

# Chasing the dragon

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Two weeks after treatment for a heroin overdose, Mr. G is growing confused and forgetful. Drug screen is negative, so what's altering his mental status?

## CASE Confusion after discharge

Mr. G, age 37, is transferred to our medical center from a local hospital for treatment of altered mental status. His wife reports that 1 month ago he had been admitted to a different hospital for a heroin overdose. His urine toxicology screen then was positive for benzodiazepines, cocaine, and opioids. Mr. G's 2-week stay was complicated by respiratory arrest, intubation, and mechanical ventilation. He also developed hypotension, acute renal failure, and aspiration pneumonia, but recovered.

His wife says 2 weeks after Mr. G was discharged home, she noticed he was becoming increasingly confused and forgetful. Initially she observed difficulty with short-term memory. He was involved in a motor vehicle accident far from home while reporting to a job he no longer held. She found him confused and watering the lawn in the rain. After she discovered him talking on the phone with no one on the line, she brought him to the emergency room (ER).

His urine toxicology screen was negative. Routine examination of cerebrospinal fluid and tests for glucose, protein, lactate, lactate dehydrogenase, red blood cell count, white blood cell count with differential, syphilis serology, Gram's stain, and bacterial culture were negative.

Brain MRI showed diffuse new white matter signal abnormality superior to the tentorium

of the cerebellum, suggestive of low-grade white matter ischemia or inflammation. Mr. G's mental status did not improve in the ER, and he was transferred to our facility.

## What is the likely cause of Mr. G's mental status changes?

- a) white matter disease
- b) metabolic injury
- c) infection
- d) exposure to toxins

## The authors' observations

Based on abnormal brain imaging findings, we initially suspect a type of white matter disorder (*Table 1, page 78*).<sup>1</sup> We attempt to conduct a thorough history.

## HISTORY Missing information

Attempts to obtain collateral information are largely unsuccessful. Mr. G denies having a history of medical or psychiatric illness. He is vague about substance use but may have a history of opioid and cocaine dependence and alcohol abuse. He says he takes no prescribed or over-the-counter medications and has no known drug allergies.

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## How would you handle this case?

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## Clinical Point

Potential causes of toxic leukoencephalopathy include radiation, chemotherapy, and substance abuse

**Table 1**

### Differential diagnoses: Types of white matter disorders

Category	Example
Genetic	Metachromatic leukodystrophy
Demyelinative	Multiple sclerosis
Infectious	AIDS dementia complex
Inflammatory	Systemic lupus erythematosus
Toxic	Toluene leukoencephalopathy
Metabolic	Vitamin B12 deficiency
Vascular	Binswanger's disease*
Traumatic	Traumatic brain injury
Neoplastic	Gliomatosis cerebri
Hydrocephalic	Normal pressure hydrocephalus

\*Degenerative dementia caused by thinning of subcortical white matter of the brain  
AIDS: acquired immune deficiency syndrome  
Source: Reference 1

Mr. G's wife provides limited additional information. She married Mr. G 6 months ago; before that, he was in jail for 3.5 years for unclear reasons. He is unemployed, and the couple has no children.

Mr. G's wife reports that Mr. G's father had a history of diabetes mellitus and dialysis and died in his 40s from "Staph infection of the brain." Mr. G is estranged from his mother. He has no family history of neurologic or psychiatric illness.

Mr. G's wife denies that her husband has had recent fever, chills, weight loss, nausea, vomiting, diarrhea, or skin rash. He has no history of alcohol withdrawal symptoms, seizures, headache, diplopia, vertigo, hearing loss, swallowing difficulty, focal weakness, or sensory or speech changes. She did not notice personality or behavior changes in her husband before his recent confusion.

#### The authors' observations

During our interview, Mr. G maintains minimal eye contact. His speech is minimal with impaired fluency; he responds to questions with 1- or 2-word answers. He

describes his mood as "fine" but exhibits an incongruent and constricted affect, alternately laughing and crying. We are unable to assess his thought process and content because Mr. G is emotionally labile and unable to respond rationally to many of our questions. Mr. G's insight and judgment are poor. His hygiene, grooming, and teeth also are poor, and he is wearing diapers for bowel/bladder incontinence.

Mr. G scores 9/30 on the Mini-Mental State Exam (MMSE), indicating severe cognitive impairment. He is not oriented to place or time, and cannot:

- spell "world" backwards
- subtract serial 7s from 100
- repeat the phrase "no ifs, ands, or buts"
- name 5 U.S. cities
- write any words
- copy a figure of intersecting pentagons.

Neurologic exam reveals apathy, inattention, impaired executive function, and generalized hyperreflexia with bilateral unsustained ankle clonus and Babinski's sign. In addition, Mr. G has a snout reflex, bilateral hand and foot grasping, and bilateral palmomental reflexes but no mydriasis or nasal septum perforation. Repeat MRI shows the same white matter changes.

Based on Mr. G's history and brain imaging findings, we suspect that he is suffering from toxic leukoencephalopathy. He meets these diagnostic criteria:

- documented exposure to a toxin
- neurobehavioral deficits
- neuroradiologic abnormalities.<sup>2</sup>

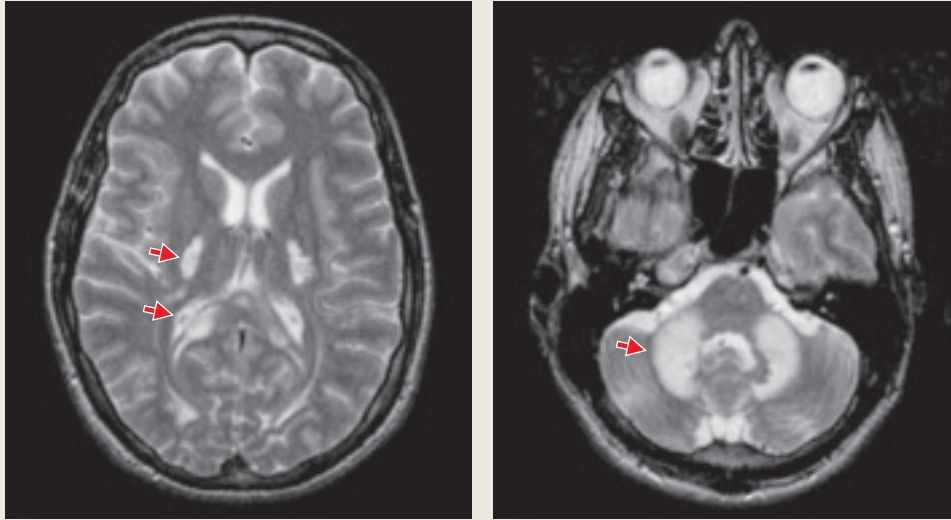
Toxic leukoencephalopathy can be caused by environmental exposure, radiation, chemotherapy, or substance abuse.<sup>3</sup> Because Mr. G has a history of substance abuse, we believe his symptoms developed as a result of heroin vapor inhalation.

### 'Chasing the dragon'

Inhaling heroin vapor is known by drug users as "chasing the dragon." Users place

## Figure

## White matter changes in a patient who inhaled heroin vapor



Seen on brain MRI as ultra-white patches, white matter hyperintensities (WMHs) are areas of increased signal intensity that indicate injury to the axons. In this typical patient (not Mr. G) who developed toxic leukoencephalopathy from heroin vapor inhalation, WMHs are evident in supra and infratentorial compartments, with characteristic involvement of the posterior limb of the internal capsule and cerebellum.

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## Table 2

## Stages of heroin vapor inhalation leukoencephalopathy

Stage	Features
Initial	Soft (pseudobulbar) speech, cerebellar ataxia, motor restlessness, apathy/bradyphrenia
Intermediate	Pyramidal tract lesions, pseudobulbar reflexes, spastic paresis, tremor/myoclonic jerks, choreoathetoid movements
Terminal	Stretching spasms, hypotonic paresis, akinetic mutism, central pyrexia, death

Source: Reference 4

a small amount of heroin powder on aluminum foil, which they heat from below with a flame. The heroin liquidizes and emits a white vapor, which users inhale.<sup>3</sup>

This method of heroin use can result in a form of toxic spongiform leukoencephalopathy. Brain imaging shows widespread white matter hyperintensities involving both supra and infratentorial compartments that are considered highly specific for this type of leukoencephalopathy (Figure). These hyperintensities are most commonly found in the:

- posterior cerebral and cerebellar white matter
- cerebellar peduncles
- splenium of the corpus callosum
- posterior limb of the internal capsule.<sup>4</sup>

Involvement of the cerebellum and posterior limb of the internal capsule while sparing the anterior limb helps to distinguish heroin vapor inhalation from other causes of toxic leukoencephalopathy.<sup>3</sup> Extensive damage to the white matter is believed to be caused by a contaminant that is activated when heroin is heated.<sup>4,5</sup>

## Clinical Point

Heroin vapor inhalation results in white matter hyperintensities highly specific for this type of toxic leukoencephalopathy

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## Related Resource

• Filley CM, Kleinschmidt-Demasters BK. Toxic leukoencephalopathy. *N Engl J Med*. 2001;345(6):425-432.

### Drug Brand Name

Methylphenidate • Ritalin

### Disclosures

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

Toxic leukoencephalopathy has not been observed in heroin users who snort or inject the drug. Despite the prevalence of heroin abuse, fewer than 100 cases of leukoencephalopathy associated with heroin vapor inhalation have been reported as of 2000, the most recent year for which data are available.<sup>6</sup> Patients with this form of leukoencephalopathy typically progress through 3 clinical stages: initial, intermediate, and terminal (*Table 2, page 79*).<sup>4</sup>

### Which treatment would you consider?

- coenzyme Q
- psychostimulants
- vitamin supplements
- supportive therapy

## TREATMENT Stimulant medication

We prescribe methylphenidate, 2.5 mg bid, to which Mr. G responds well. His cognition and mood improve, he is more goal-directed in his responses, and his MMSE score increases to 13/30. Mr. G eventually is able to converse minimally, and he confirms that he had heated heroin on a piece of foil and inhaled the vapors through his mouth.

Mr. G reports on the day of discharge that he still has cravings for illicit drugs and plans to continue using them. He is not interested in chemical dependency treatment.

### The authors' observations

Little published data exist on treating toxic leukoencephalopathy. Treatment mainly is supportive, although some researchers have suggested a role for coenzyme Q and vitamin supplements.<sup>3</sup>

Some studies have found methylphenidate beneficial in treating cognitive slowing in cancer patients.<sup>1,7</sup> The extent of Mr. G's cognitive impairment—which was severe—and evidence supporting stimulant medication prompted us to prescribe a low-dose methylphenidate trial, even though we were well aware of its abuse potential. Mr. G improved after starting methylphenidate, but unfortunately he was lost to follow-up.

### References

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## Clinical Point

We prescribe methylphenidate for Mr. G because of the drug's benefits in treating cognitive slowing in cancer patients

## Bottom Line

Heroin vapor inhalation can cause a toxic spongiform leukoencephalopathy characterized by widespread white matter hyperintensities on MRI. Suspect this condition in patients with substance use who present with new-onset mental status changes, including deficits in attention, memory, and executive function.