

CASE REPORT

> THE PATIENT

60-year-old man

> SIGNS & SYMPTOMS

- Daily episodes of confusion
- Altered behavior
- Chronic sleep deprivation

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> THE CASE

A 60-year-old man with hypertension, gout, hyperlipidemia, and chronic sleep deprivation was referred to our neurology department for evaluation because he'd recently developed episodes of confusion and altered behavior that occurred daily. According to the patient's wife, these episodes had started 4 weeks earlier while the patient was driving. He drove off the road while staring ahead with a "Joker-like" smile on his face. He was unable to utter more than a few words or respond to his wife, who was able to safely bring the car to a stop. The patient had spotty memory of this 40-minute episode.

Since then, he'd had similar but shorter episodes each morning, 20 to 75 minutes after taking his prescribed medications (lisinopril, simvastatin, and allopurinol). According to the patient's wife, during these episodes, the patient would "act childish." He would develop a voracious appetite and experience double or distorted vision, an unsteady gait, and poor muscle tone. These episodes were always followed by a long nap.

The man denied drinking, head trauma, acute illness, or taking illicit substances or any medications other than lisinopril, simvastatin, and allopurinol. Computed tomography, magnetic resonance imaging/magnetic resonance angiography, carotid Doppler ultrasound, and routine and 24-hour ambulatory electroencephalography (EEG) were normal.

Before the patient was referred to our neurology department, he had been prescribed a short course of the antiepileptic/mood stabilizer valproate and the wakefulness agent armodafinil, but neither medication had helped. The patient's episodes continued daily, usually 20 to 75 minutes after taking his regular medications. When he decided to take them at night, the episodes began to occur at night.

His neurologic exam was normal. Family history was positive for a cousin with narcolepsy but negative for seizures and obstructive sleep apnea (OSA). Polysomnography revealed moderate OSA with minimal oxygen desaturation. Inpatient video EEG monitoring captured several of the events that the patient and his wife had described; the patient seemed "uninhibited" in his behavior. His EEG, cardiac telemetry, oxygen saturation, blood pressure, and serum glucose level remained normal.

The episodes' sudden onset, peculiar symptoms, and duration—and the fact that they occurred after he took his usual medications—made complex partial seizures unlikely. The patient's chronic sleep deprivation and family history of narcolepsy raised the possibility of "sleep attacks," but the sudden onset and age of onset of his symptoms made those conditions less likely to explain the complete clinical picture. No particular hormonal disturbance could explain his presentation, and blood work was normal.

THE DIAGNOSIS

Because the patient's episodes had been occurring shortly after the patient took his lisinopril, simvastatin, and allopurinol, and because his blood pressure and lipid levels were

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INSTANT POLL

Have you ever cared for a patient whose unexplained symptoms were caused by a medication dispensing error?

Yes

No

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normal and his gout was asymptomatic, we decided to stop these medications. Later that day, the patient reported that he had discovered that his vial of lisinopril, which he had obtained from his regular pharmacy the day before his first episode, contained a different medication. He consulted a pharmacist, who determined that the vial contained extended release zolpidem 12.5 mg, and not his antihypertensive.

DISCUSSION

Although the true incidence of medication errors is difficult to determine, a 2006 Institute of Medicine report estimated that there are at least 1.5 million cases of preventable adverse drug events in the United States each year.¹ In light of these statistics, medication errors need to be near the top of our differential diagnosis when patients suddenly develop symptoms for which there is no obvious cause.

■ **Cause to pause?** If you observe a temporal association between the onset of a patient's symptoms and medication administration, consider possible adverse effects of the medication before ordering tests.

■ **In this case ...** Our patient's peculiar presentation correlated with regular ingestion of a high dose of zolpidem, a short-acting non-benzodiazepine gamma-aminobutyric acid (GABA) agonist. Zolpidem binds to the same GABA_A receptor as benzodiazepines and therefore acts as a hypnotic by increas-

ing GABA transmission.² Neuropsychiatric adverse events associated with zolpidem include hallucinations, amnesia, parasomnia, psychomotor impairment, and complex behaviors (eg, sleepwalking or sleep-driving).² Higher doses may cause coma or (rarely) death.² One case report describes a patient who heard command hallucinations and stabbed himself after ingesting a large dose of zolpidem.³

Our patient

The patient's episodes stopped after he discontinued the zolpidem. He subsequently received a correct prescription for lisinopril, and did not experience any additional episodes.

THE TAKEAWAY

Consider medication errors and adverse drug events in the differential diagnosis for patients who develop symptoms for which there is no obvious etiology. Educate patients, as well, to question their pharmacist if a recently filled prescription doesn't look like the pill they usually take or makes them feel different than usual when they take it.

Of course, patients should be reminded that a generic medication may not always look the same as a brand-name drug or a previous generic prescription. But it can't hurt for the patient to ask whether that medication that "looks different" is just a different generic—or a sign of a more worrisome mix-up. **JFP**

➤ If a patient tells you that his symptoms occur after he's taken his medication, consider whether the medication itself is to blame before ordering additional tests.

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