A Case of Nonmalignant Delirious Mania Successfully Treated With Lorazepam and Carbamazepine: A Proposed Diagnostic and Treatment Algorithm

David R. Spiegel, MD[a,*]; Abigail Barger, MD[a]; and Elizabeth Monter, DO[a]

Delirious mania is a severe but underrecognized neuropsychiatric syndrome characterized by the rapid onset of delirium, mania, and psychosis. Catatonia is often a prominent feature of the syndrome.[1] Despite the diversity of nosology, including lethal catatonia, the delirious mania construct has been relatively consistent in description in clinical reports.[2]

We present a patient with a history of bipolar disorder type 1, whom not only had been euthymic for 20 years (until presenting to our hospital) but also had been doing so with no psychotropic medication. Her phenomenology at admission warranted a thorough medical evaluation, which uncovered metastatic ovarian cancer, but was ultimately determined to be most consistent with delirious mania.

Case Report

Our patient is a 64-year-old White woman with a history of bipolar disorder type 1; she had been euthymic for 20 years, reportedly with no maintenance medications. Five days prior to admission in November 2019, the patient was found "wandering the streets" and brought to our emergency department. Premorbid, the patient was reported as fully independent, including able to perform instrumental activities of daily living. Past medical history was remarkable for diabetes mellitus type 2, treated with metformin.

The patient was described as "hard to manage," and we were consulted on hospital day 2. During our initial evaluation, our patient's mood was elated with increased energy and grandiose delusions. Her Young Mania Rating Scale (YMRS)[3] score was 31. She was also oriented ×1, with fluctuation of attention and awareness and a positive result on the Confusion Assessment Method.[4] In addition, our patient manifested behavioral stereotypies, echolalia, verbigerations, grimacing, perseverations, and catalepsy but without autonomic instability. The patient's Bush-Francis Catatonia Rating Scale (BFCRS)[5] score was 21. After the evaluation, we administered a lorazepam (1 mg) challenge, and her BFCRS score dropped to 7. On hospital day 3, we began carbamazepine titrated to 300 twice/day and lorazepam titrated up to 1.5 mg 4 times/day, both after 2 days. Her carbamazepine level at this time was 7 mcg/mL. She was started on olanzapine 2.5 mg twice/day, and based on US Food and Drug Administration prescribing information stating, "concomitant administration of intramuscular olanzapine along with benzodiazepines is not recommended due to the potential for excessive sedation and cardiorespiratory depression,"[6,7] lorazepam was discontinued.

The patient's symptoms of delirium, mania/psychosis, and catatonia decreased, and on hospital day 10, her YMRS score was 8, BFCRS was 6, CAM result was negative, and Mini-Mental State Examination[8] score was 27. Unfortunately, due to metastatic disease, at discharge (hospital day 12), the patient was placed in hospice and died 2 months later.

Discussion

Our patient demonstrated many of the symptoms of delirious mania, a syndrome of acute-onset elated mood, increase in goal-directed energy, grandiosity, emotional lability, delusions and inattention, unawareness, and fluctuation of symptoms (*DSM-5* criteria for mania and delirium, respectively). Delirious mania has been accepted to have no identifiable medical cause. Some, but not all authors, have found catatonic signs and symptoms in patients with delirious mania.[9,10] Bipolar disorder is the common diagnosis of record in patients with delirious mania, since the latter has no formal classification.[2] Figure 1 provides a proposed diagnostic and treatment algorithm for delirious mania and a review of our patient's course.[1,9–12]

In addition to psychosis, and as in our patient, catatonia is an additional common neuropsychiatric complication of delirious mania that has important prognostic and treatment implications. Figure 1 also provides an overview of malignant versus nonmalignant delirious mania and treatment differences. Curiously, the co-occurrence of catatonic symptoms in delirious mania suggests similar treatment responses between the 2 syndromes. Thus,

[a]Department of Psychiatry and Behavioral Sciences, Eastern Virginia Medical School, Norfolk, Virginia

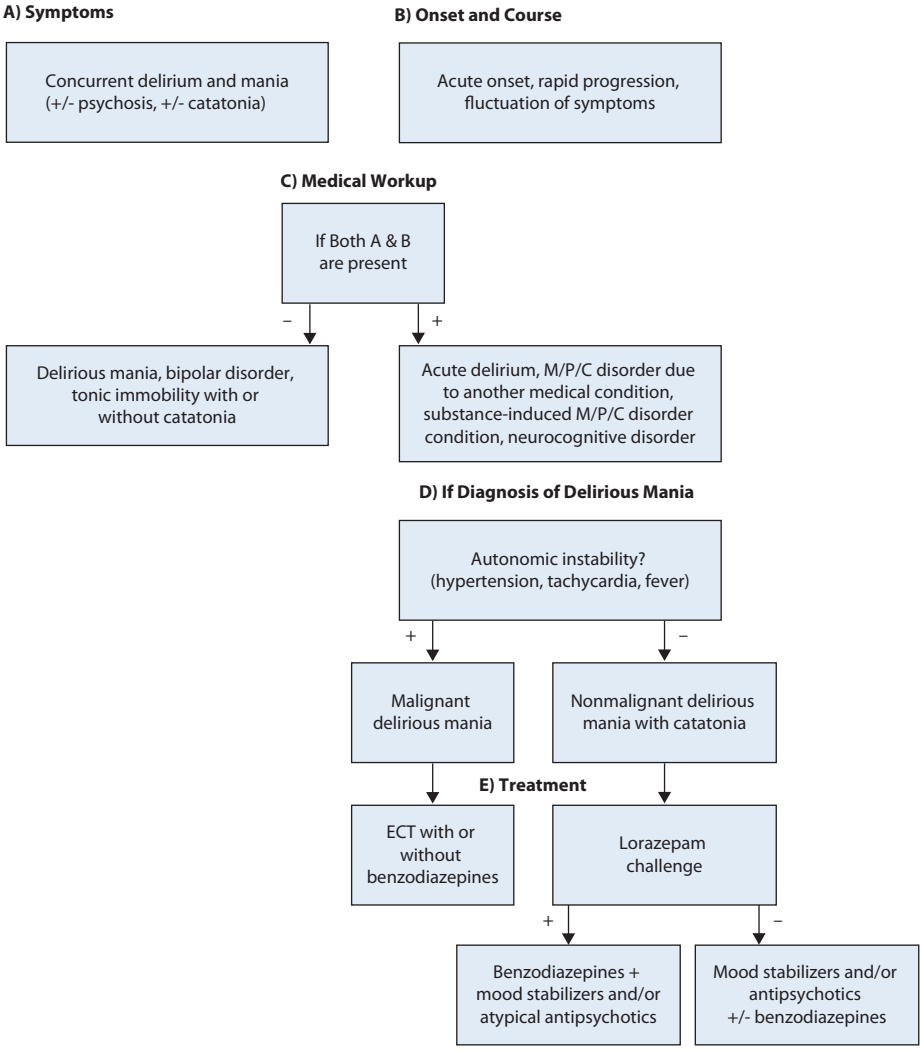
*Corresponding author: David R. Spiegel, MD, Department of Psychiatry and Behavior Sciences, Eastern Virginia Medical School, 825 Fairfax Ave, Norfolk, VA 23507 (spiegedr@evms.edu).

Prim Care Companion CNS Disord 2021;23(3):20l02764

To cite: Spiegel DR, Barger A, Monter E. A case of non-malignant delirious mania successfully treated with lorazepam and carbamazepine: a proposed diagnostic and treatment algorithm. *Prim Care Companion CNS Disord*. 2021;23(3):20l02764.

To share: https://doi.org/10.4088/PCC.20l02764

Figure 1. Diagnostic Algorithm: Evaluation and Treatment of Delirious Mania[1,9–12]



A) Our patient demonstrated most of the symptoms that have been classically associated with delirious mania, ie, acute onset of the excitement, grandiosity, emotional lability, delusions, and insomnia characteristic of mania, and the disorientation and altered consciousness characteristic of delirium.

B) Onset and course: acute, rapid with fluctuation of symptoms.

C) For a diagnosis of delirious mania, general medical, neurologic, and toxicologic causes of delirium, mania, psychosis, and catatonia are ruled out.

D) Delirious mania may be of a nonmalignant or malignant form. The latter is distinguished by significant hyperthermia, muscular rigidity, and/or autonomic instability.

E) In the malignant subtype of delirious mania, ECT with or without benzodiazepines is the primary treatment. We propose that lorazepam challenge would not be warranted in this subtype, as similar to malignant catatonia, prompt administration of ECT can decrease mortality, whereas delays to initiating ECT could result in adverse outcomes, including death.

In nonmalignant delirious mania:

1. Administration of lorazepam challenge.

2a. Positive result (ie, resolution/marked reduction of catatonic signs within 10 minutes of parenteral lorazepam administration): treatment includes benzodiazepines and mood stabilizers. Some, but not all authors, support use of atypical antipsychotics.

2b. Negative result: treatment includes mood stabilizers and atypical antipsychotics, with or without benzodiazepines.

In summary, our patient's presentation was as follows:

A) Symptoms
1. Elated mood, increased energy/excitement, and grandiosity (mania).
2. Fluctuation of attention and awareness (delirium).
3. Behavioral stereotypies, echolalia, verbigerations, grimacing, perseverations, catalepsy but without autonomic instability (nonmalignant catatonia).

B) Onset and Course
1. Symptoms developed within 5 days of admission.

C) Medical Workup
1. Remarkable for a primary ovarian tumor, metastatic to regional lymph nodes.
2. Brain magnetic resonance imaging (MRI) demonstrated no acute findings including metastasis or evidence of autoimmune/limbic encephalitis.
3. Cerebrospinal fluid evaluation was negative for cytology, growth on culture, and leukocytosis; protein and glucose levels were within normal limits and paraneoplastic antibodies were negative. She had no evidence of vital sign instability or muscular rigidity.
4. Urinalysis, complete metabolic panel, thyroid-stimulating hormone, and cyanocobalamin level were all within normal limits. Complete blood count showed a hemoglobin/hematocrit level of 9.9 g/dL/31.6%. C-reactive protein level was elevated at 16 mg/L, rapid plasma reagin was negative, and iron level was <19 µg/dL.
5. Urine drug screen and blood alcohol level were negative.

D) Diagnosis of Delirious Mania
1. No autonomic instability.
2. Diagnosis of nonmalignant delirious mania with catatonia.

E) Treatment
1. Lorazepam challenge was positive.
2. Therapeutic response to lorazepam and carbamazepine.

Abbreviations: ECT = electroconvulsive therapy, M/P/C = mood/psychotic/catatonic.

benzodiazepines/electroconvulsive therapy play a positive role and mood stabilizers provide overall benefit, regardless of the subtype of delirious mania.[10] Our patient's symptoms were consistent with nonmalignant delirious mania and were successfully treated with a combination of lorazepam and carbamazepine.

In conclusion, delirious mania is a potentially life-threatening but underrecognized neuropsychiatric syndrome. While only anecdotal-level evidence to base diagnostic and treatment recommendations exists, early recognition can significantly reduce morbidity and mortality.[13]

Published online: June 3, 2021.

Potential conflicts of interest: **Dr Spiegel** is in the speaker's bureaus of Allergen, Alkermes, Otsuka, and IntraCellular but has no conflict of interest in preparation of this manuscript. **Drs Barger** and **Monter** report no conflicts of interest related to the subject of this report.

Funding/support: None.

Patient consent: The patient provided verbal consent to publish the case report prior to her entering hospice care. Information has been de-identified to protect anonymity.

REFERENCES

1. Jacobowski NL, Heckers S, Bobo WV. Delirious mania: detection, diagnosis, and clinical management in the acute setting. *J Psychiatr Pract*. 2013;19(1):15–28.
2. Detweiler MB, Mehra A, Rowell T, et al. Delirious mania and malignant catatonia: a report of 3 cases and review. *Psychiatr Q*. 2009;80(1):23–40.
3. Young RC, Biggs JT, Ziegler VE, et al. A rating scale for mania: reliability, validity and sensitivity. *Br J Psychiatry*. 1978;133(5):429–435.
4. Inouye SK, van Dyck CH, Alessi CA, et al. Clarifying confusion: the confusion assessment method: a new method for detection of delirium. *Ann Intern Med*. 1990;113(12):941–948.
5. Bush G, Fink M, Petrides G, et al. Catatonia, I: rating scale and standardized examination. *Acta Psychiatr Scand*. 1996;93(2):129–136.
6. Marder SR, Sorsaburu S, Dunayevich E, et al. Case reports of postmarketing adverse event experiences with olanzapine intramuscular treatment in patients with agitation. *J Clin Psychiatry*. 2010;71(4):433–441.
7. Zyprexa (olanzapine) package insert. Indianapolis, IN: Lilly Research Laboratories; 2017.
8. Folstein MF, Folstein SE, McHugh PR. "Mini-mental state": a practical method for grading the cognitive state of patients for the clinician. *J Psychiatr Res*. 1975;12(3):189–198.
9. Fink M. Delirious mania. *Bipolar Disord*. 1999;1(1):54–60.
10. Karmacharya R, England ML, Ongür D. Delirious mania: clinical features and treatment response. *J Affect Disord*. 2008;109(3):312–316.
11. Vasudev K, Grunze H. What works for delirious catatonic mania? *BMJ Case Rep*. 2010;2010:bcr0220102713.
12. Walther S, Stegmayer K, Wilson JE, et al. Structure and neural mechanisms of catatonia. *Lancet Psychiatry*. 2019;6(7):610–619.
13. Lee BS, Huang SS, Hsu WY, et al. Clinical features of delirious mania: a series of five cases and a brief literature review. *BMC Psychiatry*. 2012;12(1):65.