Current PSYCHIATRY

CASES THAT TEST YOUR SKILLS

Mr. J is disoriented and seeing 'visions.' His psychiatric history suggests a substance use disorder, but a drug screen is negative. How would you diagnose him?

The consequences of sipping 'tea'

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HISTORY: A 'NEGATIVE' VIEW

Mr. J, a 50-year-old native of Fiji, has had depression and substance abuse disorder for more than 10 years, marked by irritability, poor sleep, hopelessness, and suicidality. He also suffered a traumatic brain injury in the military 25 years ago.

Police bring Mr. J to the ER after they find him wandering near traffic and speaking incoherently. His feet and hands jerk on the way to the hospital, leading police to suspect that Mr. J has suffered a grand mal seizure.

In the ER, Mr. J appears confused, has visual hallucinations, and moves his hands and feet involuntarily. His head and arms move erratically during the ER psychiatrist's interview, and he says that his pelvis is arching forward and preventing him from walking steadily. The day before, he says, he saw frightening "visions" of a being who looked "like a photo negative."

Mr. J has been seeing an outpatient psychiatrist, who has prescribed citalopram, 40 mg/d, for depression and clonazepam, 1 mg three times daily, for related anxiety symptoms.

The patient is disoriented and inattentive during the mental status examination. His cognitive deficits fluctuate in severity; at times he is aware of his surroundings, then suddenly loses this awareness.

Vital signs are stable. Physical exam shows Mr. J is approximately 30 lb underweight (97 lb) with a body mass index of 16.9 kg/m^2—nearly 2 kg/m^2 below normal. He says he has been skipping meals because of poor appetite. He also has strikingly lizard-like, scaly skin.

Urine drug screen shows no signs of recent alcohol or substance abuse. Complete metabolic profile shows elevated liver enzymes, suggesting alcohol or illicit substance toxicity, medication toxicity, hepatitis, thyroid disorder, muscle disease, or a rare liver condition. EEG shows mild encephalopathy but no ictal activity.

Mr. J suffers from:
a) substance intoxication/withdrawal
b) seizure disorder
c) depression with psychotic features
d) substance-induced delirium
e) substance-induced psychotic disorder

The authors' observations

Our psychiatric differential diagnosis is broad:

- visual and auditory hallucinations are concurrent in numerous disorders, including schizophrenia and depression
- visual hallucinations alone suggest dementia, delirium, or psychosis resulting from a medical condition, medication, or substance(s) of abuse[1]
- Mr. J's past head injury increases his risk of dementia and delirium
- his abrupt symptom onset and inattention suggest delirium.

Police feared that Mr. J suffered a seizure during transport to the ER, but EEG shows no ictal activity. Also, his abnormal motor movements appear choreoathetoid, alternating between brief, rapid, involuntary movements (chorea) and slow, continuous, writhing movements (athetosis). Choreoathetosis can result from:

- medications such as stimulants and levodopa
- toxins
- systemic diseases such as systemic lupus erythematosus, thyrotoxicosis, or stroke
- degenerative brain diseases such as Huntington's disease
- or focal brain diseases such as tumors.[2]

Given Mr. J's substance abuse history, we strongly suspect a substance-related disorder despite the negative urine drug screen. Alcohol withdrawal is unlikely because his vital signs are stable, and the negative drug screen rules out benzodiazepine withdrawal.

How would you handle this case?

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Although the test results narrow the differential diagnosis, we still have to consider numerous medical conditions that can cause delirium, such as trauma, cerebral vascular accident, intracerebral masses, CNS infection, and inflammatory disease.

Which tools could help clarify Mr. J's diagnosis?
a) additional laboratory testing
b) imaging
c) collateral information

HISTORY: COLLATERAL CONTRIBUTIONS

We refer Mr. J for lumbar puncture to rule out CNS infection and MRI to rule out tumor, abscess, or other structural brain abnormalities that could cause seizure. Results are unremarkable.

We then speak with Mr. J's outpatient psychiatrist, who reports that Mr. J has had no residual cognitive impairment from his head injury. She adds, though, that he often develops cognitive problems after consuming large amounts of a traditional South Pacific beverage containing kava (*Piper methysticum*). She explains that Mr. J socializes with fellow Fijians who drink kava at gatherings, and that he often drinks kava to excess. She attributes his dry, scaly skin to excessive kava use.

Upon questioning, Mr. J says he consumes about a half-pound of kava root per day. He says he uses the root to make a tea-like beverage that, like alcohol, induces euphoria and relaxation. He says

Box

Kava: A popular alternative to prescription anxiolytics

Kava, extracted from the roots of *Piper methysticum*, acts as a muscle relaxant, anesthetic, and anxiolytic.[5] It is among the most commonly used alternative treatments for psychiatric symptoms, with sales estimated at $17 million in the United States in 2004.[6]

Kava lactones, the pharmacologically active components of kava, might act via several pathways, including GABA-A receptor binding and dopaminergic antagonism.[7] This GABAergic CNS activity affects similar receptors as do benzodiazepines and produces kava's anxiolytic effects.

Kava is available in health food stores as capsules, tinctures, and fluid extracts and can be obtained without a prescription. The amount of active ingredient varies greatly from preparation to preparation.

he began doing this in his youth back in Fiji, and now drinks "many cups" of kava per day.

Mr. J states that his current episode of strange movements and visual hallucinations began hours after he drank several cups of kava the day before police brought him to the ER. He considers his new psychiatric symptoms Jesus' punishment for drinking kava.

The authors' observations

Mr. J's persecutory delusions suggest that he does not fully associate his symptoms with excessive kava use, but his abnormal movements, weight loss, skin changes, liver function abnormalities, and mental status changes are known adverse effects of kava.[3] We diagnose substance-induced delirium rather than substance intoxication or substance-induced psychosis because:

- Mr. J's cognitive symptoms are more severe than those caused by kava intoxication
- his psychotic symptoms occur only when he is delirious
- his disturbed consciousness, cognitive, and perceptual disturbances and the temporal relationship between symptom onset and massive kava use match DSM-IV-TR criteria for substance-induced delirium.[4]

Cultural use. Although Mr. J's kava consumption constitutes abuse, people in some cultures ingest herbal substances as part of spiritual or social rituals. Fijians, for example, commonly drink kava at social gatherings or ceremonies.

Being aware of cultural customs and beliefs in your practice area can alert you to herbal substance use in various populations, such as kava by patients from the South Pacific or echinacea, goldenseal, and burdock by some Native Americans (see *Related resources*).

Medicinal use. Patients often use kava and other herbal supplements—including fatty acids, ginkgo biloba, ginseng, St. John's wort, valerian, and others—with or instead of prescription drugs to alleviate psychiatric symptoms. Complementary and alternative medicine practitioners use kava to treat anxiety, for example (*Box*).

Anxiety and depression are among the most common reasons persons seek complementary or alternative treatment. In a national survey, 57% of respondents who suffered "anxiety attacks" and 54% of those with "severe depression" reported using such therapies.[8] Nearly 1 in 5 persons who take prescription drugs also take herbs and/or high-dose vitamin supplements.[9]

Herbal products have been shown to cause adverse effects (*Table 1*).[10] Kava, for example, has been associated with hepatotoxicity, dermopathy, movement disorders, GI disturbance, and weight loss. Standardized extracts such as capsules and tinctures appear more likely to cause adverse

Table 1

Possible adverse effects of herbal supplements used for psychiatric symptoms

Medication	Psychiatric uses	Adverse effects
Fatty acids	Depression, mania	GI upset
5-HTP (*5-hydroxytryptophan*)	Depression, anxiety	Agitation, ataxia, blurred vision, bradycardia, dyspnea, eosinophilia, headache, hypotension, insomnia, mania, psychosis, tremulousness
Ginkgo (*Ginkgo biloba*)	Cognitive enhancement	Bleeding, dizziness, GI upset, headache, palpitations, Stevens-Johnson syndrome
Ginseng (*Panax ginseng*)	Cognitive enhancement	Estrogenic effects, insomnia, mania
Kava (*Piper methysticum*)	Anxiety	Dermopathy, drowsiness, dry mouth, GI disturbance, hepatotoxicity, weight loss, movement disorders,
SAM-e (*S-adenosyl-L-methionine*)	Depression, fibromyalgia	Constipation, diarrhea, increased salivation, headache, nausea, urinary frequency, mania in patients with bipolar disorder
St. John's wort (*Hypericum perforatum*)	Depression	Anorexia, anorgasmia, anxiety, constipation, dizziness, dry mouth, fatigue, GI upset, mania, photosensitivity, pruritis, restlessness, urinary frequency
Valerian (*Valeriana officinalis*)	Insomnia	Drowsiness, GI upset, headache, hepatotoxicity

Source: Reference 10

effects than traditional extractions, such as a beverage made by infusing kava root.[5]

Kava toxicity has been reported among heavy users. Although the dosage at which kava becomes dangerous is unknown, the FDA recommends that users not exceed typical dosages (50 to 280 mg/d) and use kava only under a physician's supervision.[11]

Also, interactions between herbal products and allopathic medications can cause substantial morbidity (*Table 2, page 136*). St. John's wort, for example, can lead to serotonin syndrome when combined with selective serotonin reuptake inhibitors (SSRIs)[12] and can reduce blood levels of psychotropics metabolized by the cytochrome P-450 3A4 isoenzyme, such as alprazolam and carbamazepine.

Mr. J combined kava with clonazepam. Both substances affect gamma-aminobutyric (GABA) receptors, increasing the risk of sedation by depressing the CNS.

ASK ABOUT ALTERNATIVE MEDICINE USE

According to a national survey,[13] many patients do not tell allopathic physicians they are using complementary or alternative medications because:

Table 2

Potential adverse interactions between psychotropics and complementary/alternative medications

Herb	Interacts with …	Interaction can cause …
5-HTP	carbidopa, MAOIs, SSRIs	delirium, serotonin syndrome
Ginseng	MAOIs	mania
Kava	first- and second-generation antipsychotics, benzodiazepines, MAOIs	sedation
SAM-E	TCAs	serotonin syndrome
St. John's wort	benzodiazepines, beta blockers, buspirone, carbamazepine, clozapine, MAOIs, SSRIs, TCAs, trazodone	serotonin syndrome (w/SSRIs) reduced plasma levels of cytochrome P-450 3A4 substrates, diminishing their effectiveness
Valerian	benzodiazepines	sedation

MAOIs: Monoamine oxidase inhibitors
SSRIs: Selective serotonin reuptake inhibitors
TCAs: Tricyclic antidepressants

- "It wasn't important for the doctor to know."
- "The doctor never asked."
- "It was none of the doctor's business."
- "The doctor would not understand."
- or "The doctor would disapprove or discourage CAM use."

Kava and other herbal preparations can cause adverse side effects or interact negatively with prescription medications. Routinely ask patients if they are taking nonprescription supplements, and counsel them on intelligent use of alternative treatments.

Bottom Line

Knowing whether your patients are using complementary or alternative medications is critical to avoiding drug-drug interactions, preventing adverse side effects, and ensuring effective treatment. Yager et al[14] suggest that you:

- routinely question patients about use of alternative therapies
- discuss safety and efficacy of commonly used alternative treatments
- discuss merits of alternative treatments
- provide information on the effectiveness and risks of various treatments
- learn about alternative therapies by consulting the *Physicians' Desk Reference (PDR) for Herbal Medicines* or similar references
- help patients make decisions about alternative treatments, such as finding a qualified, licensed alternative provider.

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TREATMENT: QUICK RESOLUTION

We admit Mr. J to the inpatient psychiatry unit. There, we continue his outpatient prescription medications at the same dosages and block access to nonprescription substances. His symptoms begin to improve during the first day of hospitalization. His choreoathetosis, hallucinations, and confusion resolve within 48 hours, and he is medically stable.

We discharge Mr. J after 2 days and continue citalopram and clonazepam at the same dosages.

The authors' observations

Kava reaches peak plasma levels 1.8 hours after oral dosing and has a short (9-hour) elimination half-life. As a result, kava intoxication symptoms tend to resolve rapidly, as in Mr. J's case.

Although Mr. J is medically stable, liver damage associated with kava use can be irreversible, prompting some European countries to ban its sale. Make sure patients who report kava use are aware of its hepatotoxicity risk.

FOLLOW-UP: KICKING THE KAVA HABIT

Two weeks after Mr. J's discharge, his psychiatrist notes that his mental status has returned to baseline and that his skin has improved dramatically. The patient is following his citalopram and clonazepam regimen, and he seems more aware of kava's potential adverse effects.

Mr. J reports that he has not consumed kava since his hospitalization. He has been eating four meals per day and has gained 9 lb. He is pleased with his improved appetite and is motivated to continue abstaining from kava.

Related resources

- National Center for Complementary and Alternative Medicine. http://nccam.nih.gov.
- *Physicians Desk Reference (PDR) for herbal medicines, 3rd ed*. Montvale, NJ: Thomson PDR; 2004.
- Ernst E, Pittler MH, Stevinson C, et al. *The desktop guide to complementary and alternative medicine*. Edinburgh, UK: Mosby; 2001.

DRUG BRAND NAME

Alprazolam • Xanax
Buspirone • BuSpar
Carbamazepine • Equetro, others
Carbidopa • Lodosyn
Citalopram • Celexa
Clonazepam • Klonopin
Clozapine • Clozaril
Trazodone • Desyrel

DISCLOSURES

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

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