Depression or delirium?

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Confused and depressed, Mr. L, age 85, is admitted after threatening his wife. He has several medical conditions and receives multiple medications. What could be causing his mental status changes?

CASE Agitated and paranoid

Police bring Mr. L, age 85, to the emergency department (ED) because he threatened his wife, claiming she is having an affair. Two days earlier, he was discharged from a different hospital, where he was treated for progressive and fluctuating irritability, depressed mood, confusion, disorientation, inattention, and delusional thinking that had started 4 to 5 months earlier. He has no other psychiatric history.

Mr. L has a history of atrial fibrillation, hypertension, benign prostatic hypertrophy, and noninsulin-dependent diabetes mellitus. Several months ago, he had hip surgery, which was complicated by a surgical wound infection. Medications include digoxin, 0.125 mg/d; atenolol, 100 mg/d; warfarin, 1 mg/d on Monday, Wednesday, Friday, Saturday, and Sunday and 0.5 mg/d Tuesday and Thursday; lisinopril, 40 mg/d; tamsulosin, 0.4 mg/d; and glyburide, 1.25 mg/d. During the previous hospitalization, physicians discovered he had myasthenia gravis, which they treated with prednisone and pyridostigmine. Mr. L also was diagnosed with hyperaldosteronism. An adrenal mass was found in an abdominal CT. At that time, he also was diagnosed with major depressive disorder (MDD) with psychotic features and started on aripiprazole, 10 mg/d, mirtazapine, 30 mg/d, and trazodone, 50 mg/d for sleep.

Which diagnosis would you include in the differential?

a) psychotic disorder due to a general medical condition
b) delirium
c) dementia
d) all of the above

The authors’ observations

When evaluating mental status changes in older patients, consider the time course and characteristics of the changes, especially if the patient’s cognitive function changes. Acute mental status changes that occur over hours to days often represent delirium caused by a medical condition such as a coronary event or infection. Changes that develop over weeks to months often signal a primary psychiatric disorder such as depression, mania, or dementia. Mr. L’s mood and psychotic symptoms developed over 4 to 5 months and were thought to be a result of MDD with psychotic features. However, his fluctuating cognitive symptoms, confusion, and lack of psychiatric history suggest that the differential diagnosis should include a cognitive disorder.

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such as delirium or dementia. The hypoactive form of delirium often is unrecognized or misdiagnosed as sedation or depression, particularly in older patients.1

Multiple medical conditions and polypharmacy are important factors to consider when evaluating mental status changes in geriatric patients. In Mr. L’s case, atrial fibrillation, hypertension, and diabetes increase his risk of an acute cardiovascular or cerebrovascular event and chronic cerebrovascular disease. Hyperaldosteronism can lead to electrolyte abnormalities that may produce mental status changes. Treatment with an oral hypoglycemic raises the possibility that hypoglycemia is contributing to his mental status changes. Prednisone can cause psychosis, anxiety, and mania. Digoxin toxicity is associated with psychosis and irritability. Pyridostigmine also has been reported to cause psychosis. Use of an antidepressant, such as mirtazapine, could have exacerbated an underlying undiagnosed bipolar disorder. Antipsychotics, such as aripiprazole, may cause akathisia or activation. Substance intoxication or withdrawal should not be excluded solely because a patient is older. In older patients, medications with anticholinergic effects are common culprits for cognitive impairment (Table 1).2,3

What is the best next step?

a) continue aripiprazole and mirtazapine
b) switch to a benzodiazepine
c) switch to a selective serotonin reuptake inhibitor (SSRI)
d) initiate electroconvulsive therapy
e) complete your assessment, including history, physical examination, and laboratory workup

<table>
<thead>
<tr>
<th>Medications that could contribute to mental status changes</th>
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<tbody>
<tr>
<td>Anticholinergics (atropine, benztropine, oxybutynin, some OTC medications)</td>
</tr>
<tr>
<td>Hypnotics/sedatives (benzodiazepines)</td>
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<tr>
<td>Opiate analgesics (meperidine)</td>
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<tr>
<td>Neuroleptics (clozapine, thioridazine, olanzapine)</td>
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<tr>
<td>Antiparkinsonian medications (levodopa, selegiline, pergolide, amantadine)</td>
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<tr>
<td>Antidepressants (amitriptyline)</td>
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<tr>
<td>Anticonvulsants (phenytoin)</td>
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<tr>
<td>Histamine H2 receptor antagonists (ranitidine, cimetidine, omeprazole)</td>
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<tr>
<td>Cardiac drugs (digoxin)</td>
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<tr>
<td>Nonsteroidal anti-inflammatory drugs (aspirin)</td>
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<tr>
<td>Corticosteroids (prednisolone)</td>
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<tr>
<td>Antibiotics (penicillins, cephalosporins, quinolones)</td>
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OTC: over the counter

Source: References 2,3

Breaths per minute, and blood pressure of 164/84 mm Hg with oxygen saturation of 96% at room air. Physical exam is notable for 2+ pitting edema in the lower extremities. Mr. L is oriented to person, place, and time and is psychomotorically activated. Neurologic examination is within normal limits.

Laboratory data reveal a potassium level of 2.5 mEq/L. Other results, including complete blood count, comprehensive metabolic panel, thyroid-stimulating hormone, urinalysis, urine toxicology screen, B12, folate, venereal disease research laboratory, and ammonia are unremarkable. Chest radiography reveals an enlarged cardiomegaly. A CT scan of the brain without contrast shows cortical volume loss and periventricular white matter disease without evidence of acute intracranial abnormality. ECG shows atrial fibrillation with a rate of 67 beats per minute.

Mr. L’s hypokalemia is corrected with potassium chloride and his hyperaldosteronism is
treated with spironolactone, 25 mg/d. Physicians on the medical unit discontinue digoxin because Mr. L’s heart rate is controlled with atenolol and he is anticoagulated with warfarin.

Mr. L continues to be depressed and irritable with delusional jealousy. Mirtazapine is continued at 30 mg/d at bedtime. Aripiprazole and trazodone are discontinued and Mr. L is started on olanzapine, 10 mg/d, and haloperidol, 1 mg 4 times a day as needed for agitation. He requires multiple “as needed” haloperidol doses because of intermittent episodes of agitation. Mr. L is then transferred to the inpatient psychiatric unit for continued evaluation and treatment.

Which medications would you use to treat Mr. L’s psychiatric symptoms?
- a) continue olanzapine and trazodone
- b) continue haloperidol and trazodone
- c) continue haloperidol alone
- d) start risperidone
- e) start lorazepam

The authors’ observations
The fact that Mr. L is alert and oriented is encouraging; however, it does not rule out delirium because this condition is characterized by fluctuating levels of consciousness. Therefore, it is important to reassess him over time and perform a more thorough evaluation of cognitive function, especially attention and concentration, in addition to alertness and orientation. Psychomotor activation could suggest agitated depression, anxiety, mania, psychosis, substance intoxication, akathisia from antipsychotics, or delirium (Table 2). Initial evaluation—especially in older patients—should include a thorough history (including collateral sources) and be guided by the clinical presentation and physical examination, taking into consideration life-threatening conditions and common causes of mental status change such as infections, hypoxia, substance or medication effects, acute coronary syndromes, acute neurologic events, and metabolic conditions.

Reconsider the diagnosis
Even after being treated for hyperaldosteronism and discontinuing unnecessary medications, Mr. L continued to be treated for MDD with psychotic features despite intermittent confusion and agitation. At this point, it might have been useful to reconsider whether MDD with psychotic features was the most appropriate diagnosis to explain his mental status changes.

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Clinical Point
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EVALUATION
Poor cognitive status
Mental status examination upon admission to the psychiatric unit reveals a poorly coopera-
Cognitive testing is essential for the diagnosis and treatment of patients with mental status changes and for evaluating their response to treatment. Although the MMSE is widely used, other scales—including the Confusion Assessment Method, the Organic Brain Syndrome Scale, the Memorial Delirium Assessment Scale, and the delirium severity index—may be more sensitive for detecting delirium. All of these scales can be difficult to complete when evaluating confused and combative patients. Quick screening instruments for inattention, such as the digit span test and listing days of the week backwards, could be used as well.
ago; this was 1 month after undergoing hip replacement surgery, which was complicated by a surgical wound infection and worsened his medical illnesses. Within a month, Mr. L became withdrawn and appeared depressed. He was confused and intermittently disoriented to place and time. He became irritable and started reporting concerns about his wife having an affair. During this time different medications were introduced, including steroids and several antibiotics.

### The authors’ observations
A thorough history from the patient and caregivers, including the time course of mental status changes, new medication use, and history of medical and psychiatric disorders—especially depression and dementia—are important to obtain, especially early in the evaluation.

Although Mr. L’s irritability, delusions, and psychomotor slowing could be signs of psychotic depression, his fluctuating mental status, disorientation, poor attention, and impaired concentration suggest delirium (*Table 3*).

This diagnosis is supported by the fact that Mr. L’s symptoms emerged after orthopedic surgery. Delirium after orthopedic surgery is common among older patients. Contributing and perpetuating factors in Mr. L’s case may have included postoperative complications, hypokalemia (hypermagnesemia), medications (prednisone, digoxin, and olanzapine), and environmental unfamiliarity during hospitalization.

A delirium diagnosis should be based on a high index of suspicion and a careful clinical assessment rather than diagnostic tests.

### OUTCOME | Return home

Mr. L’s confusion and delusional jealousy decrease over time, as do his disorientation and inattention, as evidenced by improvement on MMSE scores. His last MMSE score is 27/30, failing mostly in attention and recall.

After sustained improvement in cognition and behavior, Mr. L is discharged home on haloperidol and the remainder of his nonpsychiatric medications with outpatient medical and psychiatric follow-up. Over several months, he continues to show improvement and haloperidol is discontinued.

### The authors’ observations
Delirium treatment should focus on prompt identification and management of precipitating and contributing factors. Antipsychotics are considered first-line treatment for patients with delirium, agitation, or psychosis who pose a risk to themselves or others. Benzodiazepines should be avoided in older patients unless symptoms are secondary to CNS-depressant withdrawal (ie, alcohol, benzodiazepines).
Although there are no-FDA approved medications for delirium, haloperidol has been widely studied and used for treatment of agitation and psychosis in delirium. There is no evidence that low-dose haloperidol is any less effective than olanzapine or risperidone, or is more likely to cause adverse drug effects such as extrapyramidal syndrome.10 Antipsychotic use in a confused or agitated dementia patient increases risk of mortality compared with dementia patients who do not receive antipsychotics.11 The use of typical or atypical antipsychotics for delirium should be guided by the patient’s characteristics, such as cardiovascular status and presence or absence of underlying dementia. Atypical antipsychotics should be used carefully because—as in Mr. L’s case—anticholinergic side effects of medications such as olanzapine could worsen delirium.5 Once delirium has resolved, antipsychotics should be tapered and discontinued.

Other components of delirium treatment and prevention include:

- reorientation (verbally, with clocks, calendars, etc.)
- safe ambulation
- adequate sleep, food, and fluid intake
- adaptive equipment for vision and hearing impairment
- adequate management of pain and other comorbidities.12

References

Related Resources

Drug Brand Names
- Amantadine - Symmetrel
- Amtiptyline - Elavil
- Antipiprazole - Abilify
- Atenolol - Tenormin
- Atropine - AtroPen
- Benzotropine -Cogentin
- Cimetidine - Tagamet
- Clozapine - Clozaril
- Digoxin - Lanoxin
- Glyburide - DiaBeta, Micronase
- Haloperidol - Haldol
- Levodopa/carbidopa - Parcopa, Sinemet
- Lisinopril - Prinivil, Zestril
- Lorazepam - Ativan
- Meperidine - Demerol
- Mirtazapine - Remeron
- Olanzapine - Zyprexa
- Omeprazole - Prilosec
- Oxybutynin - Ditropan
- Pergolide - Permax
- Phenytoin - Dilantin
- Phenytol
- Predisolone - Orapred
- Prednisone - Deltasone
- Pyridostigmine - Mestinon
- Ranitidine - Zantac
- Risperidone - Risperdal
- Selegiline - Elderly, Zelapar
- Spironolactone - Aldactone
- Tamsulosin - Flomax
- Thioridazine - Mellaril
- Trazodone - Desyrel
- Warfarin - Coumadin

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