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A construction worker with recent confusion, disorientation, and somnolence

A 49-YEAR-OLD construction worker is brought to the emergency department by his girlfriend, who is concerned because he is often confused, disoriented, and sleepy.

The symptoms began roughly 4 weeks ago, shortly after a large block of wood fell on his head from several feet above. At that time he was knocked to the ground, became confused, and sustained a laceration to the left lateral scalp. He was taken to another hospital's emergency department, where his wound was closed. He says that a noncontrast computed tomographic (CT) scan of the head performed at that time was negative.

For the last 2 to 3 weeks his confusion has grown. He often has trouble finding the right words and even forgets his girlfriend's name. Sometimes he does not realize where he is. He often sleeps or is difficult to arouse 12 to 14 hours a day. His appetite is decreased significantly, and he often vomits. He also reports occasional diarrhea. These symptoms appear to wax and wane.

He says he occasionally drinks alcohol on weekends. He has abused heroin intravenously in the past, but not for at least a year. He smokes 1 pack per day. He lives with his girlfriend, has not traveled recently, and has not been in contact with anyone with a similar illness. No one in his family has ever had similar symptoms. He has not undergone surgery and does not take any medications.

Physical examination

The patient, who is sitting up in bed, appears thin, slightly pale, and alert.

Vital signs: Oral temperature 100.2°F (37.9°C), pulse 112, blood pressure 168/92 mm Hg, respiratory rate 20, oxygen saturation 95% by pulse oximetry while breathing room air.

Head: He has a scar on the left temple but no signs of acute head trauma. His pupils are midrange and reactive, there is no nystagmus and no icterus, and the fundi are normal. The extraocular muscles are normal. His mucous membranes are dry. His thyroid gland is mildly enlarged; there is no nuchal rigidity and there are no bruits.

Chest: Lungs are clear to auscultation. Heart sounds are rapid and regular with no murmur, rubs, or gallops.

Abdomen: Not distended, mild epigastric tenderness, normal bowel sounds, no organomegaly.

Extremities are unremarkable. No telangiectasias or palmar erythema.

Neurologic examination: He is anxious but not agitated, and he is oriented to person, place, time, and purpose. His speech is normal. His short-term memory is mildly impaired (he can recall only two of three objects on testing). His motor strength and senses are intact, and he is globally hyporeflexic with no focal weakness. He has bilateral dysmetria with intention tremors.

Laboratory tests

- White blood cell count $9.8 \times 10^3/\mu\text{L}$ (normal 4–11)
- Hemoglobin 14.2 g/dL (13.5–17.5)
- Platelet count $100 \times 10^3/\mu\text{L}$ (150–400)

The patient says he occasionally drinks on weekends

- Mean corpuscular volume 107 fL (80–100)
- Chemistry profile: potassium 2.7 mEq/L (3.5–5.0); the concentrations of other electrolytes, glucose, blood urea nitrogen, creatinine, and thyroid-stimulating hormone are normal.
- Toxicology screen is negative for opiates, amphetamines, benzodiazepines, barbiturates, marijuana, and cocaine
- Blood alcohol level 153 mg/dL (< 100).

■ DIFFERENTIAL DIAGNOSIS

1 What is the most likely cause of the patient's symptoms?

- ☐ Intracranial hemorrhage
- ☐ Amphetamine poisoning
- ☐ Hyperthyroidism
- ☐ Hypoglycemia
- ☐ Acute schizophrenia
- ☐ Anticholinergic poisoning
- ☐ Opiate withdrawal
- ☐ Alcohol withdrawal
- ☐ Adrenocortical dysfunction

The differential diagnosis for a change in mental status is extensive,^{1–4} and only some of the possibilities are noted above.

It is important to always evaluate altered mental status in the context of potential underlying medical problems.⁵ A careful review of the history, physical examination, and pertinent data allows us to exclude most causes, and, in the case of psychiatric patients, prevent inappropriate triage in a psychiatric facility when a medical cause is present.

Unlikely causes in this patient are:

- Hyperthyroidism—his thyroid-stimulating hormone level is within normal limits
- Hypoglycemia—his blood sugar level is normal
- Acute schizophrenia—it tends to present at an earlier age
- Adrenocortical dysfunction—he has no history of steroid use and no other historical reason to suspect adrenocortical dysfunction
- Environmental causes—he has had no contact with anyone with similar symptoms
- Cocaine or amphetamine intoxication—these substances would show up on a tox-

icology screen.

Possible causes in this patient include:

- Chronic subdural hematoma—with his history of recent trauma, a repeat CT scan of the head is indicated
- Anticholinergic poisoning, which can cause delirium, dry skin, mydriasis, elevated heart rate, and high blood pressure
- Opiate withdrawal—possible, but usually accompanied by significant pain
- Acute alcohol withdrawal, which can mimic many diseases.

The history and physical examination are the keys to the diagnosis of alcohol withdrawal syndrome. The signs and symptoms of this disorder are consistent with autonomic hyperactivity and include tachycardia, hyperthermia, hypertension, hyperventilation, agitation, confusion, and tremors. Other manifestations may include nausea, vomiting, disorientation, seizures, and hyperreflexia.

Case continued

The patient is admitted to the hospital under the care of the medical service, with a diagnosis of closed head injury and possible alcohol withdrawal syndrome. A repeat CT scan of the head shows no evidence of intracranial abnormality.

■ DETECTING ALCOHOL ABUSE

In any patient with a change in mental status, if you suspect alcohol withdrawal syndrome, you should assertively ask about the patient's alcohol habits.

Uncontrolled alcoholism may be easy to detect, but a multitude of other patients are dependent on alcohol but have not reached the point where they can no longer function in society.^{6,7} Special consideration should be given to geriatric and pediatric patients, as chronic alcohol abuse is prevalent in these populations as well.⁸

Screening tests for alcohol abuse

A variety of screening tests for alcohol abuse have been developed.

CAGE. A “yes” answer to any of the four CAGE questions suggests an alcohol problem.⁹

- C: Have you ever thought you ought to

If you suspect alcohol abuse, ask about it



cut down on your drinking?

- A: Have people *annoyed* you by criticizing your drinking?
- G: Have you ever felt bad or *guilty* about your drinking?
- E: Have you ever had a drink first thing in the morning to steady your nerves or get rid of a hangover (*eye-opener*)?

TWEAK assigns points for five questions; a total score of 3 or more indicates a drinking problem.¹⁰

- *Tolerance*: How many drinks can you hold? (score 2 points if six or more)
- *Worried*: Have close friends or relatives worried or complained about your drinking in the past year? (2 points)
- *Eye-opener*: Do you sometimes take a drink in the morning when you first get up? (1 point)
- *Amnesia*: Has a friend or family member ever told you about things you said or did while you were drinking that you could not remember? (1 point)
- *Cut down*: Do you sometimes feel the need to cut down on your drinking? (1 point)

The Alcohol Use Disorders Identification Test (AUDIT) assigns 0 to 4 points for each of 10 questions; a total score of 8 or more indicates a strong likelihood of hazardous or harmful alcohol consumption.¹¹

■ ACUTE ALCOHOL WITHDRAWAL CAN KILL

2 What causes death in acute alcohol withdrawal?

- ☐ Seizures
- ☐ Respiratory failure
- ☐ Dehydration
- ☐ Cardiac dysrhythmia

Withdrawal from many substances can be physically and psychologically difficult, but very few withdrawal syndromes are as dangerous as acute alcohol withdrawal.¹² Untreated, the mortality rate ranges from 5% to 15%,¹³ but with appropriate treatment, it is close to 1%.^{3,14}

Although heavy drinkers can have many health problems, death from alcohol withdrawal is most often caused by a cardiac dysrhythmia resulting from profound hypomag-

nesemia and hypokalemia.¹³ This is most often seen in patients with delirium tremens, who often have severe vomiting, dehydration, hyperthermia, and electrolyte imbalances. Aspiration and hypoxia are also associated with higher mortality rates.

The underlying reason alcohol withdrawal is so dangerous is the way it affects the brain. Alcohol depresses neuronal activity in the brain by acting on gamma-aminobutyric acid (GABA) and *N*-methyl D-aspartate (NMDA) receptors. Over time, the brain compensates by up-regulating the number of these receptors. When alcohol is withdrawn, the autonomic system becomes hyperactive and unstable.³

Often, acute alcohol withdrawal is not the reason a patient is admitted to the hospital. However, after admission, the abrupt cessation of alcohol intake can cause withdrawal that not only is life-threatening by itself but has many associated life-threatening complications.¹³

In addition, chronic alcoholics have significantly higher morbidity and mortality rates while in the hospital for any cause.¹³ Thiamine deficiency, poor nutrition, and electrolyte abnormalities are common in these patients and may require attention.¹⁵

■ THE PRESENTATION OF ALCOHOL WITHDRAWAL

3 Which of the following should be considered when assessing the severity of alcohol withdrawal syndrome?

- ☐ Hyperthermia
- ☐ Tachycardia
- ☐ Confusion
- ☐ Hallucinations
- ☐ Seizures

Alcohol withdrawal varies in its presentation from mild and subtle to life-threatening. All of the above should be considered.

Spectrum of alcohol withdrawal

Mild alcohol withdrawal (also called “minor”) is most common. Common signs and symptoms include tremors, nausea, vomiting, anxiety, agitation, and insomnia.^{13,16,17}

Hallucinations do not predict progression to delirium tremens

Tremors can be mild to severe and tend to occur early in the course of disease, usually beginning 6 to 8 hours after cessation of alcohol use and resolving within 36 hours.^{13,16} The time course of alcohol withdrawal is highly variable, however, and can be influenced by the quantity of alcohol intake on a daily basis, comorbid conditions, and the number of withdrawal episodes in the past.³

Moderate alcohol withdrawal symptoms are the same but more pronounced. The heart rate is likely to be fast at 100 to 120 beats per minute, and the temperature 100.0 to 101.0°F (37.0–38.3°C).¹⁷ The sensorium remains clear in moderate withdrawal; however, alcoholic hallucinosis (hallucinations without delirium or impairment of consciousness) may begin 8 to 48 hours after the last drink and is the hallmark of this stage.^{13,17}

Severe withdrawal (also known as “major” withdrawal) typically occurs more than 24 hours after the last drink and is marked by confusion and further worsening of the symptoms of autonomic hyperactivity.¹⁷ Findings in severe withdrawal include more-severe hyperthermia (temperature > 101.0°F), tachycardia (heart rate > 120), and hypertension (diastolic blood pressure > 100 mm Hg).¹⁷ The absence of significant tachycardia and hypertension does not rule out severe withdrawal.

Seizures increase risk of delirium tremens

Seizures occur in up to 10% of cases of alcohol withdrawal, be it mild, moderate, or severe.⁸ Seizures in an alcoholic patient may be due to another cause such as trauma or an electrolyte disorder, however, and these should be ruled out.¹³

Classically, alcohol withdrawal seizures are short, generalized, and often limited to a single event.^{3,13} They usually occur within the first 48 hours of alcohol withdrawal. The risk of having a seizure is increased if the patient has a history of withdrawal, ie, the “kindling” phenomenon.^{3,15}

Delirium tremens, seen in severe withdrawal, occurs in up to 5% of patients with alcohol withdrawal syndrome. If unrecognized, it can carry a 10% to 15% mortality rate.¹³ It can begin 48 hours to 14 days after the last drink, most often within 4 days.³ It is characterized by severe autonomic insta-

bility and extreme confusion and disorientation, and it requires aggressive treatment.¹³

Patients with alcoholic withdrawal seizures are at increased risk of delirium tremens, and seizures can often be a manifestation or presentation of delirium tremens itself. When seizures occur with delirium tremens, the sensorium is usually clouded, but in alcohol withdrawal seizures by themselves, the sensorium is clear.³

Hallucinations are also very common, occurring in up to 25% of patients.¹³ Most often these hallucinations are visual and can occur from 1 to 6 days after alcohol cessation. These should be distinguished from alcoholic hallucinosis, which appears to have a different underlying process, although the hallucinations themselves are not significantly different.^{3,13} Hallucinations do not necessarily predict progression to delirium tremens.³

4 At which blood alcohol level does alcohol withdrawal begin?

- ☐ 100 mg/dL
- ☐ 75 mg/dL
- ☐ 50 mg/dL
- ☐ No particular level

There is no specific blood level at which alcohol withdrawal sets in. Patients can have an elevated blood alcohol level and still be in withdrawal. The important factor is how much the alcohol level has decreased, even if the patient has only cut back but not totally stopped drinking.¹³

Case continued

After some searching, family members are found. They reveal that the patient has a long history of alcohol abuse with episodes of severe alcohol withdrawal that included seizures and hallucinosis but no delirium tremens. The patient had been trying to cut back his alcohol use to one or two drinks a day from 1 gallon of vodka per day. Although that quantity of ethanol would be lethal to a nonalcoholic person, the history of an astounding daily alcohol intake by heavy drinkers is not unheard of.

Family members say he has been trying to cut down from 1 gallon of vodka per day



■ DETECTING WORSENING ALCOHOL WITHDRAWAL

5 Which of the following indicates that a mild alcohol withdrawal syndrome will likely progress to more severe withdrawal symptoms?

- ☐ Seizures
- ☐ Tachycardia
- ☐ Hyperthermia
- ☐ Hypertension
- ☐ Confusion

Approximately 25% of mild cases progress to more severe forms.^{3,13} In monitoring the clinical course, classic teaching emphasizes the signs of autonomic insufficiency, including increased temperature, heart rate, and blood pressure; tremors; and hyperreflexia, with associated hallucinations and memory deficits.^{3,13} Perhaps the most reliable indicators are confusion and attention deficits, which are often the only signs present early in the course of the disease.¹⁵

The Revised Clinical Institute Withdrawal Assessment for Alcohol Scale^{3,18} is the most objective means to measure alcohol withdrawal. Initially used in detoxification centers, it has been modified and validated for use in medical and surgical units. The scale assigns points for 10 items (see the paper by Sullivan et al¹⁸ or the review by Chang and Steinberg³ for a description of how the points are assigned):

- Nausea and vomiting (0–7 points)
- Tremor (0–7)
- Paroxysmal sweating (0–7)
- Anxiety (0–7)
- Agitation (0–7)
- Tactile disturbances (0–7)
- Auditory disturbances (0–7)
- Visual disturbances (0–7)
- Headache, fullness in head (0–7)
- Orientation and clouding of the sensorium (0–4).

Treatment should be started or intensified if the total score is greater than 20 out of a possible 67 points.

Note that this scale does not include hypertension and tachycardia. These can be absent in mild alcohol withdrawal, are poor

predictors of worsening alcohol withdrawal, and are unreliable in guiding treatment, as patients with normal blood pressure and heart rate may develop to moderate or severe withdrawal.^{14,19}

■ HOW SHOULD ALCOHOL WITHDRAWAL BE TREATED?

6 Which drug or class of drugs should be avoided in patients with alcohol withdrawal syndrome?

- ☐ Benzodiazepines
- ☐ Beta-blockers
- ☐ Clonidine
- ☐ Haloperidol
- ☐ Phenytoin
- ☐ Propofol

Benzodiazepines, the mainstays of treatment, reduce agitation and psychotic symptoms and have some anticonvulsant activity.¹³ The dosage can be on a fixed schedule or by continuous intravenous drip and should be titrated to control symptoms.^{3,13}

Other agents often used include beta-blockers, alpha agonists, antipsychotics, ethyl alcohol, antiepileptics, and propofol, which is effective in controlling agitation refractory to other measures.^{3,13} These should always be given in conjunction with a benzodiazepine, not instead of one.

Regardless of other findings, delirious or confused patients are best managed in an intensive care unit, since they have high rates of morbidity and mortality.¹⁵ There, acute alcohol withdrawal is best managed with a combination of drugs tailored to a patient's condition.¹² For example, tachycardia and hypertension could be managed with benzodiazepines and beta-blockers. This regimen causes less sedation and less risk of respiratory depression.

Haloperidol has been shown to decrease agitation in patients with alcohol withdrawal; however, it is less effective than benzodiazepines and has the side effect of lowering the seizure threshold. Thus, it should be avoided.

Case continued

The patient is given intravenous fluids, thi-

Patients can have an elevated alcohol level and still be in withdrawal



amine, folate, and magnesium and is subsequently started on lorazepam.

The lorazepam dosage is titrated so that the patient's mental status, heart rate, and blood pressure improve. He subsequently is slowly weaned off lorazepam, and our chemical dependency unit is consulted to assist in arranging an alcohol rehabilitation program.

The patient is eventually discharged in stable condition with normal vital signs and sensorium.

REFERENCES

1. **Alshekhlee A, Kaminiski HJ, Ruff RL.** Neuromuscular manifestations of endocrine disorders. *Neurol Clin* 2002; 20:35–58.
2. **Dyer KS, Shannon M.** Index of suspicion. Case 3. Diagnosis: alcohol withdrawal syndrome. *Pediatr Rev* 1999; 20:423–426.
3. **Chang PH, Steinberg MB.** Alcohol withdrawal. *Med Clin North Am* 2001; 85(5):1191–1212.
4. **American College of Emergency Physicians.** Clinical policy for the initial approach to patients presenting with altered mental status. *Ann Emerg Med* 1999; 33:251–280.
5. **Reeves RR, Pendarvis EJ, Kimble R.** Unrecognized medical emergencies admitted to psychiatric units. *Am Emerg Med* 2000; 18:390–393.
6. **Isaacson JH, Schorling JB.** Screening for alcohol problems in primary care. *Med Clin North Am* 1999; 83(6):1547–1563.
7. **McRae AL, Brady KT, Sonne SC.** Alcohol and substance abuse. *Med Clin North Am* 2001; 85(3):779–801.
8. **Fingerhood M.** Substance abuse in older people. *J Am Geriatr Soc* 2000; 48:985–995.
9. **Ewing JA.** Detecting alcoholism. The CAGE questionnaire. *JAMA* 1984; 252:1905–1907.
10. **Russell M, Martier SS, Sokol RJ, et al.** Screening for pregnancy risk-drinking. *Alcohol Clin Exp Res* 1994; 18:1156–1161.
11. **Saunders JB, Aasland OG, Bebor TF, De La Fuente JR, Grant M.** Development of the alcohol use disorders iden-

SUSPECT ALCOHOL WITHDRAWAL IN PATIENTS WITH DELIRIUM, CONFUSION

Alcohol withdrawal syndrome is common in patients admitted to the hospital and should be suspected in any patient with confusion and delirium. It is also a serious comorbidity in patients admitted to the hospital for other reasons.

The key to diagnosis is a good history, preferably confirmed by family or friends. Early diagnosis and treatment will result in shorter hospital stays with reduction in morbidity and mortality.

tification test (AUDIT): WHO collaborative project on early detection of persons with harmful alcohol consumption II. *Addiction* 1993; 88:791–804.

12. **Spies CD, Dubisz N, Neumann T, et al.** Therapy of alcohol withdrawal syndrome in intensive care unit patients following trauma: results of a prospective, randomized trial. *Crit Care Med* 1996; 24:413–421.
13. **Jenkins DH.** Substance abuse and withdrawal in the intensive care unit. *Surg Clin North Am* 2000; 80:1033–1053.
14. **Yost DA.** Alcohol withdrawal syndrome. *Am Fam Physician* 1996; 54:657–669.
15. **Zealberg JJ, Brady KT.** Substance abuse and emergency psychiatry. *Psychiatr Clin North Am* 1999; 22:803–817.
16. **Hall W, Zador D.** The alcohol withdrawal syndrome. *Lancet* 1997; 349:1897–1900.
17. **Brewer PA, D'Onofrio G.** Alcohol withdrawal syndromes: prevention, recognition, and management. *Emerg Med Rep* 1997; 18(5):45–54.
18. **Sullivan J, Sykora K, Schneiderman J, et al.** Assessment of alcohol withdrawal: The Revised Clinical Institute Withdrawal Assessment for Alcohol scale (CIWA-Ar). *Br J Addict* 1989; 84:1353–1357.
19. **Blackwood CL.** Measurement of alcohol withdrawal. *Am Fam Physician* 2000; 62:954–957.

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