Revisiting Delirious Mania in the Context of Neurosyphilis: A Case Report

Делириозная мания при нейросифилисе: клинический случай

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Case report

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ABSTRACT

BACKGROUND: Delirious mania (DM) is a severe neuropsychiatric syndrome characterized by the acute onset of delirium, psychosis and increased psychomotor activity. Its classification remains debated, with overlapping features of mania, catatonia, and delirium complicating diagnosis and treatment. The condition poses significant challenges in differential diagnosis, particularly in patients with comorbid medical conditions.

CASE REPORT: We report the case of a 52-year-old man with bipolar disorder who presented with acute agitation, disorientation, confabulation, incontinence, and severe behavioral disturbances, initially suggestive of DM. Despite targeted psychiatric treatment, his condition remained refractory until a syphilitic infection was identified, with a possible presentation of neurosyphilis, and treated with antibiotic therapy. Resolution of his symptoms followed, with the delirium persisting briefly after the mania had subsided, suggesting an organic contribution to his presentation.

CONCLUSION: This case highlights the importance of considering organic etiologies, such as neurosyphilis, in presentations of DM. It also supports the view that DM may represent a syndromic entity with both psychiatric and medical underpinnings, rather than merely a subtype of bipolar disorder. Early identification and treatment of DM, along with any underlying medical conditions, are crucial for patient recovery.

АННОТАЦИЯ

ВВЕДЕНИЕ: Делириозная мания (ДМ) — это тяжелый нейропсихиатрический синдром, характеризующийся острым возникновением делирия, психоза и повышенной психомоторной активности. Классификация заболевания остается предметом дискуссий, поскольку наличие симптомов — мании, кататонии и делирия, — присущих нескольким синдромам, усложняет его диагностику и лечение. Также это создает существенные трудности при дифференциальной диагностике, особенно у пациентов с сопутствующими заболеваниями.

КЛИНИЧЕСКИЙ СЛУЧАЙ: В представленном клиническом случае у мужчины 52 лет с биполярным расстройством наблюдались острая ажитация, дезориентация, конфабуляция, недержание мочи и выраженные поведенческие нарушения, первоначально трактовавшиеся как проявления ДМ. Несмотря на целевую психиатрическую помощь, состояние пациента оставалось рефрактерным вплоть до выявления сифилитической инфекции с возможной манифестацией нейросифилиса. После проведения антибактериальной терапии последовало разрешение симптомов. При этом после исчезновения мании кратковременно сохранялся делирий, что указывает на органическую природу заболевания.

ЗАКЛЮЧЕНИЕ: Данный клинический случай подчеркивает важность исключения органических причин (в частности, нейросифилиса) при диагностике ДМ. Кроме того, он подтверждает концепцию, согласно которой

ДМ не просто является подтипом биполярного расстройства, а может представлять собой синдромальную категорию, имеющую как психическую, так и соматическую основу. Раннее выявление и лечение ДМ, равно как и заболеваний, лежащих в ее основе, играют решающую роль в восстановлении пациента.

Keywords: *delirious mania; bipolar disorder; catatonia; neurosyphilis; electroconvulsive therapy*
Ключевые слова: *делириозная мания; биполярное расстройство; кататония; нейросифилис; электросудорожная терапия*

INTRODUCTION

Delirious mania (DM) is a severe neuropsychiatric syndrome characterized by the acute onset of delirium, increased psychomotor excitement and psychosis [1]. Delirium and psychosis are clinically distinct. The first one is defined as an acute fluctuating disturbance in attention and awareness due to an underlying medical condition, and it may be accompanied by psychotic symptoms (hallucinations or delusions) that are secondary to the confusional state [2]. In contrast, primary psychotic disorders such as schizophrenia or bipolar disorder with psychotic features typically present with preserved consciousness and sustained attention, despite marked alterations in thought content [2]. Although not formally classified in the Diagnostic and Statistical Manual of Mental Disorders, 5th Edition, Text Revision (DSM-5-TR) [3] or International Classification of Diseases, 11th Revision (ICD-11) [4], DM is extensively documented in clinical literature [5–7]. Since Calmiel's initial description in 1832, it has been identified by Kraepelin E. and, subsequently, Klerman G.L. as an extreme manifestation of mania [5, 6]. Several authors emphasize the frequent occurrence of catatonic symptoms within DM, observing that both DM and catatonia show significant responsiveness to electroconvulsive therapy (ECT) [1]. ECT is currently considered a safety first-line treatment for catatonia, including malignant and treatment-resistant forms, and in cases of DM [8–10]. Fink's classification further categorizes DM as a subtype of catatonia, alongside excited catatonia [1]. This condition closely parallels hyperactive or excited delirium, as observed in cases of neurosyphilis (NS) [11] as well as substance intoxication or withdrawal [12].

This case report outlines the clinical challenges encountered when managing presentations of suspected DM in psychiatric patients with a history of affective disorder, comorbid substance abuse, and engagement in unprotected sexual activities with multiple partners.

CASE REPORT

Patient information

A 52-year-old Caucasian male with a personal history of bipolar disorder (BD), substance abuse, and multiple sexual partners, and a family history of major affective disorders (mother and sister), presented in January 2024 with a worsening mood disorder likely exacerbated by recent cocaine use. He had been stable for seven years on valproic acid 1500 mg/day, lithium carbonate 900 mg/day, and quetiapine 300 mg/day.

Clinical findings

Following this decline, his psychiatrist recommended a short-term residential stay for therapeutic stabilization. Approximately 20 days into the stay, the patient developed an acute dysphoric mood, marked psychomotor agitation, disorientation, confabulation, incontinence, sporadic visual hallucinations, and inappropriate toileting. He also exhibited severe thought and behavioral disorganization, hypersexuality, and a tendency toward physical aggression. Consequently, he was transferred to a psychiatric emergency department.

Diagnostic assessment

Routine blood tests and a CT-scan were unremarkable, and toxicology screening ruled out recent substance use.

Preliminary diagnosis

Given his history of BD, DM was suspected as a potential diagnosis.

Relevant interventions with outcomes

The patient was admitted to the psychiatric ward, and his medication regimen was modified: risperidone was increased to 8 mg/day, delorazepam[1] 6 mg/day was added, and quetiapine was replaced with olanzapine

1 *Editor's note:* The drug is not registered in the Russian Federation.

20 mg/day, while lithium carbonate and valproic acid were continued. Despite these adjustments, his condition failed to improve over the following week; he remained persistently disoriented, restless, and displayed purposeless overactivity. Subsequently, VDRL-test returned positive, and TPHA-test confirmed syphilis while an HIV test was negative. Due to his agitation, a brain MRI and lumbar puncture could not initially be performed.

Revised diagnosis

Following the infectious disease investigations, the diagnostic orientation shifted to NS.

Therapeutic intervention

Intramuscular benzylpenicillin therapy was started, and his psychiatric medication was adjusted to monotherapy with haloperidol 6 mg/day.

Follow-up and outcomes

After three weeks of antibiotic therapy, the patient's symptoms rapidly improved, with notable reductions in agitation, and within days, a reduction in delirium. He had no recollection of events during the acute phase. Subsequent brain MRI and lumbar puncture findings were normal. He was discharged on lithium carbonate 600 mg/day and haloperidol 2 mg/day. Four months later, at follow-up, he showed no signs of mood or psychotic symptoms and reported residual memory gaps from the period of delirium.

Prognosis

The patient's prognosis appears favorable. The suspected NS was identified and treated promptly with appropriate antibiotic therapy, leading to a rapid and sustained remission of neuropsychiatric symptoms [13]. From a psychiatric perspective, the patient has a prior diagnosis of bipolar disorder, for which he is now receiving lithium prophylaxis. With therapeutic drug monitoring to ensure serum levels remain within the effective range, lithium remains a first-line mood stabilizer with well-documented efficacy in preventing relapses [14]. Continued abstinence from substance use is essential for long-term stabilization and to reduce the risk of further decompensation [15].

Timeline

The patient timeline is presented in the Figure 1.

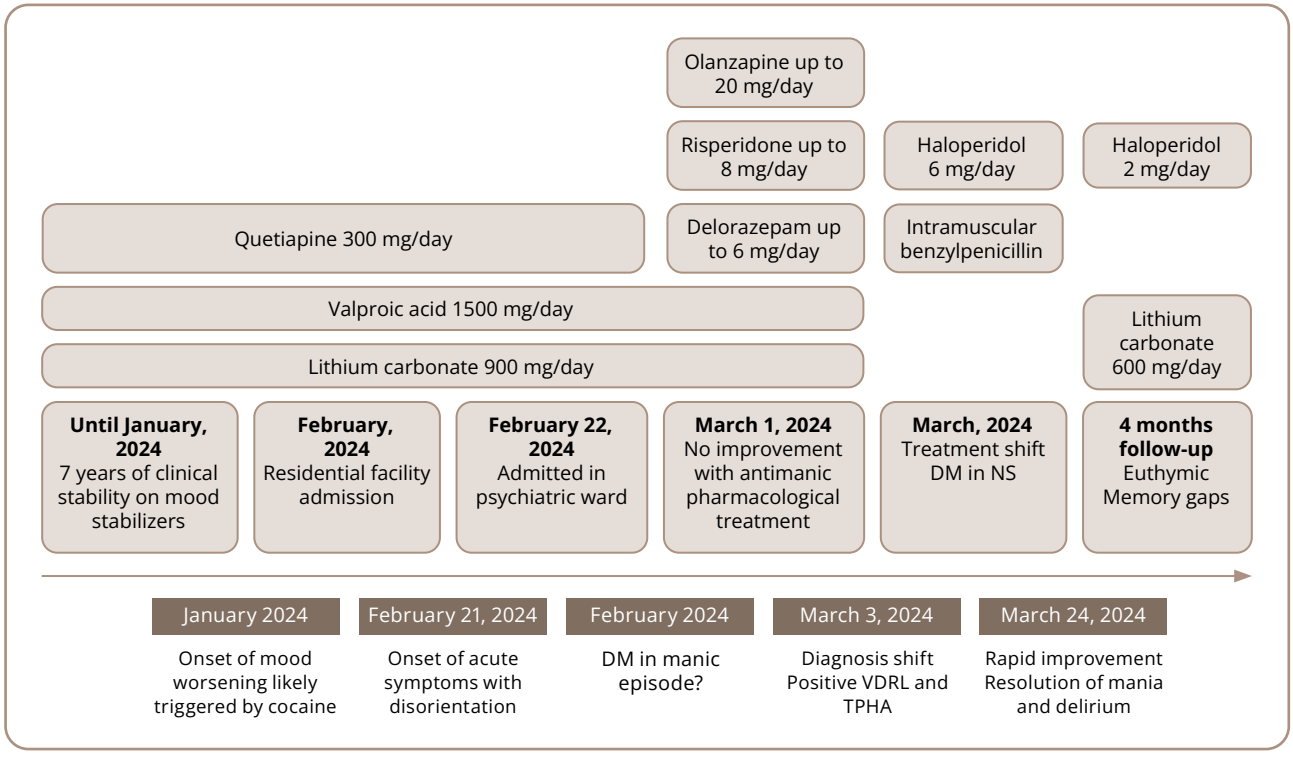

Figure 1. Chronology of the patient's disease.

Note: TPHA — Treponema pallidum hemagglutination assay; VDRL — veneral disease research laboratory test.

Source: Hirsch et al., 2025.

DISCUSSION

Case report summary

This case highlights the diagnostic complexity encountered in the assessment and management of suspected DM, given its lack of clear nosological classification and the absence of established guidelines for its differential diagnosis and treatment.

Summary interpretation of the results

Diagnostic challenges and initial hypotheses

Initially, the most probable diagnostic hypothesis was DM in the context of a manic episode, considering that our patient met 5 out of the 6 clinical criteria proposed by Bond for DM: acute onset, presence of mania at some point during the episode, features of delirium, personal history of mania or depression, and family history of major affective disorders [7].

Additionally, another characteristic that led us to consider DM was the fact that the patient exhibited a continuous tendency toward incontinence/inappropriate toileting, pouring water on the floor, and denudativeness, which were described as distinctive of DM in Karmacharya et al. study [16].

Given the impossibility of administering ECT due to difficulties in obtaining informed consent from the patient, a pharmacological treatment was established, taking into account the literature's recommendations regarding the positive role of benzodiazepines while avoiding the use of typical antipsychotics [17, 18]. Previous clinical reports had highlighted the utility of olanzapine, quetiapine, risperidone, valproate, and lithium [19], as confirmed in the study by Karmacharya et al. [16], which was the therapeutic regimen we implemented.

Alternative diagnostic hypotheses

Another diagnostic option we considered, for which the therapy we chose could have been equally effective, was excited delirium related to substance withdrawal, particularly from cocaine [12]. The patient had indeed reported to his psychiatrist that he had used cocaine before admission to the psychiatric residential facility. Although the exact signs and symptoms of excited delirium are difficult to define precisely, the criteria most frequently cited include hyperaggressive behavior with superhuman strength, a combative attitude toward the police, hyperactivity, bizarre behaviors, unusual pain tolerance, and hyperthermia [12]. However, these criteria do not occur with equal frequency, and none appear to be mandatory [12]. In our patient, hyperthermia was never present.

Most cases of excited delirium occur in the context of psychoactive substance abuse or among psychiatric patients [20]. In more than 90% of cases, toxicology screening tests are positive, and 50% of patients have a pre-existing psychiatric background [21]. Benzodiazepines or classic antipsychotics, such as haloperidol, are the most frequently proposed treatments [20]. Recently, ketamine has also been suggested as an alternative for acutely agitated patients, offering the added benefit of maintaining airway patency and spontaneous ventilation [22].

Shift toward neurosyphilis

Given the lack of improvement with standard therapy for a manic episode, as expected under Bond's sixth criterion [7], together with the absence of response to the withdrawal hypothesis and the positive TPHA test, we considered a diagnostic reorientation toward possible NS to be appropriate, based on our clinical judgment.

NS is an infection of the central nervous system caused by the spirochete *Treponema pallidum* [23]. The frequency of psychiatric signs and symptoms associated with NS ranges from 33 to 86% [24]. Personality changes, dementia, abnormal behavior, and emotional problems are the most common psychiatric manifestations, though depression, psychosis, and mania have also been noted [25]. In a study of 52 NS patients, 34% presented with cognitive impairment, and 25% showed signs of delirium [26]. Although these conditions may coexist, they represent distinct clinical phenomena. Cognitive decline typically develops progressively and manifests as a stable disturbance of memory, attention, or executive function, with preserved consciousness [27]. In contrast, delirium is an acute, fluctuating disturbance in attention and awareness, often accompanied by altered consciousness and disorganized thinking [28]. This variable, non-specific presentation not only creates diagnostic challenges but also leads to potential therapeutic missteps. A case report very similar to ours by Wahab et al. described a male patient in his 40s who was disoriented to time, place, and person, agitated, aggressive, and exhibiting bizarre behavior, initially diagnosed and treated for psychosis with a poor response to antipsychotic therapy, later testing positive for VDRL and improving with antibiotic treatment [29].

Therapeutic approach

In our patient, once the hypotheses of DM in the context of mania and excited delirium due to cocaine withdrawal became less likely, the clinical picture of delirium associated with NS became predominant. As a result, haloperidol was introduced as monotherapy alongside antibiotic therapy. A recent review has shown that, in patients with delirium, haloperidol may reduce mortality and likely results in little to no difference in the occurrence of serious adverse events or serious adverse reactions compared with placebo [30].

The sequence of clinical improvement — mania first, followed by delirium — further supports the hypothesis that delirium was not driven by mania but rather by the underlying infection [10].

Limitations in diagnostic confirmation

Although the VDRL serum test is a screening test for syphilis, the Centers for Disease Control and Prevention (CDC) outline the need to satisfy two diagnostic criteria for the diagnosis of NS: one being a reactive cerebrospinal fluid (CSF)-VDRL test and the second being CSF abnormalities with clinical signs and symptoms consistent with syphilis [31]. In our case, a limitation was the inability to perform a lumbar puncture due to psychomotor agitation. However, the negativity of the CSF after antibiotic treatment does not exclude a diagnosis of NS, as serological and CSF abnormalities after treatment may become ambiguous and difficult to interpret [32]. Similarly, regarding the negative brain MRI, the literature indicates that brain MRIs in most NS patients are normal or show non-specific changes [33].

Implications for clinical practice

Based on our clinical experience, we believe that, similar to catatonia, it may be more appropriate to conceptualize DM as a syndrome with both psychiatric and organic underpinnings, rather than solely as a manifestation of BD. Likewise, as with catatonia, the treatment could target DM itself, such as with ECT and benzodiazepines, and its underlying cause. Adopting such a perspective could broaden diagnostic frameworks and guide more effective treatment strategies.

In terms of distinguishing catatonia from DM — considering that some authors have classified DM as a subtype of catatonia [1] — tools such as spatial-temporal psychopathological assessments and the concept of *personal experience* might prove valuable [34]. Northoff et al. argue that patients with catatonia often report feeling overwhelmed by emotions and frequently retain memories of the acute phase, recalling, for example, specific interactions with medical staff during episodes of psychomotor agitation or immobility [34]. In contrast, patients with DM typically experience profound memory gaps, rendering them unable to recall most events during the acute phase, such as family visits or medical interventions [16, 35].

Finally, regarding the relationship between DM and excited delirium, it is evident that the lack of a universal and objective definition of excited delirium remains a major obstacle [12]. Developing such a definition is urgently needed to enable more structured and standardized research with higher levels of evidence, such as prospective cohorts investigating toxic, metabolomic, and genetic factors [12].

CONCLUSION

This case illustrates the need for a broader, integrative approach to understanding and managing DM. A critical objective for future research is to harmonize the definitions of DM and its specific signs, while also developing clear thresholds for making a diagnosis. Studies of spatiotemporal psychopathology could contribute significantly to refining these criteria. Additionally, there is an urgent need for clinical trials focused on DM, as current treatment data are predominantly derived from small case reports, which limits the generalizability of findings.

Informed consent: Written informed consent for publication of clinical details was obtained from the patient, as well as for the publication of any data in this article that could potentially identify him. This consent was provided after the resolution of the delirious mania, when the patient had fully regained decision-making capacity.

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