# Persistent Delirium Following Cessation of Heavy Alcohol Consumption: Diagnostic and Treatment Implications

**David Hersh, M.D., Henry R. Kranzler, M.D., and Roger E. Meyer, M.D.**

The treatment of alcoholism has undergone a series of major shifts since the modern approach emerged in the late 1940s (1, 2). During the past 50 years the decriminalization of public intoxication, a growing recognition that alcohol dependence is responsive to treatment, and the availability of health insurance coverage for alcohol rehabilitation have led to a dramatic increase in the number of programs devoted to alcoholism treatment. Although increased availability of alcoholism treatment occurred largely through an expansion of inpatient services, recent efforts to reduce the cost of alcoholism treatment have emphasized outpatient care, both for rehabilitation and detoxification. Studies comparing the relative effectiveness of inpatient and outpatient rehabilitation have generally failed to show significant differences related to the setting in which treatment is provided (3). Whereas outpatient detoxification has been shown to be safe and effective for alcohol-dependent patients who are without serious medical or psychiatric comorbidity (4), inpatient detoxification remains the treatment of choice for patients with major comorbid disorders or for those with a history of serious withdrawal-related phenomena (e.g., recurrent seizures, hallucinations, delirium tremens).

Received Oct. 25, 1996; revision received Jan. 21, 1997; accepted Jan. 27, 1997. From the Department of Psychiatry, University of Connecticut Health Center, Farmington; and the Association of Academic Health Centers, Washington, D.C. Address reprint requests to Dr. Hersh, 584 Castro St., Suite 405, San Francisco, CA 94114.

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Approximately 5% of patients hospitalized for alcohol withdrawal go on to develop delirium tremens (5, 6). DSM-IV describes delirium as a disturbance of consciousness characterized by diminished awareness of the environment, distractibility, and impaired attention and accompanied by changes in cognition such as disorientation, memory impairment, and language disturbance. Delirium develops over a period of hours to days, with signs and symptoms fluctuating over the course of the day, often including an altered sleep-wake cycle, changes in psychomotor activity, emotional lability, and perceptual disturbances. Alcohol withdrawal delirium (also called delirium tremens) is defined as a delirium accompanied by autonomic hyperactivity and tremor occurring during or shortly after alcohol withdrawal. The syndrome typically develops 2 to 4 days after the cessation of heavy alcohol intake (7, 8), although the range can be quite large.

Although delirium tremens typically remits over a period of several days (9, 10), cases persisting for weeks have been reported (11). Several decades ago, the mortality rate for patients with untreated delirium tremens was estimated to be as high as 15% (12). More recent estimates range from 2% to 5% (9, 13), the decrease presumably due to the availability of superior pharmacological and supportive measures. Advanced age and comorbid medical or surgical disorders are associated with increased risk of death (14). Feuerlein and Reiser (15) found the mortality rate to be 6% to 8.5% in patients between 20 and 54 years of age, and it climbed to 27% for individuals experiencing delirium tremens at age 55 or older. The importance of increasing age for the seriousness of alcohol withdrawal delirium is relevant to the case we describe.

The case involves an episode of protracted delirium following the cessation of alcohol use in an elderly man. It illustrates the diagnostic complexity of protracted delirium in the context of alcohol dependence. In this case, alcohol withdrawal delirium (delirium tremens) was a diagnosis of exclusion, occurring in the absence of medical or surgical illness and despite benzodiazepine treatment. In addition, the syndrome persisted well beyond the 2–5-day course typically cited in the literature. These observations raise a series of complex questions as to the pathogenesis, diagnosis, and most effective treatment of delirium tremens. They also underscore the need for careful clinical monitoring of patients undergoing medical detoxification, particularly insofar as the initial presentation of the patient described herein would likely have been viewed as appropriate for outpatient detoxification (4, 16).

## CASE PRESENTATION

### *History of Present Illness*

**The patient was a 71-year-old married man, who at the time of admission was living with his wife and maintained an insurance agency. He had been managing his own office until several months before admission when, because of his alcohol use, his family began taking on an increasing role in the business. He was admitted to an inpatient substance abuse treatment unit in a university hospital for medical detoxification from alcohol. He described himself as having been a "social drinker" who, over the preceding 2 years, had substantially increased his drinking in response to escalating job-related stress. On admission, he reported drinking between a pint and a quart of scotch daily, beginning each morning. He acknowledged having withdrawal tremor and tolerance, an inability to control his intake of alcohol, and the presence of alcohol-related interpersonal and vocational prob-**

lems. His last drink had been several hours before admission. He had previously been treated once for alcoholism. That was a failed effort at detoxification several months earlier, at which time he left treatment against medical advice on the second day. He denied a history of seizures or delirium; during the preceding year he had not gone more than a day without consuming alcohol. His wife reported that recently she had noted a global deterioration in his functioning and that he had taken several falls. He denied the use of any substances other than alcohol and nicotine, the use of any medications, and the presence of any psychiatric or medical problems.

### *Initial Assessment*

On admission, the patient was neatly dressed in a business suit. He weighed 207 pounds and stood 5 feet 10 inches tall. His complexion was ruddy, and on examination he was found to have a mild tremor of his eyelids, tongue, and extremities. Although the patient was afebrile, his pulse rate was 104 bpm, and his blood pressure was 170/100 mm Hg; breath alcohol level was 83 mg/dl. Results of the admission physical examination were otherwise unremarkable. Specifically, the patient was found to be anicteric; results of cardiac, lung, and abdominal examination were normal. Furthermore, a neurological examination revealed no focal abnormalities, nystagmus, abnormal ocular movements, gait disturbance, or peripheral neuropathy. Mental status examination revealed the patient to be alert, cooperative, and oriented in all spheres. He was euthymic, and his thinking was logical. He showed no evidence of gross cognitive deficits: short- and long-term memory were intact, as were attention, concentration, and executive functions. On the basis of his vocabulary, the patient was judged to be of above-average intelligence.

### *Hospital Course*

Considering his age, the extent of his alcohol consumption, and the degree of tolerance that he reported, the patient was considered to be at risk for a moderate-to-severe alcohol withdrawal syndrome. Consequently, treatment was initiated with 100 mg i.m. of thiamine, intramuscularly administered magnesium sulfate, oral folate, and chlordiazepoxide at a starting dose of 50 mg p.o. every 4 hours. Admission laboratory work revealed a slightly elevated mean corpuscular volume; otherwise, the CBC, electrolytes, magnesium, calcium, and liver function test results were all within normal limits.

The patient's first 3 hospital days were relatively uneventful. On the first hospital day, his pulse ranged from 100 to 110 bpm, and his diastolic blood pressure ranged from 90 to 100 mm Hg. However, both decreased to normal by the third hospital day, consistent with the usual course of uncomplicated alcohol withdrawal. Medications during this period included chlordiazepoxide, 50 mg p.o. every 4 hours on days 1 and 2, tapered to 50 mg p.o. every 6 hours on day 3. Additional doses were available as needed. The patient received a total of 350 mg of chlordiazepoxide over the first 24-hour period, 350 mg over the second day, and 250 mg over the third day. After an initial 100 mg i.m. of thiamine, he continued to receive 100 mg p.o. of thiamine daily. Although throughout this period the patient continued to have a mild tremor, he ate and slept well and was alert and oriented, with a clear sensorium and intact cognitive functioning.

On the fourth hospital day the patient's condition deteriorated. He became increasingly confused, and by evening he was agitated and disoriented to place and time. The following several days were marked by global confusion, disorientation, a reversed sleep-wake cycle, suspiciousness, and periods of agitation alternating with a decreased level of consciousness. The confusion and agitation were more pronounced in the evening and necessitated the use of restraints. Although the presentation was consistent with alcohol withdrawal delirium, a search was initiated for other medical causes of the delirium. Parenteral administration of thiamine was resumed. Results of all laboratory work, including serum electrolyte levels, magnesium, calcium, CBC, and liver function tests (transaminases, bilirubin, ammonia), were within normal limits. Results of thyroid function tests were normal, and serologic testing for syphilis was negative. Physical examination revealed no evidence of infection or trauma; and there were no neurological signs consistent with a focal central nervous system process or Wernicke's encephalopathy (evidence of which might include oculomotor abnormalities or ataxia).

The onset of delirium approximately 72 hours after cessation of alcohol consumption in an individual physically dependent on alcohol, as well as the absence of evidence for an alternative diagnosis, supported the working diagnosis of delirium tremens. Once delirium tremens has developed, appropriate management consists of 1) treatment of autonomic hyperactivity, 2) use of supportive measures such as fluid and electrolyte replacement, 3) management of behavioral dyscontrol and perceptual disturbances, and 4) an ongoing search for medical or surgical conditions that may contribute to the delirium. The longer the delirium persists, the greater the concern for the survival and well-being of the patient.

Autonomic hyperactivity was well controlled with chlordiazepoxide, and the benzodiazepine was gradually tapered over the initial 9 days of hospitalization. Intravenous hydration became necessary, since the patient's agitation limited his ability to take oral fluids or nutrition. Managing the intermittent agitation and combativeness proved to be difficult. Initially as-needed doses of chlordiazepoxide, and then lorazepam, were given, but the benzodiazepines produced either extreme sedation or a worsening of the confusional state. On the eighth hospital day (i.e., the fifth day of delirium), with the patient still receiving benzodiazepine therapy, oral haloperidol was begun. Despite the recognition that antipsychotic medications reduce seizure threshold, the decision was made to administer haloperidol because of the significant risk to the patient from episodic agitation, which responded poorly to benzodiazepine therapy. Doses of 0.5 mg to 1 mg were initially given on an as-needed basis but were then converted to a standing dose of 1.5 mg of haloperidol daily, with additional 0.5-mg doses as needed. While the haloperidol had a calming effect and appeared to diminish the patient's confusion, at times even small doses resulted in marked sedation, while at other times oral doses up to 4 mg had little effect. The patient received his final dose of a benzodiazepine on the 11th hospital day, by which time the risk of a seizure was deemed to be negligible.

On the eighth hospital day (i.e., the fifth day of delirium), results of a computed tomographic (CT) scan of the head were unremarkable; there was no evidence of the presence of a mass or fluid collection and no evidence of cerebral atrophy. A chest radiograph revealed bilateral lower-lobe infiltrates, consistent with either pneumonia or atelectasis. Although the patient was afebrile and without a cough, a course of cephalexin was initiated. Despite this treatment and a clear chest radiograph 1 week later, the delirium persisted.

By the second week of the delirium, because of a concern that the diagnosis of protracted alcohol withdrawal delirium might have been incorrect and that a potentially treatable condition might have existed, a neurological consultation was obtained. The consultant's opinion was that the patient suffered from a nonspecific encephalopathy, alcohol withdrawal delirium being most likely. No further evaluation was recommended. Although the neurological examination revealed neither ocular abnormalities nor ataxia, parenteral administration of thiamine was continued to ensure adequate levels of the vitamin, given the possibility that malabsorption of thiamine might prevent adequate treatment of Wernicke's encephalopathy. Despite consideration by the treatment team of the possible presence of dementia or an amnestic syndrome (e.g., Korsakoff's syndrome), the ongoing delirium made it impossible to assess these possibilities. The patient remained disoriented, confused, and unable to walk or feed himself.

Although during the next 2 weeks the patient's level of alertness, psychomotor activity, orientation, and understanding continued to wax and wane, there was a gradual overall improvement in these areas. On the basis of this evidence of improvement, the hospital's utilization review service (which had been monitoring the patient's progress and eligibility for continued inpatient coverage by Medicare) established that continued services could be provided in a less intensive setting. Consequently, on the 18th

**hospital day, the patient was discharged to a skilled nursing facility. He remained intermittently disoriented to time, scoring only 23 (maximal score=30) on the Mini-Mental State (17). DSM-IV axis I discharge diagnoses were as follows: alcohol dependence and alcohol withdrawal delirium (protracted) (rule out delirium not otherwise specified [i.e., Wernicke's encephalopathy], alcohol-induced persisting dementia, and alcohol-induced persisting amnestic disorder [Korsakoff's syndrome]).**

**At the time of discharge, the patient was receiving the following medications orally: haloperidol, 0.5 mg in the afternoon and 1 mg at bedtime; thiamine, 50 mg b.i.d.; and folate, 1 mg daily.**

### *Second Hospitalization*

**Five days later, the patient was brought to the emergency department by ambulance. While at the nursing facility he had refused to take any medication and became increasingly agitated, disorganized, and disorientated. He was admitted to the general psychiatric unit, and treatment with haloperidol was resumed, resulting in a substantial improvement in behavior.**

**Psychological testing was performed on the eighth day of this second hospitalization (25 days since his last alcoholic drink). At the time of testing the patient was described as fully oriented, with a normal level of psychomotor activity and a full range of affect. His concentration was erratic, and he was easily distracted and was at times circumstantial, but he was able to follow instructions when they were repeated. His frustration tolerance and insight were limited. Results of the Cognitive Status Examination (18) showed the patient to have adequate word recall and recognition and short-term spatial memory. He read well and was able to acquire new information readily. His ability to reason and his overall executive functioning were generally unimpaired. He showed some impairment of concentration and attention, expressive language, and spatial functioning and had a slight motor apraxia. His functioning was interpreted to be at the lower end of the age-appropriate range and consistent with a diagnosis of delirium. The mild impairments observed did not support a diagnosis of an underlying dementia or Korsakoff's syndrome.**

**During the next 2 weeks the patient's mental status and level of functioning continued to improve, and after 17 days of inpatient psychiatric care he was discharged to return home. Discharge medications included haloperidol, 1.5 mg in the morning and 2 mg at bedtime. At the time of discharge he was fully oriented, calm, and cooperative. Although he scored 26 of 30 on the Mini-Mental State, he continued to show impaired judgment, insight, and ability to abstract. He did not return for scheduled follow-up visits. However, 3 months later he appeared at the emergency department intoxicated, confused, and exhibiting left-sided weakness. A CT scan of the head revealed a subdural hematoma, which had not been present during his previous hospitalization. He was transferred to another hospital for neurosurgery and was lost to our follow-up.**

## DISCUSSION

Although delirium tremens was first described in the late 1700s, it was not until 1953 that alcohol withdrawal was identified as the cause of the disorder (12). Shortly thereafter, Isbell et al. (19) described the effects of the abrupt cessation of drinking in 10 healthy volunteers who consumed approximately 15 to 30 standard drinks daily for periods of 7 to 87 days. These investigators found that four subjects who drank at the lower end of the quantity-duration spectrum experienced tremulousness, nausea, diaphoresis, and insomnia during abstinence from alcohol. The six subjects who consumed more than 20 drinks per day for 48 or more consecutive days experienced more numerous and more severe withdrawal signs and symptoms, including tremor, marked weakness, vomiting, fever, and hypertension. Four of these subjects also experienced hallucinations, two had seizures, and three developed frank delirium. These results provided evidence for a correlation between the quantity and duration of alcohol consumption and the severity of withdrawal phenomena.

Although the timing and quality of the confusional state described herein were consistent with alcohol withdrawal delirium (delirium tremens), it was clinically necessary to consider medical and surgical problems that might have caused or worsened the patient's altered mental status. Metabolic abnormalities, hepatic encephalopathy, infection, and an intracranial process such as a subdural hematoma deserved special consideration. Physical examination, blood work, and a normal CT of the head essentially excluded these conditions as being of etiological significance. Given concern that benzodiazepine treatment might have contributed to the patient's confusional state, once his vital signs were stable, the medication was tapered and discontinued.

Wernicke's encephalopathy, which in its classic form consists of the triad of oculomotor abnormalities (e.g., rectus paralysis, nystagmus, conjugate palsies), ataxia, and a confusional state, must also be considered in an alcoholic with altered mental status. The confusional state is typically described as apathetic and is characterized by inattention, disorientation, and sleepiness. Although the presence of ocular signs was once considered pathognomonic, it is now recognized that the syndrome may present with encephalopathy alone (20). Associated features include hypotension, hypothermia, and polyneuropathy. Wernicke's encephalopathy has been shown to result from thiamine deficiency (20). Rapid improvement in the ocular abnormalities and some aspects of the confusional state following treatment with thiamine supports the vitamin's role in the etiology of the disorder (21). However, the ataxia and delirium may respond more gradually to thiamine treatment or, in some instances, not at all. Although thiamine deficiency occurs commonly in alcoholic patients (9), Wernicke-Korsakoff's syndrome is diagnosed in only 3% to 10% of cases (22). Since malabsorption is thought to play a key role when thiamine deficiency is seen in alcoholic patients, it is recommended that the medication be given parenterally for several days before oral therapy is initiated (23). If Wernike's encephalopathy is untreated, the mortality rate is 10%–20% (23).

Many patients with Wernicke's encephalopathy (as many as 80%) will develop Korsakoff's syndrome (24). The syndrome is characterized primarily by anterograde amnesia (with a consequent inability to assimilate new information), confabulation, and decreased spontaneity and initiative (20, 24). The point at which Wernicke's encephalopathy ends and Korsakoff's syndrome begins is difficult to ascertain; a sizable proportion of patients develop Korsakoff's syndrome insidiously, without clear-cut episodes of Wernicke's encephalopathy (7).

Differentiating between Wernicke's encephalopathy and other causes of delirium, including alcohol withdrawal delirium, can be difficult. Although the time course and associated features are helpful in the differential diagnosis, the syndromes share many features. In addition, they can occur simultaneously in the same individual. In the present case, the onset of the delirium approximately 72 hours after the last alcoholic drink, the high degree of agitation, and the lack of associated neurological findings argued in favor of withdrawal delirium and against Wernicke's encephalopathy. The fact that the patient received parenteral thiamine before the development of delirium and that parenteral thiamine did not improve his mental status also argues against a di-

agnosis of Wernicke's encephalopathy. Nonetheless, given the variable expressions of Wernicke's encephalopathy, the possibility of an atypical presentation of that disorder could not be excluded. Although Korsakoff's syndrome would not explain the patient's agitated delirium, it could have played a role later in the patient's course.

In the United States, benzodiazepines are the treatment of choice for the prevention and treatment of alcohol withdrawal phenomena, including delirium tremens (9, 25, 26). They are efficacious in reducing anxiety, restlessness, and tremor, as well as the risk of seizures associated with alcohol withdrawal (27). Other agents that have been widely used to treat alcohol withdrawal include alcohol, paraldehyde, and the barbiturates. However, the dosage of alcohol and paraldehyde is very difficult to titrate, while barbiturates have a significant potential for abuse and are lethal in overdose. In addition, paraldehyde has an offensive odor and a potential for hepatotoxicity and is a mucosal irritant with a limited shelf life (13). In a controlled study of the treatment of delirium tremens, paraldehyde appeared to be more toxic, but no more effective, than diazepam (28).

There is no evidence favoring any specific benzodiazepine for the treatment of alcohol withdrawal (26). The ideal benzodiazepine is rapidly and completely absorbed after either oral or intramuscular administration, has an intermediate half-life, and is eliminated in a manner that is unaffected by liver or renal disease. Although chlordiazepoxide and diazepam have been the most widely used agents for the treatment of alcohol withdrawal, lorazepam may be preferable to these medications, since it is the only benzodiazepine that is reliably absorbed intramuscularly and is without active metabolites than can accumulate over time. Nonetheless, the longer-acting benzodiazepines are often used, typically with good results.

The degree to which benzodiazepines actually prevent or treat delirium tremens, beyond providing sedation and thus reducing cardiopulmonary stress and allowing for other supportive measures, has been an area of some debate (7). The development and persistence of delirium tremens despite high-dose benzodiazepine therapy are not uncommon (8). Hemmingsen and Kramp (29) hypothesized that the efficacy of benzodiazepines may be limited by saturation kinetics, such that a ceiling is reached above which additional doses of benzodiazepines provide no additional pharmacological benefits. These investigators found a trend for barbital to show superior efficacy to diazepam and suggested that barbiturates may be less limited by saturation kinetics than the benzodiazepines. There is also evidence that chronic heavy drinkers may have alterations in their γ-aminobutyric acid benzodiazepine system, rendering them less responsive to benzodiazepines (30, 31). Although this may mean that barbiturates have greater therapeutic potential in delirium tremens, they also present a greater risk for respiratory depression and coma.

The development of delirium tremens despite adequate control of the minor symptoms of alcohol withdrawal with benzodiazepine treatment raises a question of the relationship between minor withdrawal symptoms and alcohol withdrawal delirium. If delirium represents the final stage of a withdrawal cascade in which minor symptoms such as autonomic hyperactivity trigger the development of more severe phenomena, prevention or control of the early, minor symptoms would theoretically prevent development of the major symptoms. Although the cessation of alcohol consumption is a necessary antecedent to the development of delirium tremens, it appears that the syndrome runs a course separate from that of minor withdrawal phenomena (14, 29, 32). It has been hypothesized that whereas withdrawal symptoms such as autonomic hyperactivity are the result of recent physical dependence on alcohol, delirium tremens results from irreversible, cumulative changes in the central nervous system caused by years of heavy alcohol consumption. Therefore, a preset "point of no return" determined by the patient's drinking and withdrawal history may exist and for some individuals may make delirium an inevitable result of the abrupt cessation of alcohol intake (32, 33).

Since medical illness appears to increase both the likelihood that delirium tremens will develop and its severity and duration, rapid identification and treatment of infections, hepatic insufficiency, and traumatic injuries are crucial. Although cerebrospinal fluid examination has been advocated as part of the workup of the patient with suspected delirium tremens, even in the absence of physical signs of meningeal irritation, a lumbar puncture rarely yields positive findings (14). The detection and correction of metabolic abnormalities such as hyponatremia or hypernatremia, hypokalemia, hypomagnesemia, and hypocalcemia (which is often secondary to hypomagnesemia) are also important, since these conditions may contribute to mental status changes that may predispose the individual to delirium tremens (34).

Hypomagnesemia results from several mechanisms, including decreased intake, intestinal malabsorption, and reduced tubular reabsorption (resulting in increased urinary excretion) of magnesium. Observations in the 1950s that magnesium deficiency in animals resulted in a syndrome resembling delirium tremens led Sullivan et al. (35) to hypothesize a relationship between hypomagnesemia and alcohol withdrawal delirium. Stendig-Lindberg and Rudy (10) found an association between hypomagnesemia and the severity of delirium tremens. Whereas some investigators have found that magnesium replacement attenuates minor withdrawal symptoms and reduces the risk of withdrawal seizures and delirium (34, 36), others have found it to be of no benefit (37–39). Despite conflicting data, the relative safety of magnesium replacement argues for correction of hypomagnesemia as one element in the treatment of alcohol withdrawal.

In addition to advanced age and comorbid medical or surgical illness, a history of alcohol withdrawal seizures or delirium is also a risk factor for the development of delirium tremens (13, 15, 40). This suggests that kindling may play a role in alcohol withdrawal delirium; that is, past episodes of delirium may lower the threshold for future episodes by sensitizing the neural structures that underlie the syndrome (41). Therefore, medication that suppresses kindling, such as carbamazepine, may have particular efficacy in the prevention of delirium tremens. Several investigators (42, 43) have found carbamazepine to be of comparable efficacy to oxazepam in the treatment of minor withdrawal symptoms and in the prevention of seizures. Although in the study by Stuppaeck et al. (43), two patients in the oxazepam group developed withdrawal delirium, the syndrome was too uncommon to provide convincing evidence that carbamazepine serves to prevent or treat delirium tremens.

As demonstrated by the case presented herein, agitation, combativeness, and psychotic features are often part of alcohol withdrawal delirium. Control of these symptoms is necessary to ensure the safety of both the patient and the treatment staff, to minimize cardiopulmonary stress and fluid loss,

and to allow for the administration of fluids, electrolytes, and medications. Ordinarily, the treatment of delirium rests on the identification and correction of causative factors such as intracranial disease, metabolic abnormalities, systemic disease, or toxic effects of medications or other exogenous agents. In the case of alcohol withdrawal delirium, there is no clear abnormality to correct. Although benzodiazepines are effective in reducing autonomic hyperactivity and seizure risk, as mentioned, they have limited efficacy in the treatment of alcohol withdrawal delirium. Despite their beneficial effects (e.g., sedation), benzodiazepines may contribute to the confusion and behavioral dyscontrol that are central elements of withdrawal delirium. In the case of a delirium of unknown etiology, low-dose treatment with a high-potency antipsychotic, such as haloperidol, is warranted, even in the absence of frank psychotic symptoms (44–47). The use of high-potency antipsychotics in this context is, however, not without risk, in that they can exacerbate the confusional state through anticholinergic effects, increase agitation as a result of akathisia, produce dystonic reactions, and lower the patient's seizure threshold. In the case reported herein, the deterioration following cessation of haloperidol, followed by a fairly rapid response to resumption of treatment with the antipsychotic, suggests that haloperidol provided both behavioral control and improved cognitive functioning. Pretreatment with a benzodiazepine may have helped to prevent the development of seizures or akathisia.

Although the case described herein appears to involve a protracted alcohol withdrawal delirium, the validity of that diagnosis may be questioned. That is, can a delirium that persists beyond 10 days following the cessation of heavy drinking still be considered an alcohol withdrawal delirium? Consistent with the literature, DSM-IV allows that withdrawal delirium can persist for up to 4 weeks (7, 8, 10, 11). Feuerlein and Reiser (15) found that among almost 800 cases of delirium tremens, 62% resolved in 5 days or less, and 6% of the cases persisted for 10 days or more. Although in that series, patients experiencing protracted withdrawal delirium often had comorbid medical or surgical illness, that was not always the case. Miller (11) described a case of an individual who experienced two episodes of protracted alcohol withdrawal delirium. The first episode lasted approximately 6 weeks and was complicated by neurosurgical problems. The second episode, occurring almost a year later, persisted for nearly 3 weeks in the absence of comorbid medical or surgical illness.

The possibility that the persistent mental status changes seen in the case presented here could be explained, even in part, by a protracted Wernicke's encephalopathy or the development of Korsakoff's syndrome or both deserves consideration. In their evaluation of 32 cases of Wernicke's encephalopathy, Wood and Currie (21) found that despite parenteral thiamine therapy, 16% of patients continued to evidence globally clouded thinking, and 56% remained disoriented to time and place. It is unclear whether these persistent impairments represented ongoing low-grade Wernicke's encephalopathy, atypical Korsakoff's syndrome, another process (e.g., dementia), or a combination of these conditions.

Some authors contend that a delirium persisting beyond several weeks should be considered dementia (47). Dementia and delirium often occur concomitantly and can be difficult to differentiate. Unlike dementia, however, delirium usually has an acute onset with marked fluctuations in mental status over the course of the day. The presentation of the patient whose case is described herein was consistent with delirium. An important finding is that cognitive testing failed to reveal an underlying dementia (alcohol-related or otherwise) or Korsakoff's syndrome. Although alcoholics often show significant short-term and long-term memory impairments (48), these deficits do not explain a persistent delirium.

In addition to its value in the identification of an intracranial process such as a subdural hematoma, neuroimaging may be useful for the evaluation of delirium. Some investigators have found cerebral atrophy to be associated with the development and severity of delirium tremens (49). While others failed to find such an association, the degree of cerebral atrophy was found to be directly related to a history of prior episodes of alcohol withdrawal, leading to the hypothesis that repeated episodes of withdrawal may produce cumulative cerebral damage (40). Therefore, the absence of cortical atrophy in the present case is consistent with the patient's relatively short history of heavy drinking and the fact that he had experienced no previous episodes of alcohol withdrawal. Studies have also shown a strong association between Wernicke's encephalopathy and cerebral atrophy (20, 21), providing further evidence against a diagnosis of Wernicke-Korsakoff's syndrome in the case presented here. Finally, several investigators have found mamillary body volume to be smaller in patients with Wernicke-Korsakoff's syndrome than in both patients with Alzheimer's disease and normal comparison subjects; this finding suggests that magnetic resonance imaging may be useful in differentiating the two syndromes (50, 51).

In addition to neuroimaging, an EEG might have proved useful in the clarification of the diagnostic picture. While the EEG in the delirious patient usually shows diffuse slowing of background activity, in the case of alcohol withdrawal delirium, the EEG often shows excessive low-amplitude fast activity (52, 53).

The case described herein reflects the difficulty of deriving a conclusive clinical diagnosis for protracted delirium in an alcohol-dependent patient. Although the available evidence points to a protracted alcohol withdrawal delirium, the absence of a pathologic diagnosis prevents us from drawing a definitive conclusion as to the etiology of the delirium. It underscores the potential for a case of routine treatment of alcohol withdrawal, which is increasingly being conducted on an outpatient basis, to develop into a complex diagnostic problem that strains the clinical decision-making process and requires intensive inpatient management.

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