Persistent headache plagues an immunocompromised patient

Imaging studies and laboratory tests were negative, but lumbar puncture revealed a pathogen you should suspect in patients with unexplained neurologic symptoms.

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CASE

Mr. V., a 65-year-old African American, with multiple myeloma presented to the emergency department (ED) with a persistent headache. His multiple myeloma was diagnosed 18 months ago, and he was placed on weekly low-dose dexamethasone therapy approximately 1 year ago. Mr. V. began lenalidomide and bortezomib 6 months ago. One month prior to his presentation in the ED, a bone marrow biopsy showed a remission marrow. However, the lenalidomide and bortezomib were discontinued due to difficulty with grade II peripheral neuropathy. Mr. V. was referred for high-dose chemotherapy and autologous hematopoietic progenitor stem cell transplant.

Extensive pretransplant laboratory test results were all within the normal range except for a tuberculin skin test, which showed 14 mm induration. Chest radiography was negative. Isoniazid (INH) and Vitamin B6 were initiated for tuberculosis (TB) prophylaxis.

The next week, Mr. V. called the office and reported accidentally taking eight furosemide 20 mg tablets that he had mistaken for dexamethasone. Laboratory tests the next day showed a normal BUN and creatinine; but



The patient was infected with the fungus Cryptococcus neoformans (inset).

his BUN-to-creatinine ratio (>20:1) indicated dehydration. Mr. V. also reported having an intense headache for the past 2 days. The headache was believed to be related to the dehydration, and IV fluids were administered. Mr. V. felt much better the next day and even went to work, but the headaches persisted despite taking naproxen or ibuprofen. Mr. V. came to the ED 2 days later.

CT of the head was negative, and MRI of the brain was also negative. CBC and BMP were within normal limits. The next day Mr. V. was noted to be slightly disoriented, and then he had a seizure. Repeat CT of the head was negative, but a lumbar puncture returned positive for cryptococcal meningoencephalitis.

DISCUSSION

Cryptococcal meningoencephalitis is an invasive fungal infection with Cryptococcus neoformans or Cryptococcus gattii. The incidence is about 4.9 cases per 100,000 persons. The infection is more prevalent in immunocompromised conditions, especially acquired immune deficiency syndrome (AIDS), prolonged therapy with glucocorticoids, organ transplantation, malignancy, or sarcoidosis. Most cases occur in African Americans.1

C gattii and C neoformans are airborne infections. The organism has a tendency to localize in the central nervous system (CNS). The inflammatory response in the brain is usually milder than in cases of bacterial meningitis. Disease outside of the CNS (disseminated) can also occur. Clinical presentation is highly variable. Approximately 50% of patients present with a fever. Other symptoms

include headache, lethargy, personality changes, and memory loss over 2 to 4 weeks.¹

Definitive diagnosis is established by culture of the cerebrospinal fluid (CSF) via lumbar puncture. If papilledema, focal neurologic signs, or impaired mentation manifests, presence of CNS lesions should be ruled out via CT or MRI of the brain first. Increased intracranial pressure or hydrocephalus is often evident.¹

Treatment goals for patients with cryptococcal meningoencephalitis are to reduce immunosuppressive therapy, manage intracranial pressure, and administer antifungal therapy. Antifungal therapy is given as induction therapy, consolidation therapy, and maintenance therapy. Amphotericin B (Amphotec, Abelcet, Ambisome, generic) and flucytosine (Ancoban, generic) are the antifungal agents of choice for induction therapy; however, amphotericin B is highly nephrotoxic and should be avoided in patients with renal insufficiency. Repeat lumbar puncture is usually obtained 2 weeks later, but can be performed sooner to reduce intracranial pressure if needed. If CSF cultures remain positive after 2 weeks of induction therapy, continue the induction regimen with serial lumbar punctures every 2 weeks until the CSF becomes

TEACHING POINTS

This case reinforced these important nursing concepts:

- Cryptococcal meningoencephalitis should be suspected if an immunocompromised patient complains of unexplained persistent headache, fever, or other neurologic symptoms.
- Immunocompromised patients with cancer are at increased risk for cryptococcal meningoencephalitis.
- Definitive diagnosis is confirmed via culture of *Cryptococcus neoformans* or *Cryptococcus gattii* obtained through lumbar puncture.
- Treatment goals are to lower immunosuppression, manage intracranial pressure, and provide antifungal therapy.
- Prognosis is very poor for patients with cancer who develop cryptococcal meningoencephalitis.

sterile. Once the CSF cultures return negative, then fluconazole (Diflucan, generics) is used for consolidation and maintenance therapy.²

Prognosis for patients with cryptococcal meningoencephalitis is very poor, especially if an underlying malignancy is present. One study reported a median survival of about 2 months for patients with a malignancy compared with 9 months for patients with AIDS.²

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