Terrifying visions
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Mrs. L, age 82, is agitated by vivid new-onset visual hallucinations, but delirium, dementia, and medication effects are ruled out. What could be the cause?

CASE Seeing things
Family members bring Mrs. L, age 82, to the emergency room (ER) because she is agitated, nervous, and carries a knife “for protection.” In the past few months, she has been seeing things her family could not, such as bugs in her food and people trying to break into her house. Mrs. L becomes increasingly frightened and angry because her family denies seeing these things. Her family is concerned she might hurt herself or others.

Despite some hearing loss, Mrs. L had been relatively healthy and independent until a few years ago, when her vision decreased secondary to age-related macular degeneration and diabetic retinopathy. In addition to sensory impairment and diabetes mellitus, her medical history includes mild hypothyroidism and intervertebral disc herniation. She has no history of liver disease or alcohol or substance abuse. A few weeks ago Mrs. L’s primary care physician began treating her with donepezil, 5 mg/d, because he suspected dementia was causing her hallucinations. Otherwise, she has no psychiatric history.

On exam, Mrs. L is easily directable and cooperative. She seems angry because no one believes her; she reports seeing a cat that nobody else could see in the ER immediately before being evaluated. She is frightened because she believes her hallucinations are real, although she is unable to explain them. Mrs. L reports feeling anxious most of the time and having difficulty sleeping because of her fears. She also feels sad and occasionally worthless because she cannot see or hear as well as when she was younger.

A mental status examination shows partial impairment of concentration and short-term memory, but Mrs. L is alert and oriented. No theme of delusions is detected. She has no physical complaints, and physical examination is unremarkable.

What diagnosis do Mrs. L’s symptoms suggest?
   a) schizophrenia
   b) dementia with behavioral disturbance
   c) mood disorder with psychotic features
   d) delirium, causing a perceptual disturbance

The authors’ observations
Mrs. L presented with new-onset agitation, visual hallucinations, and mildly decreased concentration and short-term memory. Our next step after history and examination was to perform laboratory testing to narrow the diagnosis (Table 1).

A basic electrolyte panel including kidney function can point toward electrolyte imbalance or uremia as a cause of delirium.
um. Mrs. L’s basic metabolic panel and liver function were normal. Urinalysis ruled out urinary tract infection.

Mrs. L’s thyroid-stimulating hormone (TSH) level was mildly elevated at 5.6 mU/L (in our laboratory, the upper normal limit is 5.2 mU/L). Hypothyroidism and hyperthyroidism are not associated with hallucinations, but hyperthyroidism is an important medical cause of anxiety and hypothyroidism can cause a dementia-like presentation. CT of the head to rule out a space-occupying lesion or acute process—such as cerebrovascular accident—shows only chronic vascular changes.

Based on Mrs. L’s history, physical examination, and lab results, we provisionally diagnose dementia, Alzheimer’s type with psychotic features, and prescribe quetiapine, 25 mg at bedtime. We offer to admit Mrs. L, but she and her family prefer close outpatient follow-up. After discussing safety concerns and pharmacotherapy with the patient and her family, we discharge Mrs. L home and advise her to follow up with the psychiatric clinic.

**Table 1**

**Suggested workup for elderly patients with hallucinations**

<table>
<thead>
<tr>
<th>History and physical exam</th>
</tr>
</thead>
<tbody>
<tr>
<td>History of dementia, mood disorder, Parkinson’s disease, or drug abuse</td>
</tr>
<tr>
<td>Presence of delusions or mood/anxiety symptoms</td>
</tr>
<tr>
<td>Detailed medication history</td>
</tr>
<tr>
<td>Level of consciousness, alertness, and cognitive function assessment (eg, MMSE)</td>
</tr>
<tr>
<td>Vital signs (instability may reflect delirium, meningitis/encephalitis, or intoxication)</td>
</tr>
<tr>
<td>Physical exam (may confirm acute medical illness causing delirium)</td>
</tr>
<tr>
<td>Neurologic exam (may show focal neurologic signs reflecting space-occupying lesion, signs of Parkinson’s disease, vitamin B12 deficiency)</td>
</tr>
<tr>
<td>Ophthalmologic history/exam</td>
</tr>
</tbody>
</table>

**Investigations**

- Electrolyte imbalance, especially calcium
- Glucose level
- Uremia, impaired liver function, and increased ammonia
- CBC
- Urine drug screen
- Urinalysis, culture, and sensitivity

**Additional tests**

- VDRL
- Arterial blood gas
- ECG and cardiac enzymes
- Chest radiography
- Vitamin B12/folate
- TSH
- EEG
- Serum drug levels
- CT/MRI of the head
- Lumbar puncture and cerebrospinal fluid analysis
- Heavy metal screen
- HIV screen

**Clinical Point**

Although not associated with hallucinations, hyperthyroidism is a cause of anxiety.

**EVALUATION**

**Lasting hallucinations**

Quetiapine improves Mrs. L’s sleep and agitation but does not reduce her hallucinations. She sees a helicopter planting wires on a tree next to her house, a snake in the house, children in her room (some are “beautiful”), fire, and creatures with scary faces. These hallucinations occur mostly when she is alone. She denies hearing or touching the things she sees but continues to feel fear and anxiety when she sees them, although this diminishes with education and reassurance.

**The authors’ observations**

In Mrs. L’s subsequent psychiatry clinic visits, we gather additional information that helped us rule out several differential diagnoses (*Table 2, page 72*).

The most common causes of new-onset psychosis in later life are:
Table 2  
Differential diagnosis of hallucinations in elderly patients  

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Delirium</td>
<td>Secondary to a generalized medical condition, substance-induced, or substance withdrawal</td>
</tr>
<tr>
<td>Dementia</td>
<td>Alzheimer’s, vascular, Lewy body, or less common types</td>
</tr>
<tr>
<td>Parkinson’s disease</td>
<td>Medications can induce visual hallucinations</td>
</tr>
<tr>
<td>Brain tumor/mass/CVA</td>
<td>Usually accompanied by other neurologic symptoms and signs</td>
</tr>
<tr>
<td>Schizophrenia</td>
<td>Usually starts in early adulthood</td>
</tr>
<tr>
<td>Mood disorder with psychotic features</td>
<td>Depression can present as pseudodementia in elderly patients</td>
</tr>
<tr>
<td>Drug abuse/withdrawal or side effect</td>
<td>Numerous medications are known to worsen delirium in elderly patients</td>
</tr>
<tr>
<td>Other causes</td>
<td>HIV, tertiary syphilis, Charles Bonnet syndrome</td>
</tr>
</tbody>
</table>

CVA: cerebrovascular accident; HIV: human immunodeficiency virus

- dementia-related syndromes with psychosis, delirium, or drug-induced psychosis
- primary psychiatric disorders, most commonly depression.  

Alzheimer’s disease has been associated with up to a 60% incidence of psychotic symptoms at some point in the disease course. Although Mrs. L’s short-term memory had declined in recent years, she does not have aphasia, apraxia, agnosia, or decrease in mental executive functioning to meet Alzheimer’s dementia criteria.

Perceptual disturbance is a feature of delirium that can cause agitation and hallucinations in elderly patients. However, Mrs. L did not have a decreased level of consciousness or an acute medical illness that would explain delirium.

Despite Mrs. L’s symptoms and progressive hearing and vision loss with resultant disability, she generally was organized in terms of basic self-care, hygiene, and activities of daily living. She was able to have a conversation when she could hear the physician. Surprisingly, her Mini-Mental State Examination (MMSE) score was within normal limits or only mildly impaired at office visits. This was not compatible with the initial diagnosis of dementia, although it may suggest mild cognitive impairment.

Mrs. L took donepezil as prescribed by her primary care physician for only a few weeks before we stopped it. We attributed Mrs. L’s slightly impaired concentration and short-term memory in the ER to the anxiety and stress of oscillating visual hallucinations.

Schizophrenia is another cause of psychosis, but Mrs. L had no history of negative symptoms, delusions, disorganized speech/behavior, or family history of psychotic disorders. In addition, schizophrenia is most likely to appear in a patient’s third decade. Although more common in women than men, late-onset schizophrenia—defined as onset after age 40—has a 1-year prevalence rate of 0.6% and therefore is an unlikely cause of Mrs. L’s symptoms.

Mrs. L had no history of neurologic deficit to suggest cerebrovascular disease or space-occupying brain lesion. Her TSH, which was slightly increased when she presented in the ER, was normal on subsequent testing. Folic acid and vitamin B12 were normal. We ordered brain MRI to rule out organic causes not seen with CT, but Mrs. L felt claustrophobic in the machine and could not finish the test.

EEG was ordered to rule out epilepsy. Hallucinations can be a prominent component of seizures and are more common continued on page 75
when the seizure focus is in the left temporal lobe. However, the development of psychotic symptoms often follows the onset of seizures by approximately 14 to 17 years. Although Mrs. L never obtained the ordered EEG, the absence of a history of clinical seizures or focal neurologic signs makes it unlikely that epilepsy accounted for her hallucinations. The normal workup ruled out most possible medical/organic causes of Mrs. L’s visual hallucinations.

We considered depression with psychotic features because Mrs. L had occasional depressed mood, feelings of worthlessness, and low self-esteem. These symptoms started only after she began losing her vision and hearing and she did not experience them most of the time. Furthermore, her predominant negative feeling was anxiety related to the hallucinations. Mrs. L had no other depressive symptoms such as guilt or loss of appetite.

**A diagnosis of exclusion**

We began to suspect that Mrs. L had Charles Bonnet syndrome (CBS), a condition in which visually impaired persons experience visual hallucinations without other known mental illnesses. These hallucinations tend to be complex, vivid, and elaborate, lasting from a few seconds to most of the day. CBS occurs in 10% to 15% of patients with visual impairment, including up to 3.5% of elderly patients referred to psychiatrists for visual hallucinations. CBS is most common among the elderly because of the high prevalence of visual impairment in this population.

Many patients with CBS are aware that their hallucinations are not real. Mrs. L’s presentation was atypical because she believed what she was seeing was real and because most images were terrifying, which also is not usually the case in CBS.

CBS frequently goes unrecognized in clinical practice. Patients who admit to experiencing hallucinations often are labeled demented or psychotic. The course of CBS is categorized in 3 patterns:

- episodic (in this least common pattern, hallucinations occur over days to months and then resolve)
- periodic (hallucinatory activity alternates with phases of remission)
- continuous (patients experience no hallucination-free intervals)

The pathophysiology of CBS is not fully understood. The deafferentation hypothesis suggests that reduced or absent visual system stimulation leads to increased excitability of areas of the cerebral cortex associated with vision, resulting in phantom vision.

CBS has no universally accepted diagnostic criteria; it is a diagnosis of exclusion. Because we ruled out medical and organic causes, dementia, delirium, schizophrenia, and depression with psychotic features—and because Mrs. L had advanced macular degeneration and retinopathy—we believed CBS was a likely diagnosis. We referred her to an ophthalmologist, who confirmed the CBS diagnosis.

**What pharmacologic treatment would you consider for Mrs. L’s hallucinations?**

- a) benzodiazepine
- b) increased quetiapine dosage
- c) a different atypical antipsychotic
- d) mood stabilizer

**TREATMENT Temporary improvement**

We prescribe low-dose lorazepam, 0.5 to 1 mg every 8 hours as needed for agitation, and increase quetiapine to 50 mg up to twice a day as needed. These approaches fail because of excessive sedation and delayed onset of action in relation to the fast onset of Mrs. L’s hallucinations.

Based on a published report, we prescribe gabapentin, 100 mg bid, which seems to help Mrs. L. For several months, her hallucinations are reduced, and she occasionally experiences a hallucination-free day. After several months, however, the frequency of her hal-
Charles Bonnet syndrome (CBS) is characterized by vivid, complex visual hallucinations in patients with impaired vision but no mental illness. Careful evaluation is essential because CBS is a diagnosis of exclusion. Effective treatments may include anticonvulsants, increased social interaction, and brighter lighting.