

66-Year-Old Woman With Falls and Confusion



Jordan K. Schaefer, MD; Hassan B. Alkhateeb, MD; and Carrie A. Thompson, MD

A 66-year-old woman with a medical history of vertigo, nicotine dependence, hypertension, and hyperlipidemia presented to the emergency department with recent-onset generalized weakness, headache, confusion, and frequent falls, which had progressed over the past months. She did not have visual symptoms, tongue biting, incontinence, dysarthria, cardiopulmonary symptoms, or constitutional symptoms. Her home medications consisted of aspirin, atenolol, citalopram, gemfibrozil, lisinopril, lovastatin, omeprazole, and a multivitamin.

On physical examination, her temperature was 36.5°C, blood pressure was 158/60 mm Hg, pulse rate was 50 beats/min and regular, respiratory rate was 18 breaths/min, and oxygen saturation was 96% while the patient breathed room air. She appeared drowsy and was oriented only to person. On neurologic examination, her speech was normal. She had left greater than right anisocoria, slight left-sided weakness, a left pronator drift, and Babinski sign on the left toe. She required assistance for ambulation. Cardiopulmonary and abdominal examination findings were normal.

Computed tomography (CT) of the head revealed areas of low attenuation in the right temporal lobe and basal ganglia with a mass in the right basal ganglia and thalamus. Subsequent magnetic resonance imaging (MRI) of the brain showed multiple enhancing lesions with surrounding edema and local mass effect; the largest of these lesions measured 2×1×1 cm in the right basal ganglia.

The results of stereotactic brain biopsy were preliminarily believed to be consistent with a high-grade glioma. The patient's clinical presentation and radiographic findings were felt to be congruent with the initial pathologic interpretation. This opinion, in conjunction with her subacute neurologic decline, prompted the immediate initiation of therapy before the final pathologic diagnosis was available. External-beam whole-brain radiation therapy was initiated. She had received a total of 900 cGy in 3

fractions when the final pathologic review was reported. The tumor cells were large with irregular nuclei and single or multiple nucleoli. Areas of focal necrosis and glial fibrillary acidic protein positivity were seen, which support the diagnosis of high-grade glioma. However, on immunohistochemical examination, cells were CD20-positive and CD3-negative with a distinct perivascular arrangement consistent with diffuse large B-cell lymphoma, and the glial fibrillary acidic protein positivity was secondary reactive gliosis. Staging with CT/positron emission tomography and bilateral bone marrow biopsy did not reveal any other sites of lymphoma. With the diagnosis of primary central nervous system (CNS) lymphoma, radiation therapy was discontinued, and high-dose methotrexate, rituximab, and temozolomide chemotherapy was initiated.

Through her first cycle of chemotherapy, the patient's confusion persisted. When she was readmitted for the next dose of chemotherapy, it was noted that her mental status "was a little odd... [she] unpacked her bag for several minutes while I waited to finish my exam." Magnetic resonance imaging performed for further evaluation showed that the lymphomatous masses were improving. The neurology service was consulted, but the evaluation was unrevealing. The patient was discovered to have a 2-year history of heavy alcohol use. Therefore, she was treated with several days of oral thiamine dosed at 100 mg/d while an inpatient.

When she presented for evaluation before another cycle of chemotherapy, her family noted worsening confusion at home. Repeated MRI indicated ongoing improvement in her lymphoma. On examination, she was alert and oriented to person, place, time, and recent events. She answered questions, gave explanations, or told stories that seemed appropriate, but the content was confirmed by her family to be inaccurate. On mental status examination, she gave an incorrect home address. She successfully repeated 4 random digits, adding "that is my husband's phone number." She had particular difficulty

See end of article for correct answers to questions.

Residents in Internal Medicine (J.K.S.) and Hematology (H.B.A.), Mayo School of Graduate Medical Education, Rochester, MN; Advisor to residents and Consultant in Hematology, Mayo Clinic, Rochester, MN (C.A.T.).

with mathematics. She answered “What is $7 + 4$ ” with “2005.” The question of $8 + 3$ was answered with “a quarter past 9.” When asked what was similar between an orange and a banana, she said “I enjoy eating both of them.” She then gave the same answer when asked the similarities between a horse and dog. Her score on the short test of mental status developed by Kokmen et al¹ was 11/38. Neurologic examination findings were notable for gait disturbance.

1. Which one of the following is the most likely primary cause of the patient’s ongoing altered mental status?

- a. CNS lymphoma
- b. Complications of cranial irradiation
- c. Corticosteroid-induced psychosis
- d. Wernicke encephalopathy (WE)
- e. Delirium

The patient presented with a new diagnosis of CNS lymphoma and subacute onset of confusion. Therefore, the lymphoma could be partially responsible for her confusion. However, improvement of the lymphoma was evident on 2 MRIs after starting therapy, but her mental status continued to worsen, making CNS lymphoma unlikely to be the main issue. Complications of radiation would also be unlikely because the patient had confusion that preceded her therapy. She received a relatively low-dose partial course of treatment that would not account for her degree of subsequent cognitive and motor issues. Corticosteroids are a typical treatment for cerebral edema associated with metastatic brain tumors. They are also given along with chemotherapy and can be associated with psychiatric disturbances, including psychosis. However, these effects should be more temporally related to corticosteroid administration. Unlike this case, corticosteroid-induced psychosis will often involve hallucinations or delusions. Confabulation, as indicated by the patient providing false testimony regarding her history, is typically not a part of corticosteroid-induced psychosis. Wernicke encephalopathy is a neurologic disorder caused by thiamine deficiency typically caused by chronic alcoholism or persistent vomiting and marked by mental confusion, abnormal eye movements, and unsteady gait. Although oral thiamine supplementation produced no improvement in our patient’s mental status, this would not exclude

WE as a diagnostic consideration, and at this point, WE is the most likely cause of her altered mental status. The patient did not have a change in her level of consciousness or a typical time course to support delirium.

A presumptive diagnosis of WE was ultimately made on the basis of the patient’s history of alcohol abuse, gait disturbance consistent with ataxia, and altered mental status. Although she reportedly had a long history of regular alcohol use, the extent of her use was unknown and her history was unreliable. Her history was not suggestive of alcohol dependence, and she was recently sober. These factors called into question the diagnosis of WE. Although WE is often associated with alcohol use, it has been reported in other populations as well. Its diagnosis requires a high index of clinical suspicion.

2. Aside from heavy alcohol use, which one of the following, if present, would be most suggestive of WE in this patient?

- a. Cancer
- b. Hyperemesis gravidarum
- c. History of gastrointestinal bypass procedure
- d. AIDS
- e. Chronic renal disease

When WE has been reported in nonalcoholic patients, cancer was the most common associated condition (18%), followed by gastrointestinal operations (16.8%), hyperemesis gravidarum (12.2%), AIDS (5%), and dialysis and renal disease (3.8%).^{2,3} Starvation and malnutrition combined were associated with WE in 14.4% of nonalcoholic patients. Even without knowledge about this patient’s alcohol use, her comorbid cancer and subsequent worsening while receiving chemotherapy should raise concerns for WE in this context.

Wernicke encephalopathy is well known to have a variable clinical presentation. This patient had an evolution in her symptoms and examination findings over time, which led to considering WE as a diagnosis.

3. For a diagnosis of WE, which one of the following would be the most likely examination findings?

- a. Ataxia
- b. Nystagmus or ophthalmoplegia
- c. Confusion

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