Mr. E, age 55, has a 2-week history of altered mental status, sleep disturbance, and decreased appetite and speech. Medical workup does not reveal an underlying cause. How would you proceed?

Mr. E, age 55, presents to the emergency department (ED) with a 2-week history of altered mental status (AMS). His wife reports, “He was normal one day and the next day he was not.” Mr. E also presents with sleep disturbance, decreased appetite and speech, and a 20-lb weight loss. His family reports no recent stressors or head trauma. Mr. E is agitated in the ED and receives a single dose of IV haloperidol, 5 mg. He exhibits paranoia and is afraid to get a CT scan. The medical team attempts a lumbar puncture (LP), but Mr. E does not cooperate.

His laboratory values are: potassium, 3.0 mEq/L; creatinine, 1.60 mg/dL; calcium, 10.6 mg/dL; thyroid-stimulating hormone, 0.177 IU/L; vitamin B12, >1500 pg/mL; folate, >20 ng/mL; and creatine kinase, 281 U/L. Urine drug screen is positive for benzodiazepines and opiates, neither of which was prescribed, and blood alcohol is negative.

Mr. E is admitted for further workup of AMS. His daughter-in-law states that Mr. E is an alcoholic and she is concerned that he may have mixed drugs and alcohol. The medical service begins Mr. E on empiric antimicrobials—vancomycin, ceftriaxone, and acyclovir—because of his AMS, and performs an LP to rule out intracranial pathology. His LP results are unremarkable.

Mr. E appears to be confused during psychiatric evaluation. He requests to be “hypnotized on a helicopter to find out what is wrong with me.” His wife states that Mr. E drank vodka daily but decreased his alcohol consumption after surgery 5 months ago. Before his current admission, he was drinking approximately half a glass of vodka every few days, according to his wife. Mr. E says he has no prior psychiatric admissions. During the mental status exam, his eye contact is poor, with latency of response to questions, thought blocking, and psychomotor retardation. He is alert, oriented to time, place, and person, and cooperative. He cannot concentrate or focus during the interview. He denies suicidal or homicidal ideation.

What would be your working diagnosis?

a) delirium not otherwise specified (NOS)
b) psychosis NOS
c) delusional disorder
d) substance-induced mood disorder
e) Wernicke-Korsakoff syndrome

The authors’ observations

Mr. E appeared to be delirious, as evidenced by the sudden onset of waxing and waning changes in consciousness, attention deficits, and cognition. He also had a history of daily alcohol use and decreased...
his alcohol intake after a surgery 5 months ago, which puts him at risk for Wernicke’s encephalopathy.\textsuperscript{1-3} The type of surgery and whether he received adequate thiamine supplementation at that time was unclear. Because Mr. E is older, he has a higher risk of mortality and morbidity from delirium.\textsuperscript{4,5} We started Mr. E on quetiapine, 50 mg/d, for delirium and an IV lorazepam taper, starting at 2 mg every 8 hours, because the extent of his alcohol and benzodiazepine use was unclear—we weren’t sure how forthcoming he was about his alcohol use. He received IV thiamine supplementation followed by oral thiamine, 100 mg/d.

Which test(s) would you order?
   a) electroencephalography (EEG)
   b) MRI
   c) cerebrospinal fluid (CSF) workup
   d) all of the above

\textbf{The authors’ recommendations}

We requested a neurology consult, EEG, CSF cultures, and brain MRI (\textit{Table 1}).\textsuperscript{6} EEG, chest radiography, thyroid scan, and CT scan were normal and MRI showed no acute intracranial process. However, there was a redemonstration of increased T1 signal seen within the bilateral basal ganglia and relative diminutive appearance to the bilateral mamillary bodies, which suggests possible liver disease and/or alcohol abuse. These findings were unchanged from an MRI Mr. E received 10 years ago, were consistent with his history of alcohol abuse, and may indicate an underlying predisposition to delirium. A CT scan of the abdomen showed hepatic cirrhosis with prominent, tortuous vessels of the upper abdomen, subtle ill-defined hypodensity of the anterior aspect of the liver, and an enlarged spleen.

Mr. E’s mental functioning did not improve with quetiapine and lorazepam. Further evaluation revealed a negative human immunodeficiency virus test and normal heavy metals, ammonia, ceruloplasmin, and thiamine. We suspected limbic encephalitis because of Mr. E’s memory problems and behavioral and psychiatric manifestations,\textsuperscript{7} but CSF was unremarkable and limbic encephalitis workup of CSF and paraneoplastic antibody panel were negative.

Mr. E’s primary care physician stated that at an appointment 1 month ago, Mr. E was alert, oriented, and conversational with normal thought processing. At that time he had presented with rectal bleeding, occult blood in his stool, and an unintentional 25-lb weight loss over 2 months. It was not clear if his weight loss was caused by poor nutrition—which is common among chronic alcoholics—or an occult disease process.

After 10 days, Mr. E was discharged home from the medicine service with no clear cause of his AMS.

\textbf{EVALUATION | Worsening behavior}

One week later, Mr. E presents to the ED with continued AMS and worsening behavior at home. Two days ago, he attempted to strangle his dog and cut himself with a knife. His para-

\begin{table}
\centering
\caption{Suggested workup for altered mental status}
\begin{tabular}{|l|}
\hline
Complete blood count, basic metabolic profile, creatine kinase \\
Thyroid-stimulating hormone, thyroid scan \\
Vitamin B12, folate, thiamine \\
Blood alcohol, urine drug screen \\
Urine analysis and cultures \\
Lumbar puncture—CSF staining and cultures \\
Chest radiography \\
CT and MRI scan of brain \\
Electroencephalography \\
Neuropsychiatric testing \\
CSF: cerebrospinal fluid  \\
\textbf{Source:} Reference 6  \\
\hline
\end{tabular}
\end{table}
noia was worsening and his oral intake continued to decrease. In the ED, Mr. E does not want a chest radiograph because, “I don’t like radiation contaminating my body”; his family stated that he had been suspicious of radiography all of his life. He receives empiric ceftriaxone because of a possible urinary tract infection. Urine culture is positive for *Pseudomonas aeruginosa* and he is switched to ciprofloxacin. Mr. E is admitted for further workup.

Mr. E’s mother states, “I think this change in behavior is related to my son drinking alcohol for 20 years. This is exactly how he acted when he was on drugs. I think he is having a flashback.” She also reports her son purchased multiple chemicals—the details of which are unclear—that he left lying around the house. His wife says that after discharge a week ago, Mr. E was stable for 1 or 2 days and then “he started going downhill.” He became more paranoid and he started talking about cameras watching him in his house. Mr. E took quetiapine, 50 mg/d, for a few days, then refused because he thought there was something in the medication. Mr. E’s family feels that at times he is responding to internal stimuli. He makes statements about his DNA being changed and reports that he has 2 wives and the wife in the room was not the real one, which suggests Capgras syndrome. His wife provides a home medication list that includes vitamin B complex, vitamins B12, E, and C, a multivitamin, zinc, magnesium, fish oil, garlic, calcium, glucosamine, chondroitin, herbal supplements, and gingko. The psychiatry team recommends switching from quetiapine to olanzapine, 15 mg/d, because Mr. E was paranoid about taking quetiapine.

We determine that Mr. E does not have medical decision-making capacity. Because his symptoms do not improve, Mr. E is transferred to the psychiatric intensive care unit. His mental status shows little change while there. Neuropsychiatric testing shows only “cognitive deficits.” He shows signs consistent with neurologic dysfunction in terms of stimulus-bound responding and perseveration, which is compatible with the bilateral basal ganglia lesion seen on MRI. However, some of his behaviors suggest psychiatric and motivationally driven or manipulative etiology. During this testing he was difficult to evaluate and needed to be convinced to engage. At times he was illogical and at other times he showed good focus and recall. It is difficult to draw more definitive conclusions and Mr. E is discharged home with minor improvement in his symptoms. He

### Table 2

<table>
<thead>
<tr>
<th>Symptoms</th>
<th>Treatment</th>
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</thead>
<tbody>
<tr>
<td><strong>First ED visit</strong></td>
<td><strong>Empiric antimicrobials for possible meningitis</strong></td>
</tr>
<tr>
<td>Agitation</td>
<td>Haloperidol for agitation</td>
</tr>
<tr>
<td>Confusion</td>
<td>Quetiapine for delirium</td>
</tr>
<tr>
<td>Sleep disturbance</td>
<td>Lorazepam taper</td>
</tr>
<tr>
<td>Decreased appetite and speech</td>
<td>Thiamine supplementation</td>
</tr>
<tr>
<td>20-lb weight loss</td>
<td></td>
</tr>
<tr>
<td><strong>Second ED visit</strong></td>
<td>Switch from ceftriaxone to ciprofloxacin for <em>Pseudomonas aeruginosa</em></td>
</tr>
<tr>
<td>Violent behavior</td>
<td>Switch from quetiapine to olanzapine</td>
</tr>
<tr>
<td>Worsening paranoia</td>
<td></td>
</tr>
<tr>
<td>Responding to internal stimuli</td>
<td></td>
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<tr>
<td>Mr. E believes he has 2 wives, but the wife in the room is not the real one, which suggests possible Capgras syndrome</td>
<td></td>
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<tr>
<td>Cognitive deficits on mental status exam</td>
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ED: emergency department
didn’t attend follow-up appointments. During a courtesy call a few months after his admission, his wife revealed that Mr. E had died after shooting himself. It is unclear if it was an accident or suicide.

**The authors’ observations**

Mr. E’s diagnosis remains unclear (for a summary of his clinical course, see Table 2). Although his initial presentation was consistent with delirium, the lack of an identifiable medical cause, prolonged time course, and lack of improvement with dopamine blocking agents suggest additional diagnoses such as Wernicke-Korsakoff syndrome, rapidly progressive dementia, or a substance-induced disorder. He displayed paranoia and bizarre delusions, which would suggest a thought disorder. However, he also had a history of substance use. A few months after we saw Mr. E, “bath salt” (methylenedioxypyrovalerone) abuse gained national attention. Patients with bath salt intoxication present with confusion, paranoia, and behavioral disturbances as well as a prolonged course.

Mr. E’s CT and MRI scans, history of alcohol use, and cirrhosis also point to Wernicke-Korsakoff syndrome as an underlying diagnosis. It is unclear whether Mr. E experienced alcohol withdrawal and IV glucose without adequate thiamine replacement during a prior surgery. However, MRI findings were unchanged from a previous study 10 years ago.

It is puzzling whether Mr. E’s AMS was a first psychotic break, a result of drug and alcohol use, rapidly progressing dementia, or another neurologic problem that we have not identified. Our tentative diagnosis was Wernicke-Korsakoff syndrome because of his history of alcohol use and imaging findings.

Although we used a multidisciplinary team approach that included psychiatry, internal medicine, neurology, neuropsychology, and an aggressive and thorough workup, we could not establish a definitive diagnosis. Unsolved cases such as this can leave patients and clinicians frustrated and may lead to unfavorable outcomes. Additional resources such as a telephone call after the first missed appointment may have been warranted.

**Related Resources**


**Drug Brand Names**

<table>
<thead>
<tr>
<th>Acyclovir - Zovirax</th>
<th>Olanzapine - Zyprexa</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ceftriaxone - Rocephin</td>
<td>Quetiapine - Seroquel</td>
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<tr>
<td>Ciprofloxacin - Cipro</td>
<td>Thiamine - Betaxin</td>
</tr>
<tr>
<td>Haloperidol - Haldol</td>
<td>Vancomycin - Vancocin</td>
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<tr>
<td>Lorazepam - Ativan</td>
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**Disclosure**

The authors report no financial relationship with any company whose products are mentioned in this article or with manufacturers of competing products.

**Clinical Point**

Mr. E’s CT and MRI scans, history of alcohol use, and cirrhosis point to Wernicke-Korsakoff syndrome as an underlying diagnosis.

**Bottom Line**

Paranoia and altered mental status (AMS) may be multifactorial. Teasing out an exact cause can be difficult and frustrating. Closely monitor patients who present with AMS for harm to themselves or others, even if their history doesn’t suggest suicidality or homicidality.


Clinical Point
Although we used a multidisciplinary team approach, we could not establish a definitive diagnosis.