An overlooked cause of catatonia
Roy Ibrahim, BS, Enjie El Rassi, MD, Rosette Jabbour, MD, and Rita Khoury, MD

Ms. L, age 40, develops severe headache, vomiting, altered mental status, and signs of catatonia. Is this a new-onset psychiatric disorder, or is it something else?

CASE  Agitation and bizarre behavior
Ms. L, age 40, presents to the emergency department (ED) for altered mental status and bizarre behavior. Before arriving at the ED, she had experienced a severe headache and an episode of vomiting. At home she had been irritable and agitated, repetitively dressing and undressing, urinating outside the toilet, and opening and closing water faucets in the house. She also had stopped eating and drinking. Ms. L’s home medications consist of levothyroxine 100 mcg/d for hypothyroidism.

In the ED, Ms. L has severe psychomotor agitation. She is restless and displays purposeless repetitive movements with her hands. She is mostly mute, but does groan at times.

HISTORY  Multiple trips to the ED
In addition to hypothyroidism, Ms. L has a history of migraines and asthma. Four days before presenting to the ED, she complained of a severe headache and generalized fatigue, with vomiting and nausea. Two days later, she presented to the ED at a different hospital and underwent a brain CT scan; the results were unremarkable. At that facility, a laboratory work-up—including complete blood count, urea, creatinine, C-reactive protein, electrolytes, magnesium, phosphorus, calcium, full liver function tests, amylase, lipase, bilirubin, thyroid function test, and beta-human chorionic gonadotropin—was normal except for low thyroid-stimulating hormone levels (0.016 mIU/L). Ms. L was diagnosed with a severe migraine attack and discharged home with instructions to follow up with her endocrinologist.

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Cases That Test Your Skills

Catatonia is a behavioral syndrome with heterogeneous signs and symptoms. According to DSM-5, the diagnosis is considered when a patient presents with ≥3 of the 12 signs outlined in Table 1. It usually occurs in the context of an underlying psychiatric disorder such as schizophrenia or depression, or a medical disorder such as CNS infection or encephalopathy due to metabolic causes. Ms. L exhibited mutism, negativism, mannerism, stereotypy, and agitation and thus met the criteria for a catatonia diagnosis.

EVALUATION Unexpected finding on physical exam

In the ED, Ms. L is hemodynamically stable. Her blood pressure is 140/80 mm Hg; heart rate is 103 beats per minute; oxygen saturation is 98%; respiratory rate is 14 breaths per minute; and temperature is 37.5° C. Results from a brain MRI and total body scan performed prior to admission are unremarkable.

Ms. L is admitted to the psychiatric ward under the care of neurology for a psychiatry consultation. For approximately 24 hours, she receives IV diazepam 5 mg every 8 hours (due to the unavailability of lorazepam) for management of her catatonic symptoms, and olanzapine 10 mg every 8 hours orally as needed for agitation. Collateral history rules out a current mood episode or onset of psychosis in the weeks before she came to the ED. Diazepam improves Ms. L’s psychomotor agitation, which allows the primary team an opportunity to examine her.

A physical exam reveals small vesicular lesions (1 to 2 cm in diameter) on an erythematous base on the left breast associated with an erythematous plaque with no evident vesicles on the left inner arm. The vesicular lesions display in a segmented pattern of dermatomal distribution.

Based on these new findings, what is the next step in managing Ms. L’s catatonia?

a) Perform a lumbar puncture (LP)
b) Initiate another second-generation antipsychotic such as risperidone
Cases That Test Your Skills

The authors’ observations
Catatonic symptoms, coupled with psychomotor agitation in an immunocompetent middle-aged adult with a history of migraine headaches, strong family history of severe mental illness, and noncontributory findings on brain imaging, prompted a Psychiatry consultation and administration of psychotropic medications.

A thorough physical exam revealing the small area of shingles and acute altered mental status prompted more aggressive investigations to explore the possibility of encephalitis.

Physicians should have a low index of suspicion for encephalitis (viral, bacterial, autoimmune, etc) and perform a lumbar puncture (LP) when necessary, despite the invasiveness of this test. A direct physical examination is often underutilized, which can lead to the omission of important information.

Additional lab results establish the diagnosis
An LP reveals Ms. L’s protein levels are 44 mg/dL, her glucose levels are 85 mg/dL, red blood cell count is 4/µL, and white blood cell count is 200/µL with 92% lymphocytes and 1% neutrophils. Ms. L’s CSF analysis profile indicates a viral CNS infection (Table 2).

What is the next step to treat Ms. L?
- a) Start an antibiotic
- b) Start an antiviral
- c) Adjust the psychotropic dosage
- d) Perform electroconvulsive therapy (ECT)

Table 2
Patterns of findings of cerebrospinal fluid analysis in bacterial, viral, and fungal encephalitis

<table>
<thead>
<tr>
<th>CSF analysis</th>
<th>Normal findings</th>
<th>Bacterial</th>
<th>Viral</th>
<th>Fungal</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pressure</td>
<td>5 to 15 cm water</td>
<td>Increased</td>
<td>Normal or mildly increased</td>
<td>Normal or mildly increased</td>
</tr>
<tr>
<td>Cell counts (cells/L)</td>
<td>0 to 5</td>
<td>&gt;1,000 to 2,000, mostly neutrophils</td>
<td>&lt;2,000, mostly lymphocytes</td>
<td>100 to 500, mostly lymphocytes</td>
</tr>
<tr>
<td>Glucose</td>
<td>&gt;40% serum or &gt;40 mg/dL</td>
<td>&lt;45 mg/dL</td>
<td>Normal</td>
<td>Low to normal</td>
</tr>
<tr>
<td>Protein</td>
<td>15 to 45 mg/dL</td>
<td>&gt;250 mg/dL</td>
<td>&lt;150 mg/dL</td>
<td>Normal</td>
</tr>
</tbody>
</table>

Source: Reference 3

Clinical Point
Direct physical examination of a patient is often underutilized, which can lead to the omission of important information.

EVALUATION

Varicella-zoster virus with clustered vesicles on an erythematous base

Source: Reference 5

Figure

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continued
Cases That Test Your Skills

**The authors’ observations**

Varicella-zoster virus (VZV) and herpes simplex virus (HSV) are human neurotropic alphaherpesviruses that cause lifelong infections in ganglia, and their reactivation can come in the form of encephalitis. VZV encephalitis can present with atypical psychiatric features, including catatonic symptoms.

Ms. L’s clinical presentation most likely implicated VZV. Skin lesions of VZV may look exactly like HSV, with clustered vesicles on an erythematous base [Figure, page 43](#). However, VZV rash tends to follow a dermatomal distribution (as in Ms. L’s case), which can help distinguish it from herpetic lesions.

Cases of VZV infection have been increasing worldwide. It is usually seen in older adults or those with compromised immunity. Significantly higher rates of VZV complications have been reported in such patients. A serious complication is VZV encephalitis, which is rare but possible, even in healthy individuals.

Ms. L’s case shows the importance of early recognition of VZV infection. The diagnosis is confirmed through CSF analysis. There is an urgency to promptly conduct the LP to confirm the diagnosis and quickly initiate antiviral treatment to stop the progression of the infection and its life-threatening sequelae.

In the absence of underlying medical cause, typical treatment of catatonia involves the sublingual or IM administration of 1 to 2 mg lorazepam that can be

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**Table 3**

**Acute psychiatric presentations of VZV encephalitis**

<table>
<thead>
<tr>
<th>Case</th>
<th>Sex, age (y)</th>
<th>Immunity</th>
<th>Previous health status</th>
<th>Presentation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Psychosis&lt;sup&gt;13&lt;/sup&gt;</td>
<td>Female, 57</td>
<td>Immunocompetent</td>
<td>Previously healthy</td>
<td>Delusional thoughts, short episodes of confusion, depersonalization, showing short moments of spatial and temporal disorientation</td>
</tr>
<tr>
<td>Mania&lt;sup&gt;14&lt;/sup&gt;</td>
<td>Male, 31</td>
<td>Immunocompetent (HIV positive)</td>
<td>Previously healthy</td>
<td>Irritable, erratic, verbally aggressive, grandiose, talkative</td>
</tr>
</tbody>
</table>

**Table 4**

**Delayed neuropsychiatric presentations after VZV encephalitis**

<table>
<thead>
<tr>
<th>Case</th>
<th>Sex, age (y)</th>
<th>Immunity</th>
<th>Previous health status</th>
<th>Date of onset</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dementia&lt;sup&gt;15&lt;/sup&gt;</td>
<td>Female, 71</td>
<td>Immunocompetent</td>
<td>Previously healthy</td>
<td>10 months post-VZV encephalitis that was successfully treated with antiviral medication 10 days after diagnosis</td>
</tr>
<tr>
<td>Delirium with manic symptoms&lt;sup&gt;16&lt;/sup&gt;</td>
<td>Female, 38</td>
<td>Immunocompetent</td>
<td>Panic disorder, dysthymia, 1 manic episode</td>
<td>6 weeks post-VZV reactivation causing herpes-zoster ophthalmicus that was successfully treated with corticosteroid eye drops</td>
</tr>
</tbody>
</table>

LP: lumbar puncture; PCR: polymerase chain reaction; VZV: varicella-zoster virus
Cases That Test Your Skills

Clinical Point

Delay in the diagnosis and treatment of VZV encephalitis can be fatal

OUTCOME Prompt recovery with an antiviral

Ms. L receives IV acyclovir 1,200 mg every 8 hours for 14 days. Just 48 hours after starting this antiviral medication, her bizarre behavior and catatonic features cease, and she returns to her baseline mental functioning. Olanzapine is discontinued, and lorazepam is progressively decreased. The CSF polymerase chain reaction assay indicates Ms. L is positive for VZV, which confirms the diagnosis of VZV encephalitis. A spine MRI is also performed and rules out myelitis as a sequela of the infection.

The authors’ observations

Chickenpox is caused by a primary encounter with VZV. Inside the ganglions of neurons, a dormant form of VZV resides. Its reactivation leads to the spread of the infection to the skin innervated by these neurons, causing shingles. Reactivation occurs in approximately 1 million people in the United States each year. The annual incidence is 5 to 6.5 cases per 1,000 people at age 60, and 8 to 11 cases per 1,000 people at age 70. In 2006, the FDA approved the first zoster vaccine (Zostavax) for use in nonimmuno-compromised, VZV-seropositive adults age >60 (later lowered to age 50). This vaccine reduces the incidence of shingles by 51%, the incidence of postherpetic neuralgia by 66%, and the burden of illness by 61%. In 2017, the FDA approved a second VZV vaccine (Shingrix, recombinant nonlive vaccine). In 2021, Shingrix was approved for use in immunosuppressed patients.

Reactivation of VZV starts with a prodromal phase, characterized by pain, itching, numbness, and dysesthesias in 1 to 3 dermatomes. A maculopapular rash appears on the affected area a few days later, evolving into vesicles that scab over in 10 days. Dissemination of the virus leading specifically to VZV encephalitis typically occurs in immunosuppressed individuals and older patients. According to the World Health Organization, encephalitis is a life-threatening complication of VZV and occurs in 1 of 33,000 to 50,000 cases. Delay in the diagnosis and treatment of VZV encephalitis can be detrimental or even fatal. Kodadhala et al. found that the mortality rate for VZV encephalitis is 5% to 10% and ≤80% in immunosuppressed individuals.
Cases That Test Your Skills

Sometimes, VZV encephalitis can masquerade as a psychiatric presentation. Few cases presenting with acute or delayed neuropsychiatric symptoms related to VZV encephalitis have been previously reported in the literature. Some are summarized in Table 3\textsuperscript{13,14} (page 44) and Table 4\textsuperscript{15,16} (page 44).

To our knowledge, this is the first case report of catatonia as a presentation of VZV encephalitis. The catatonic presentation has been previously described in autoimmune encephalitis such as N-methyl-D-aspartate receptor encephalitis, due to glutamatergic hypofunction.\textsuperscript{17}

References


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Related Resources


Drug Brand Names

<table>
<thead>
<tr>
<th>Acyclovir - Sitavig</th>
<th>Levothyroxine - Levoxyl</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diazepam - Valium</td>
<td>Olanzapine - Zyprexa</td>
</tr>
<tr>
<td>Haloperidol - Haldol</td>
<td>Risperidone - Risperdal</td>
</tr>
<tr>
<td>Lorazepam - Ativan</td>
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</table>

Clinical Point

Few cases of neuropsychiatric symptoms related to VZV encephalitis have been previously reported.

Bottom Line

In the setting of a patient with an abrupt change in mental status/behavior, physicians must be aware of the importance of a thorough physical examination to better ascertain a diagnosis and to rule out an underlying medical disorder. Reactivation of varicella-zoster virus (VZV) can result in encephalitis that might masquerade as a psychiatric presentation, including symptoms of catatonia.