Manic after having found a ‘cure’ for Alzheimer’s disease
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Mr. A, age 73, has been irritable, impulsive, grandiose, and sleeping very little. He claims to have found a ‘cure’ for Alzheimer’s disease. What could be causing his symptoms?

CASE Reckless driving, impulse buying
Mr. A, age 73, is admitted to the inpatient psychiatric unit at a community hospital for evaluation of a psychotic episode. His admission to the unit was initiated by his primary care physician, who noted that Mr. A was “not making sense” during a routine visit. Mr. A was speaking rapidly about how he had discovered that high-dose omega-3 fatty acid supplements were a “cure” for Alzheimer’s disease. He also believes that he was recently appointed as CEO of Microsoft and Apple for his discoveries.

Three months earlier, Mr. A had started taking high doses of omega-3 fatty acid supplements (10 to 15 g/d) because he believed they were the cure for memory problems, pain, and depression. At that time, he discontinued taking nortriptyline, 25 mg/d, and citalopram, 40 mg/d, which his outpatient psychiatrist had prescribed for major depressive disorder (MDD). Mr. A also had stopped taking buprenorphine, 2 mg, sublingual, 4 times a day, which he had been prescribed for chronic pain.

Mr. A’s wife reports that during the last 2 months, her husband had become irritable, impulsive, grandiose, and was sleeping very little. She added that although her husband’s ophthalmologist had advised him to not drive due to impaired vision, he had been driving recklessly across the metropolitan area. He had also spent nearly $15,000 buying furniture and other items for their home.

In addition to MDD, Mr. A has a history of chronic kidney disease, Leber’s hereditary optic neuropathy, and chronic pain. He has been taking vitamin D3, 2,000 U/d, as a nutritional supplement.

What is the most likely cause of Mr. A’s psychiatric symptoms?

- a) late-onset bipolar disorder
- b) behavioral changes due to a neurodegenerative disorder (eg, frontotemporal dementia)
- c) thyrotoxicosis
- d) high-dose omega-3 fatty acid supplements
- e) abrupt withdrawal of antidepressant medications

How would you handle this case?
Answer the challenge questions at MDedge.com/psychiatry and see how your colleagues responded.
The authors’ observations

Mr. A met the DSM-5 criteria for a manic episode (Table 1). His manic and delusional symptoms are new. He has a long-standing diagnosis of MDD, which for many years had been successfully treated with antidepressants without a manic switch. The absence of a manic switch when treated with antidepressants without a mood stabilizer suggested that Mr. A did not have bipolarity in terms of a mood disorder diathesis. In addition, it would be unusual for an individual to develop a new-onset or primary bipolar disorder after age 60. Individuals in this age group who present with manic symptoms for the first time are preponderantly found to have a general medical or iatrogenic cause for the emergence of these symptoms. Mr. A has a history of chronic kidney disease, Leber’s hereditary optic neuropathy, and chronic pain.

Typically a sedentary man, Mr. A had been exhibiting disinhibited behavior, grandiosity, insomnia, and psychosis. These
symptoms began 3 months before he was admitted to the psychiatric unit, when he had started taking high doses of omega-3 fatty acid supplements.

**EVALUATION** Persistent mania

On initial examination, Mr. A is upset and irritable. He is casually dressed and well-groomed. He lacks insight and says he was brought to the hospital against his will, and it is his wife “who is the one who is crazy.” He is oriented to person, place, and time. At times he is found roaming the hallways, being intrusive, hyperverbal, and tangential with pressured speech. He is very difficult to redirect, and regularly interrupts the interview. His vital signs are stable. He walks well, with slow and steady gait, and displays no tremor or bradykinesia.

What laboratory investigations should be ordered for Mr. A?

- a) brain MRI
- b) thyroid-stimulating hormone test
- c) serum docosahexaenoic acid (DHA) and eicosapentaenoic acid (EPA) levels
- d) comprehensive metabolic panel
- e) urine drug screen

**The authors’ observations**

In order to rule out organic causes, a complete blood count, comprehensive metabolic panel, thyroid profile, urine drug screen, and brain MRI were ordered. No abnormalities were found. DHA and EPA levels were not measured because such testing was not available at the laboratory at the hospital.

Mania emerging after the sixth decade of life is a rare occurrence. Therefore, we made a substantial effort to try to find another cause that might explain Mr. A’s unusual presentation (**Table 2, page 52**).

**Clinical Point**

Very limited evidence suggests that omega-3 fatty acid supplements, particularly those with flaxseed oil, can induce hypomania or mania. This association was first reported by Rudin in 1981, and later reported in other studies. How omega-3 fatty acids might induce mania is unclear.

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Mr. A was reportedly taking high doses of an omega-3 fatty acid supplement. We hypothesized that the antidepressant effect of this supplement may have precipitated a manic episode. Mr. A had no history of manic episodes in the past and was stable during the treatment with the outpatient psychiatrist. A first episode mania in the seventh decade of life would be highly unusual without an organic etiology. After laboratory tests found no abnormalities that would point to an organic etiology, iatrogenic causes were considered. After a review of the literature, there was anecdotal evidence for the induction of mania in clinical trials studying the effects of omega-3 supplements on affective disorders.

This led us to ask: How much omega-3 fatty acid supplements, if any, can a patient with a depressive or bipolar disorder safely take? Currently, omega-3 fatty acid supplements are not FDA-approved for the treatment of depression or bipolar disorder. However, patients may take 1.5 to 2 g/d for MDD. Further research is needed to determine the optimal dose. It is unclear at this
time if omega-3 fatty acid supplementation has any benefit in the acute or maintenance treatment of bipolar disorder.

**Cases That Test Your Skills**

**Differential diagnoses considered for Mr. A**

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<thead>
<tr>
<th>Diagnosis</th>
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<tbody>
<tr>
<td>Opiate withdrawal</td>
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<tr>
<td>Late-onset mania</td>
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<tr>
<td>Neurodegenerative disorder (e.g., frontotemporal dementia)</td>
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<tr>
<td>Hyper/hypothyroidism</td>
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<tr>
<td>Substance-induced mania due to omega-3 fatty acid toxicity</td>
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<tr>
<td>Schizoaffective disorder</td>
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<td>Abrupt withdrawal of antidepressant medications</td>
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<tr>
<td>Delirium</td>
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<tr>
<td>Substance-induced psychotic disorder</td>
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**Over-the-counter agents that may be associated with manic symptoms**

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<tr>
<th>Agent</th>
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<tbody>
<tr>
<td>St. John’s wort</td>
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<tr>
<td>Ginseng</td>
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<tr>
<td>Tyrosine</td>
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**TREATMENT** Nonadherence leads to a court order

On admission, Mr. A receives a dose of hydrocodone/acetaminophen (10 mg/325 mg, by mouth every 4 hours as needed) and lorazepam. His intake of omega-3 fatty acid supplements is discontinued during treatment. He is alert but tangential with loosening of associations. His speech is rapid; he continues to be grandiose and oblivious to the reason for his hospitalization. He is able to spontaneously discuss recent life events. After a week-long period of nonadherence to treatment, Mr. A requires a court order for psychiatric treatment and undergoes inpatient treatment for a total of 30 days.

How would you acutely treat Mr. A’s symptoms?

a) lithium  
b) anticonvulsant  
c) antipsychotic  
d) lithium with antipsychotic  
e) anticonvulsant with antipsychotic  
f) lithium with anticonvulsant

**The authors’ observations**

During an acute manic episode, the goal of treatment is urgent mood stabilization. Monotherapy can be used; however, in emergent settings, a combination is often used for a rapid response. The most commonly used agents are lithium, anticonvulsants such as valproic acid, and antipsychotics. In addition, benzodiazepines can be used for insomnia, agitation, or anxiety. The decision to use lithium, an anticonvulsant, or an antipsychotic depends upon the specific medication’s adverse effects, the patient’s medical history, previous medication trials, drug-drug interactions, patient preference, and cost.
Because Mr. A has a history of chronic kidney disease, lithium was contraindicated. Therefore, risperidone was initiated and titrated up to 6 mg/d. Mr. A showed some improvement, but his response was not optimal, as he experienced continued irritability, insomnia, and delusions. Valproic acid was started, and the dose was titrated to 1,000 mg/d, which equates to a serum blood level of 54.2 mg/dL.

**What would be the most effective maintenance treatment for this patient?**

a) lithium  

b) anticonvulsant  

c) antipsychotic  

d) anticonvulsant with antipsychotic  

e) lithium with antipsychotic  

f) anticonvulsant with lithium

**The authors’ observations**

After the acute episode of mania resolves, maintenance pharmacotherapy typically involves continuing the same regimen that achieved mood stabilization. Monotherapy is typically preferred to combination therapy, but it is not always possible after a manic episode. A reasonable approach is to slowly taper the antipsychotic after several months of dual therapy if symptoms continue to be well-controlled. Further adjustments may be necessary, depending on the medications’ adverse effects. Moreover, further acute episodes of mania or depression will also determine future treatment.

**OUTCOME** Resolution of delusions  

Mr. A is discharged 30 days after admission. At this point, his acute manic episode has resolved with non-tangential, non-pressured speech, improved sleep, and decreased impulsivity. His grandiose delusions also have resolved. He is prescribed valproic acid, 1,000 mg/d, and risperidone, 6 mg/d at bedtime, under the care of his outpatient psychiatrist.

**Related Resource**


**Drug Brand Names**

<table>
<thead>
<tr>
<th>Buprenorphine</th>
<th>Lithium</th>
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<tbody>
<tr>
<td>Buprenex, Buprenex CR, Suboxone, Subutex, Subutex CR</td>
<td>Eskalith, Lithobid</td>
</tr>
<tr>
<td>Citalopram</td>
<td>Lorazepam-Alprazolam</td>
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<tr>
<td>Ciolex</td>
<td>Nortriptyline-Pamelor</td>
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<tr>
<td>Hydrocodone/acetaminophen</td>
<td>Risperidone-Risperdal</td>
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<tr>
<td>Vicodin</td>
<td>Valproic acid-Depakote</td>
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**Clinical Point**

The most commonly used agents for a manic episode are lithium, anticonvulsants, and antipsychotics.

**REFERENCES**


7. Su KP, Shen WW, Huang SY. Are omega3 fatty acids beneficial in depression but not mania? Arch Gen Psychiatry. 2000;57(7):716-717.


**Bottom Line**

Initial presentation of a manic episode in an older patient is rare. It is important to rule out organic causes. Weak evidence suggests omega-3 fatty acid supplements may have the potential to induce mania in certain patients.