The psychotic pot smoker

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How would you handle this case?

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When police bring Mr. C to the emergency department, he's agitated, confused, and hallucinating. He claims someone tampered with his marijuana. What's causing his psychosis?

CASE Scared and confused

Mr. C, age 28, presents to the emergency department (ED) in police custody with agitation and altered mental status. Earlier that evening, Mr. C's girlfriend noticed he was talking to himself while watching television. A few hours later, Mr. C thought someone was breaking into his house. Mr. C ran out of the house screaming for help, broke his neighbor's window, and eventually called the police. When the police arrived Mr. C was wearing only his underwear, shaking, and bleeding from his hands. He said he was afraid and refused to respond to police instructions. Police officers used an electronic stun gun to facilitate transport to the hospital.

Mr. C admits to smoking 3 to 4 marijuana joints daily for the past 16 years. His last drug use was 2 hours before his symptoms began. Mr. C suggests that someone may have adulterated his marijuana joint but he has no factual basis for this accusation. He denies using alcohol and other illicit drugs and has no personal or family psychiatric history. He denies recent fever, loss of consciousness, chest pain, weakness, myalgia, or headache. Medically stable, his only complaint is mild hand pain.

Mr. C is alert, awake, and oriented to his name, and he responds properly to questions. He is tachycardic (101 bpm), his blood pressure is 149/57 mm Hg with normal S1 and S2 sounds, and he has no meningismus or nystagmus. Glasgow Coma Scale score is 15. He has increased deep tendon reflexes on the right upper and lower limb with good handgrip and multiple abrasions and lacerations on his hands.

Which condition would you consider as part of the differential diagnosis?

a) cannabis-induced psychosis
b) phencyclidine (PCP) intoxication
c) acute psychosis not otherwise specified (NOS)
d) embalming fluid intoxication
e) complex partial seizure

The authors' observations

New-onset psychosis can have a wide differential diagnosis, particularly when reliable history is not available. Mr. C's allegation that someone tampered with his marijuana raises 2 possibilities: embalming fluid (formaldehyde) toxicity or PCP intoxication.

Embalming fluid toxicity can cause:

- agitation and sudden unpredictable behavior
- confusion or toxic delirium
- coma or seizure
- cerebral and pulmonary edema or death in severe cases.

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The terms "wet," "sherm," "fly," "amp," or "illy" are used to describe a marijuana cigarette that has been dipped into embalming fluid, dried, and then smoked.[1] The effect is similar to that of PCP and causes extreme hallucinations. Reported highs last 30 minutes to 1 hour.[2]

Symptomatology of PCP intoxication may be indistinguishable from functional psychosis ***(Table 1)***.[3] Visual, auditory, and tactile misperceptions are common and highly changeable disorientation often is accompanied by alternating periods of lethargy and fearful agitation. These patients typically show catatonic posturing and/or stereotyped movement. Somatic sensations appear to be disassociated; patients may misperceive pain, distance, and time. Patients taking PCP rarely admit to true hallucinations; however their thinking usually is grossly disoriented.[4] Symptoms of delirium may last from 30 minutes to 6 hours in 80% of cases; 12% of patients may remain symptomatic for 12 hours. Violent behavior and agitation usually lasts only a few hours.[5]

Long-term marijuana abuse can lead to psychosis[6] but acute onset is not typical, and recent prospective trials raised doubts that cannabis would be a sole factor.[7] Instead, cannabis may be 1 of several factors that contribute to psychosis, particularly in patients who are predisposed.

Possible neurologic causes

Complex partial seizures—also known as psychomotor epilepsy—are caused by a surge of electrical activity in the brain. Seizures often involve 1 of the brain's temporal lobes but can affect any brain region. Symptoms include:

- impaired social interaction
- inability to control one's movements
- alogia
- amnesia.

Episodes typically start with a blank stare followed by automatisms. The actions and movements often are unorganized or confused. Motor symptoms typically last for 1 to 2 minutes and confusion persists for another 1 to 2 minutes.[8] In rare cases, a patient may become agitated or engage in behaviors such as undressing. Complex partial seizures may cause a person to run in apparent fear, cry out, or repeat a phrase.[9] Electroencephalogram, CT, MRI, or positron-emission tomography scan could reveal any intracranial focus of complex partial seizures.

We suspect PCP or embalming fluid intoxication and initiate supportive therapy.

Table 1

Phencyclidine (PCP) intoxication: What to look for

Findings	Percentage of cases
Nystagmus	57.4%
Hypertension	57.0%
Delirium	36.9%
Violent behavior	35.4%
Agitation	34.0%
Tachycardia	30.0%
Bizarre behavior	28.5%
Hallucinations/delusions	18.5%
Unconsciousness	10.6%
Lethargy/stupor	6.6%
Hypothermia	6.4%
Generalized rigidity	5.2%
Profuse sweating	3.9%
No behavior effect	3.5%
Grand mal seizure	3.1%

Source: Reference 3

EVALUATION Still confused

Initial baseline labs include a urine drug screen (UDS), chest radiography, ECG, and head CT. Mr. C's UDS is positive for cannabis. A specific PCP assay is negative. White blood cell count (WBC) is 22,000/µL with high neutrophil count (88%), creatine kinase (CK) is 458 U/L, and urinalysis reveals protein 75 mg/dL and ketone

Clinical Point

PCP intoxication may be indistinguishable from functional psychosis; visual, auditory, and tactile misperceptions are common

Table 2

DSM-IV-TR criteria for psychotic disorder, not otherwise specified

This category includes psychotic symptomatology (ie, delusions, hallucinations, disorganized speech, grossly disorganized or catatonic behavior) about which there is inadequate information to make a specific diagnosis or about which there is contradictory information, or disorders with psychotic symptoms that do not meet the criteria for any specific psychotic disorder. Examples include:
1. Postpartum psychosis that does not meet criteria for mood disorder with psychotic features, brief psychotic disorder, psychotic disorder due to a general medical condition, or substance-induced psychotic disorder
2. Psychotic symptoms that have lasted for less than 1 month but that have not yet remitted, so that the criteria for brief psychotic disorder are not met
3. Persistent auditory hallucinations in the absence of any other features
4. Persistent nonbizarre delusions with periods of overlapping mood episodes that have been present for a substantial portion of the delusional disturbance
5. Situations in which the clinician has concluded that a psychotic disorder is present, but is unable to determine whether it is primary, due to a general medical condition, or substance induced

Source: Reference 10

Clinical Point

Long-term marijuana use can lead to psychosis but acute onset is not typical

50 mg/dL. Head CT is negative for any acute process (visit this article at CurrentPsychiatry.com for detailed description of Mr. C's hospital course while in the ED).

During psychiatric evaluation 7 hours after presentation, Mr. C's speech is loose and somewhat pressured, but intelligible. He cannot follow commands. Mr. C is delusional and appears to be hallucinating. He can repeat 3 words immediately but not after 3 minutes. We start Mr. C on divalproex, 1,500 mg/d, haloperidol, 6 mg/d, and IV lorazepam, 2 mg as needed for agitation. Although mildly disoriented, he gradually becomes less agitated.

What tool would you use next to help you make a diagnosis?

a) MRI of the brain
b) take a more detailed history
c) lumbar puncture (LP)
d) repeat UDS or serum PCP detection
e) EEG

The authors' observations

At this point further evaluation is needed. Mr. C's elevated WBC count could explain his fluctuating symptoms. He cannot provide further history and his family denies any past psychiatric episodes. Thyroid-stimulating hormone, B12, and folate levels are within normal limits. A negative LP rules out meningitic infection. We give Mr. C a diagnosis of psychosis NOS ***(Table 2)***.[10]

TREATMENT Medication choices

After 8 hours in the ED, Mr. C is transferred to the medical unit, where he becomes agitated and complains of auditory and visual hallucinations. He receives divalproex, 750 mg, haloperidol, 3 mg, and IM diphenhydramine, 50 mg, to calm him. He remains agitated but not violent until bedtime. At midnight he is agitated and violent and receives another dose of haloperidol and IM diphenhydramine with IV lorazepam, 2 mg. These medications calm him and he is able to sleep until morning.

Morning labs reveal CK is 674 U/L and WBC decreased to 13,200/µL. Mr. C denies any distress but after the fourth dose of haloperidol, he develops dystonia of his arms so we discontinue this medication. We start aripiprazole, 10 mg/d gradually increased to 30 mg/d, and Mr. C receives 1 injection of diphenhydramine. He responds well to the treatment.

The next few hours are uneventful but then Mr. C becomes verbally abusive to his relatives and sitter; physical restraints are ordered and he receives IM ziprasidone, 20 mg, and IV lo-

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ONLINE ONLY

Visit this article at CurrentPsychiatry.com for a detailed description of Mr. C's hospital course

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Table 3

Criteria for sedative, hypnotic, or anxiolytic withdrawal

A. Cessation of (or reduction in) sedative, hypnotic, or anxiolytic use that has been heavy and prolonged
B. Two (or more) of the following, developing within several hours to a few days after Criterion A: 1. autonomic hyperactivity (eg, sweating or pulse rate greater than 100) 2. increased hand tremor 3. insomnia 4. nausea or vomiting 5. transient visual, tactile, or auditory hallucinations or illusions 6. psychomotor agitation 7. anxiety 8. grand mal seizures
C. The symptoms in Criterion B cause clinically significant distress or impairment in social, occupational, or other important areas of functioning
D. The symptoms are not due to a general medical condition and are not better accounted for by another mental disorder

Source: Reference 10

Clinical Point

Mr. C admits to using illegally obtained alprazolam for sleep for months, but stopped when he could no longer afford the drug

razepam, 2 mg. He remains awake and babbling. His perception continues to wax and wane and his words are jumbled. He remains calm until the next morning (visit this article at CurrentPsychiatry.com for detailed description of Mr. C's hospital course while on the medical unit).

After 4 days on the medical unit Mr. C is transferred to the psychiatry unit, where he is angry, belligerent, and hostile, but not placed in restraints. His symptoms resolve in 2 days without any further episodes of violent behavior.

OUTCOME Solving the puzzle

When Mr. C becomes cooperative, he gives a detailed history. He repeats his suspicion of smoking adulterated marijuana, but during detailed questioning, he admits to using alprazolam, which he purchased illegally, to sleep for the past 6 to 7 months. He started with 1 or 2 "footballs" (1 to 2 mg) and gradually increased to 3 or 4 "bars" (6 to 8 mg) each day. Mr. C could no longer afford the drug and last took alprazolam 6 days before his symptoms began. He says that after stopping alprazolam he felt anxious and could not sleep. His girlfriend adds that he was irritable and "he had not been acting himself" several days before admission. She says he complained of hearing the voice of God, particularly when he was not taking alprazolam.

Mr. C's hand wounds heal and his vitals are normal during his 1-week stay on the psychiatric unit. His interactions with staff and peers improve. Aripiprazole is tapered and discontinued; divalproex is reduced to 1,000 mg/d. Mr. C is discharged 11 days after presentation and prescribed divalproex, 1,000 mg/d, with instructions to taper the drug over several days to prevent withdrawal seizures before stopping it in 1 week.

Mr. C does not return for his follow-up appointment; however, in a telephone follow-up 6 months later, he denies experiencing withdrawal symptoms after discharge. Mr. C is now undergoing drug rehabilitation.

The authors' observations

Benzodiazepine withdrawal symptoms occur 7 to 10 days after abrupt cessation ***(Table 3)***.[10] Symptoms are similar to those of alcohol withdrawal and include tachycardia, hypertension, clouding of consciousness, and auditory and visual hallucinations.[11] Serious reactions to ben-

Related Resource

- Vikander B, Koechling UM, Borg S, et al. Benzodiazepine tapering: a prospective study. Nord J Psychiatry. 2010; 64(4):273-282.

Drug Brand Names

Alprazolam • Xanax
Aripiprazole • Abilify
Chlordiazepoxide • Librium
Diazepam • Valium
Diphenhydramine • Diphenhydramine injection
Divalproex • Depakote
Haloperidol • Haldol
Lorazepam • Ativan
Ziprasidone • Geodon

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zodiazepine withdrawal include seizures and death.[12]

Because of the high prevalence of polysubstance misuse, obtain a detailed substance use history in patients undergoing benzodiazepine withdrawal to determine the likelihood of polysubstance withdrawal.[13] A cross-tolerant sedative such as clonazepam could prevent withdrawal symptoms as the dose is gradually decreased. Long-acting benzodiazepines such as clonazepam or diazepam are recommended.[14]

In Mr. C's case, minor withdrawal symptoms, such as disturbed sleep and irritability, began 3 to 4 days after discontinuing benzodiazepines[15] and preceded development of psychosis. Withdrawal symptoms usually resolve after 2 weeks.[16] Mr. C responded only partially to IV lorazepam because he did not receive the total replacement dose. Had we known he was experiencing benzodiazepine withdrawal, Mr. C could have been managed with detoxification of the primary drug, alprazolam, with diazepam substitution and tapering over 3 weeks.[17]

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Clinical Point

A cross-tolerant sedative could prevent benzodiazepine withdrawal as the dose is gradually decreased

Bottom Line

Benzodiazepine withdrawal could lead to dramatic symptomatology that can mimic psychosis, with agitation, hallucinations, and confusion. Symptoms typically resolve within 2 weeks. Ease withdrawal symptoms with a short-acting benzodiazepine followed by a long-acting benzodiazepine.

Table 1

Mr. C's hospital course in the emergency department

Time after presentation	Description
2 hours	Mr. C is alert and oriented to his name and place. He rests comfortably but asks questions about his girlfriend and uncle, falsely believing they are in the emergency department
4 hours	Hand lacerations are repaired, but Mr. C continues to dig in his wounds with the opposite hand and place it over his mouth despite constant redirection. He reports hearing his uncle's voice behind the curtain. He then uses the pulse oximeter as a telephone and holds a conversation with his uncle on the other side of the curtain. On redirection, Mr. C replies that the pulse oximeter looks like a telephone and begins mumbling to himself
5 hours	Mr. C continues to mumble but responds when directly questioned. He keeps insisting that the pulse oximeter is a telephone and that he can tell his uncle to come over from the other side of the curtain. He continues to act inappropriately despite the presence of family members but he is aware of their identities
6 hours	Mr. C becomes disoriented and agitated and pulls out his IV line. Because of the high WBC count, we order blood cultures and a urine culture and give him IV antibiotics

WBC: white blood cell count

Table 2

Mr. C's hospital course on the medical unit

Time after presentation	Description
54 hours	He is oriented to person and place. Staff notices he is talking to someone in the room but no one is present. Mr. C appears to be responding to visual hallucinations, but upon questioning he denies any symptoms. Restraints are discontinued. Divalproex is increased to 2,000 mg/d
62 hours	Mr. C remains calm for several hours but later begins hallucinating and calls to his mother and others when no one is in the room. He receives IV lorazepam, 2 mg, without much response. Again he is placed in restraints and receives another dose of IV lorazepam, 3 mg, and IM ziprasidone, 20 mg. He becomes calmer. Restraints are continued as a precautionary measure. Mr. C calms down after several hours but cannot sleep
78 hours	The next morning, Mr. C remains agitated and aggressive with loud speech. He denies any further hallucinations but talks to an invisible person. He remains in restraints and receives his routine medications. His blood pressure is 141/99 mm Hg and pulse is 110. Pulse rate normalizes during the day and he becomes calmer but seclusive