENCE

隱球菌腦膜腦炎併腦膜脊髓炎：一病例報告

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摘要

隱球菌是一種造成侵入性中樞神經感染的重要黴菌。隱球菌腦膜腦炎甚至發生在後天免疫不全症候群的病人中，都已被認為是極特殊的臨床表現。以往發表的文獻以脊髓症候群表現的隱球菌感染中，都是造成隱球菌椎體脊髓炎的病例。本文報告一病例為49歲男性病患，過去並無免疫功能不全的病史，臨床表現為隱球菌腦膜腦炎與腦膜脊髓炎，合併第6、7、8對腦神經侵犯。

關鍵字：隱球菌，腦膜腦炎，腦膜脊髓炎，中樞神經感染