

# Malignant catatonia and aphasia follow multiple-drug overdose

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Two weeks after an overdose, Ms. M, age 37, develops malignant catatonia. Although her catatonic symptoms resolve with ECT, she shows word-finding difficulty. How would you proceed?



## How would you handle this case?

Answer the **challenge questions** throughout this article

### CASE Improvement, then decline

Ms. M, age 37, is brought to the hospital after her husband found her at home, after an unknown duration of impaired consciousness. Her husband reports that Ms. M had normal cognitive functioning before this event, with no difficulty completing activities of daily living. Ms. M's medical and psychiatric histories are notable for type 2 diabetes mellitus, unspecified bipolar disorder, and opioid, cocaine, and alcohol use disorders. Her medications include paroxetine, 40 mg/d, and gabapentin, 1,200 mg/d.

**First admission.** Poor inspiratory effort and oxygen saturation of 70% leads to emergent intubation. Serum laboratory studies reveal a white blood cell (WBC) count at 10,900/ $\mu$ L and creatinine phosphokinase level of 25,000 U/L. Urine drug screen is positive for tetrahydrocannabinol, cocaine, and opioids.

Ms. M is admitted to the ICU for management of rhabdomyolysis and multi-organ system failure, including acute hypoxic kidney injury.

By hospital Day 7, the tube is extubated with no recorded physical neurologic deficits. Mental status exam is normal, except for impaired memory of events surrounding the admission. Ms. M is discharged home with a recommendation for outpatient follow-up.

**2 Weeks later.** Ms. M is brought to the emergency department after a progressive decrease in social interaction, limited oral intake, decline in activities of daily living, and urinary incontinence. Results from laboratory studies are within normal limits; brain MRI is negative; EEG shows generalized moderate slowing.

During psychiatric evaluation, Ms. M is mute and staring continuously. Examination reveals oppositional paratonia (gegenhalten), catalepsy, prominent negativism, and waxy flexibility, all suggestive of catatonia. IV lorazepam is initiated at 1 mg every 8 hours, titrated to 2 mg, 3 times a day.

Ms. M is transferred to a psychiatric hospital for further treatment of catatonia.

**Second admission.** Evaluation with the Bush-Francis Catatonia Rating Scale supported a diagnosis of catatonia, with the presence of >3 features from the 14-item screen and a score of 16 on the 23-item rating scale.<sup>1</sup> After titrating lorazepam to 9 mg/d with minimal therapeutic impact, the psychiatry team consults the

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### Disclosures

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

### Clinical Point

In approximately 25% of cases, catatonia is caused by a general medical condition; as such, a comprehensive medical workup is vital

**Table 1**

## Differential diagnosis and workup for Ms. M

Possible diagnosis	Evaluation
Dementia	Initial studies: B <sub>12</sub> , folate, thyroid-stimulating hormone; brain MRI
Delirium	Initial studies: CBC with differential, complete metabolic panel, urinalysis
Toxins <ul style="list-style-type: none"> <li>• Heroin inhalation encephalopathy</li> <li>• Carbon monoxide poisoning</li> <li>• Heavy metals</li> </ul>	Urine drug screen; comprehensive drug screen; history Brain MRI
Infection <ul style="list-style-type: none"> <li>• Viral encephalopathy</li> <li>• Pneumonia</li> <li>• Urinary tract infection</li> <li>• HIV</li> <li>• Neurosyphilis</li> </ul>	Lumbar puncture with cytology (protein, glucose, cell count, bacterial cultures) Chest radiography, CBC with differential Urinalysis with culture Rapid HIV test Rapid plasma reagin test
Multiple sclerosis	Lumbar puncture, brain MRI
Nutritional deficiencies	B <sub>12</sub> , folate
Nonconvulsive status epilepticus Seizures	EEG
Stroke (hemorrhagic vs ischemic)	Brain MRI
Tumor/metastasis	Brain MRI
Posterior reversible encephalopathy syndrome	Brain MRI
Autoimmune <ul style="list-style-type: none"> <li>• Vasculitis</li> <li>• Acute disseminated encephalomyelitis</li> </ul>	Brain MRI
Creutzfeldt-Jakob disease	CSF analysis, EEG, and (rarely) brain biopsy

CBC: complete blood count; CSF: cerebrospinal fluid

electroconvulsive therapy (ECT) service, who deems Ms. M to be an appropriate candidate and petitions for court-ordered ECT.

On hospital Day 8, Ms. M has a fever of 104°F, tachycardia at 180 beats per minute, increased rigidity, and a WBC count of 17,800/μL. She is transferred to the ICU, with a presumptive diagnosis of malignant catatonia.

The medical evaluation, including general laboratory studies, EEG, and spinal fluid analysis, is unremarkable. Because of vital sign instability, 2 ECT treatments are completed in the general hospital before Ms. M resumes psychiatric inpatient care.

By the tenth ECT treatment, Ms. M is no longer febrile and experiences no further

autonomic instability or psychomotor features of catatonia. Despite these improvements, she is noted to have persistent word-finding difficulty.

**Which test would you order as the next step in your work up?**

- EEG
- lumbar puncture
- MRI
- CT

### The authors' observations

In approximately 25% of cases, catatonia is caused by a general medical condition<sup>2</sup>;



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as such, a comprehensive medical workup is vital for assessment and management of catatonic patients. In Ms. M's case, we considered several medical causes, including nutritional deficiency, infection, a toxin, renal or hepatic impairment, hypothyroidism, seizure, and stroke. Evaluation included measurement of thyroid-stimulating hormone, vitamin B<sub>12</sub>, and folic acid levels; urinalysis and urine drug screen; chest radiography; lumbar puncture; neuroimaging; and EEG (Table 1).

Several conditions in the differential diagnosis were noteworthy. Ms. M's severe and sudden neurologic decline, along with a positive urine drug screen for substances of abuse, raised concern about overdose leading to toxic encephalopathy or hypoxic brain injury. Ms. M's oxygen saturation when she was found was moderately hypoxic at 70%, which is not a level associated with hypoxic brain damage.

We also considered posterior reversible encephalopathy syndrome (PRES), which presents variably with nausea, visual impairment, disturbance in consciousness, seizures, and focal neurologic signs.<sup>3</sup> Although 67% to 80% of patients with PRES also have acute hypertension, blood pressure elevation is not necessary for the diagnosis.<sup>4</sup> Similar to toxic leukoencephalopathy, PRES is diagnosed by brain MRI, with classic signs of posterior white-matter edema.

Case reports also describe an uncommon demyelinating syndrome, delayed post-hypoxic leukoencephalopathy (DPHL), which develops several weeks or months after a cerebral anoxic insult.<sup>5</sup> In Ms. M's case, brain MRI performed during her second medical hospitalization, 7 days after the initial neuropsychiatric decline, was unremarkable. Using this result to rule out DPHL would have been premature because pathognomonic abnormalities can appear as long as 40 days after the anoxic insult. Given our differential diagnosis, we ordered a repeat MRI.

Table 2

### Mechanisms of anoxic injury

Anoxic anoxia	Low environmental oxygen tension or pulmonary function
Anemic anoxia	Low oxygen-carrying capacity of blood
Ischemic anoxia	Failure of cerebral blood flow

Source: Reference 7

### Etiology and pathophysiology

First described in 1979, DPHL is rare, posing diagnostic challenges for clinical providers.<sup>6</sup> Although the exact incidence of DPHL is unknown, the precipitating event typically involves cerebral anoxia, which can occur through carbon monoxide (CO) poisoning, strangulation, cardiac arrest, respiratory failure, and overdose from sedatives and narcotics (Table 2).<sup>7</sup> DPHL was first observed in a small percentage (2.75%) of patients suffering from CO poisoning.<sup>8,9</sup> Progression of the disease generally includes a period of unconsciousness, then a lucid interval that can last 2 to 40 days, followed by the abrupt onset of neuropsychiatric symptoms.<sup>10</sup> The specific pathophysiologic mechanism is unknown, but has been hypothesized to involve inferior

### Clinical Point

**Although the exact incidence of DPHL is unknown, the precipitating event typically involves cerebral anoxia**

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- A man, age 42, slowly deteriorating with schizophrenia, reports a throbbing headache; his family fears that he might grow violent

How would you proceed with their care?

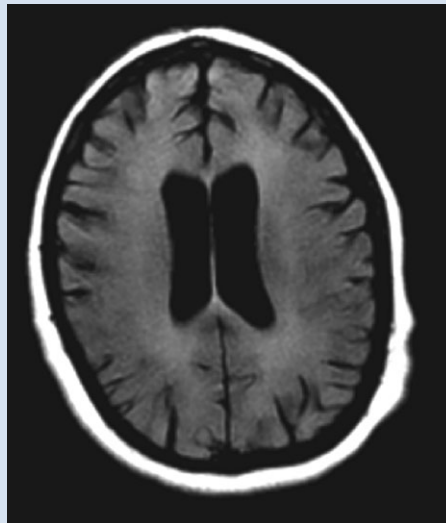
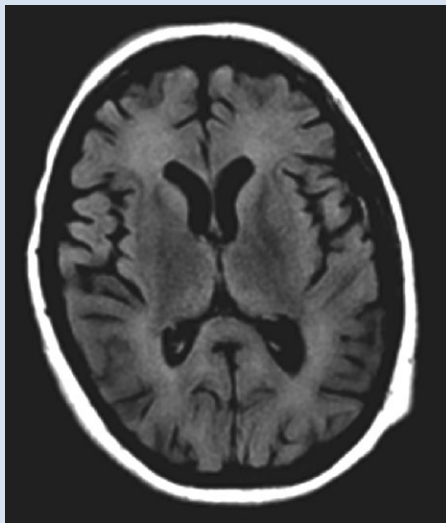
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**Clinical Point**

DPHL is a diagnosis of exclusion.

A careful history is critical to establish the possibility of a recent anoxic event

**Figure****Second brain MRI (T2/FLAIR)**

Diffuse hyperintensities are seen in the white matter

compensatory response to decreased oxygenation in the white matter.

**Diagnosis and clinical features**

DPHL can be divided into 2 clinical variations: parkinsonism and akinetic mutism. The former consists of conventional parkinsonian features along with agitation, apathy, hallucinations, dystonic posturing, and odd behaviors. The latter variant presents with apathy, minimal response to pain, functional bowel and bladder incontinence, mutism, and, at times, inappropriate laughter or tearfulness.<sup>5</sup> Both variants share similar features with hypokinetic forms of catatonia.

DPHL is a diagnosis of exclusion. A careful history is critical to establish the possibility of a recent anoxic event. MRI findings, including hyperintensities in the cerebral white matter on T2-based sequencing, are suggestive of the disease. A choline peak on magnetic resonance spectroscopy also might be present in patients with DPHL, although it is not specific to the diagnosis.

Early reports of DPHL suggested an associated deficiency of arylsulfatase A, an enzyme required in the modulation of myelin; however, more recent case reports are conflicting.<sup>11</sup> Familial mutations in the gene for arylsulfatase A also result in metachromatic leukodystrophy, and adult onset can present with psychiatric symptoms, including delusions and hallucinations.<sup>12</sup>

**Treatment and prognosis**

The treatment of DPHL consists primarily of supportive care and rehabilitation with physical, occupational, and speech therapy.<sup>11</sup> With these measures, most patients improve after 3 to 6 months; however, a large percentage sustain some long-term cognitive deficit, the most prevalent symptom being frontal executive dysfunction.<sup>5</sup>

**OUTCOME Supportive care**

A second MRI shows diffuse hyperintensities in the white matter that spare the cerebellum and brainstem (**Figure**). This finding is pathognomonic for DPHL.

ECT is discontinued because there is no evidence to support ECT-associated improvement in DPHL. Moreover, ECT might worsen the clinical course through increased stress and metabolic demand on the brain.<sup>13</sup>

Because the primary treatment of DPHL is early rehabilitation, we consider that Ms. M would benefit most from increased supportive care and therapy. She is discharged to a brain injury rehabilitation facility, where metoprolol is prescribed for mild tachycardia, along with thiamine and vitamins B<sub>12</sub> and D. Physical, occupational, and speech therapy are continued.

Approximately 3 weeks after admission to the rehabilitation program, Ms. M is discharged home. Although she improves in overall activities of daily living, she continues to experience moderate communication deficits and occasional external distractibility.

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## Related Resources

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#### Drug Brand Names

Gabapentin • Neurontin	Metoprolol • Lopressor
Lorazepam • Ativan	Paroxetine • Paxil

## Clinical Point

The treatment of DPHL consists primarily of supportive care and rehabilitation with physical, occupational, and speech therapy

## Bottom Line

Although delayed post-hypoxic leukoencephalopathy is considered rare, consider it in the differential diagnosis when a patient has a recent history of an anoxic event followed by the abrupt onset of neuropsychiatric symptoms. Keep in mind that the condition can be missed if an MRI is obtained too early, and the clinical signs can mimic hypokinetic catatonia.