Clinical Characteristics and Treatment Responses of Patients Presenting with Delirious Mania: Case Series

Клинические характеристики и ответ на лечение у пациентов с делириозной манией: серия клинических случаев

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Case report

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ABSTRACT

BACKGROUND: Delirious mania (DM) is a severe psychiatric condition having rapid onset of delirium, mania, and psychosis. It is an emergency condition as it has acute onset and is characterized by extreme hyperactivity. Catatonic signs may also be present. Very few cases have been reported from India, hence making it imperative to study its clinical characteristics and possible treatment, which can help in providing care to such patients in emergency settings.

CLINICAL CASES DESCRIPTION: This paper describes four cases with a diagnosis of DM — demography, clinical features, investigations, treatment. All the patients had an acute onset and rapid progression of symptoms, with clinical symptoms of talkativeness, increased psychomotor activity, decreased need for sleep, aggressive and violent behavior, increased libido, increased appetite with delusion of grandiosity, disorientation to time/place/person, impaired memory of recent events, impaired attention with fluctuating course, negativism, echolalia, and echopraxia.

CONCLUSION: There is a high likelihood of misdiagnosing DM in the absence of diagnostic guidelines. There should be an active search for the underlying aetiology in all cases of DM. Atypical antipsychotics and mood stabilizers may be used to treat less severe forms of DM. Modified electric convulsive treatment and intravenous benzodiazepines elicit a good response.

АННОТАЦИЯ

ВВЕДЕНИЕ: Делириозная мания (ДМ) — это тяжелое психическое нарушение, характеризующееся быстрым возникновением и сочетанием делирия, мании и психоза, также возможны симптомы кататонии. Такое состояние является неотложным ввиду характерных для него острого начала и крайнего возбуждения. В Индии зарегистрировано очень мало случаев этого расстройства, поэтому важно изучать его клинические характеристики и приемлемые методы лечения, чтобы иметь возможность обеспечить таким пациентам адекватную неотложную помощь.

ОПИСАНИЕ КЛИНИЧЕСКИХ СЛУЧАЕВ: В статье описано 4 случая пациентов с диагнозом ДМ — их демографические характеристики, клинические особенности, лабораторные и инструментальные данные, лечение. У всех пациентов отмечали острое начало и быстрое прогрессирование клинических симптомов. Частыми проявлениями были многоречивость, повышенная и психомоторная активность, сниженная потребность во сне, агрессивное и буйное поведение, усиление либидо, повышенный аппетит, бред величия, дезориентация во времени/пространстве/

личности, нарушение памяти на недавние события, нарушение внимания по типу неустойчивости, негативизм, эхолалия, эхопраксия.

ЗАКЛЮЧЕНИЕ: В связи с отсутствием специфических диагностических рекомендаций для делириозной мании высока вероятность допущения диагностической ошибки. Во всех подобных случаях необходимо активно искать этиологические факторы, лежащие в основе ДМ. Для лечения менее тяжёлых форм ДМ могут применяться атипичные антипсихотические препараты и нормотимики. Хороший терапевтический эффект дают модифицированная электросудорожная терапия и внутривенное введение бензодиазепинов.

Keywords: *mania; delirious mania; delirium; electroconvulsive therapy; case report*
Ключевые слова: *мания; делириозная мания; делирий; электросудорожная терапия; клинический случай*

INTRODUCTION

Delirious mania (DM) was previously known as Bell's mania. Delirium, mania, and psychosis constitute the main clinical features of this condition. It is a severe psychiatric syndrome in which the clinical features have a rapid onset. It can morph into an emergency situation, as it may lead to the sudden onset of severe agitation. It can be described as "a syndrome of the acute onset of hyperactivity, emotional lability, grandiosity and insomnia characteristic of mania, and the disorientation and altered consciousness characteristic of delirium" [1]. Catatonic signs and autonomic dysfunction may accompany the condition. Catatonic signs and symptoms may include mutism, grimacing, stereotypy, mannerisms, rigidity, negativism, automatic obedience, and echopraxia/echolalia (i.e., mimicking of the examiner's movements/speech) [2]. Kraepelin used the term DM; however, Calmeil described these cases extensively. He identified high morbidity and mortality in cases of DM [3, 4]. This was also found by Bell in 1849, who reported a 75% mortality rate in admitted patients with DM [5]. Carlson and Goodwin published a case series wherein 6 out of 20 patients with a diagnosis of mania were not oriented to time and place [6]. Ritchie et al. have found that the incidence of delirium in hospitalized patients with bipolar disorder is 35.5% [7]. In the absence of a consensus on the diagnostic criteria of DM, the incidence of DM varies across studies. There are no standardized diagnostic guidelines or clinical assessment measures. Very few cases have been reported from India, hence making it imperative to study its clinical characteristics and possible treatment, which can help in providing care to such patients in emergency settings. The profound hyperactivity encountered in this condition is distressing to both the caregivers and clinicians providing treatment. Unfortunately, the information gathered so far has remained limited to case reports, which provide a similar picture. We hope this work will be of help to clinicians in successfully diagnosing and treating patients with DM.

Our aim was to examine the clinical profile and treatment responses of patients presenting with delirium and mania at a government psychiatric inpatient unit.

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CLINICAL CASES

Case 1

Patient information

Mr. N., a 40-year-old married male, educated to class 8th, unemployed, belonging to a Muslim nuclear family of lower socio-economic status. He presented with complaints of over-talkativeness, increased goal directed activity, decreased need for sleep, violent behavior, increased libido, increased appetite, and decreased self-care since 3 days. He had a past history of manic episode 9 years prior, which resulted in 20 days of treatment and was taken off treatment after remission. He had a nil significant family and personal history.

Clinical findings

At the time of admission, the patient was conscious but had no orientation to time or place. He showed increased psychomotor activity, talked excessively, was extremely irritable, and sometimes exhibited disinhibited behavior of disrobing in front of others. He talked very highly of himself. He had impaired attention span and poor memory of recent events. He refused to follow commands like putting out his tongue or extending his hands in front of him for examination. He would repeat words spoken to him and sometimes mimic his examiner's behavior.

Diagnostic assessment

Diagnostic testing: Upon investigation there was increased Total Leucocyte Count (TLC) — 15,940/mm^3 (normal — 4,000–11,000/mm^3), increased Absolute Neutrophil Count (ANC) — 14,940/mm^3 (normal — 2,500–6,000/mm^3), increased Serum Glutamic Oxaloacetic Transaminase (SGOT) — 223 U/L (normal — 8–45 U/L), increased Serum Glutamic Pyruvic Transaminase (SGPT) — 142 U/L (normal — 7–56 U/L). All routine haematological investigations other than these were within normal range. Non-Contrast Computed Tomography of the head did not show any anomaly.

Diagnostic challenges: As the testing was done in a government-funded health institution, the patient did not face any financial burden related to bearing the diagnostic cost.

Diagnosis: A provisional diagnosis of DM with a differential diagnosis of bipolar disorder and current episode of mania with psychotic symptoms. Encephalitis was also considered.

Therapeutic intervention

The patient was administered several doses of injections. Haloperidol 5 mg intramuscularly with injections. Promethazine 25 mg intramuscularly, but the patient responded poorly to it, after which he was started on injections. Lorazepam 2 mg intravenously repeated doses (maximum — 8 mg/d) to which his response was good. He was also started on Lithium, which was optimized to 900 mg/d and Thioridazine optimized to 500 mg/d.

Follow-up and outcomes

By day 6 of admission, there was a 50% reduction in symptoms (reduction in Young Mania Rating Scale, YMRS, — from 36 to 20). The patient was febrile on day 7 and exhibited shortness of breath. He was referred for this and was diagnosed with pulmonary tuberculosis, with pleural effusion. He was discharged on medical grounds.

Case 2

Patient information

Mrs. S., a 22-year-old married female, uneducated, a homemaker belonging to a Hindu nuclear family of lower socio-economic status. She presented with complaints of hyperactivity, abusive and agitated behaviour, excessive talkativeness, hypersexuality-sexual gestures, disrobing, sleep disturbance since 4 days and no significant family and personal history. She is a known case of bipolar affective disorder.

Clinical findings

At the time of admission, the patient was conscious but was not oriented to time and place. She suffered from impaired attention span and poor memory of recent events. She was extremely restless and would get up from her bed purposelessly. She talked rapidly, and sometimes it was difficult to make sense of what she was saying. She displayed a labile affect and would go from crying to bursting into laughter in an instant. She displayed delusion of grandiosity, flight of ideas, poor insight, and impaired judgement. She often repeated the words spoken to her and sometimes mimicked her examiner's behavior. All routine haematological investigations like complete blood count, liver function test, renal function test, thyroid function test, and blood sugar were within normal range except.

Creatine phosphokinase (CPK) — 202 mcg/L (normal — 10–120 mcg/L). The neuroimaging finding was non-significant.

Therapeutic intervention

Upon treatment the patient showed no response to intravenous Lorazepam up to 12 mg/d in divided doses: hence, she was started on a Modified Electric Convulsive Treatment (MECT), to which she showed a good response. She went through 6 sessions of MECT, which resulted in a reduction in the YMRS score from 48 to 8. Delirium resolved by the 2nd day of MECT. She was discharged on Lithium 900 mg/d, Risperidone 8 mg/d, and Trihexyphenidyl (THP) 2 mg/d in divided doses.

Follow-up and outcomes

The patient was discharged with significant improvement.

Case 3

Patient information

Mr. K., a 35-year-old married male, educated to class 5th, unemployed, belonging to a Muslim nuclear family of lower socio-economic status, with a past history of pulmonary tuberculosis (treated) and no significant personal or family history. He had undergone an episode of DM 6 years prior. Currently, he displays over-talkativeness, increased goal-directed activity-overspending, increased libido, aggressive behavior, grandiosity, and a decreased need for sleep for 10 days.

Clinical findings

On examination, the patient was not oriented to time, place, or person. He had impaired attention span and poor memory of recent events. No medical cause was identified for his delirium. He often repeated the words spoken to him and sometimes mimicked his examiner's behavior. All routine haematological investigations and neuroimaging findings were within normal range.

Therapeutic intervention

The patient was started on intravenous Lorazepam optimized up to 6 mg/d in divided doses and showed improvement in delirium within the next 3 days. Later, he was treated with Sodium Valproate optimized up to 1,500 mg/d, Lithium optimized up to 900 mg/d, Risperidone optimized up to 8 mg/d, and was discharged 25 days after admission with a change in YMRS from 32 to 6.

Follow-up and outcomes

This patient was discharged with significant improvement.

Case 4

Patient information

Mr. A., a 38-year-old male, educated to class 12th, working as a factory helper, belonging to an Hindu nuclear family of lower socio-economic status with a history suggestive of multiple manic episodes dating back 15 years, with current presentation from 7 days with abrupt onset of aggression, over religiosity, always ready to engage in some activity, decreased need for sleep, grandiosity, poor personal hygiene, and decreased appetite.

Clinical findings

He was not oriented to time during admission. He had impaired attention span and poor memory of recent events. He had no significant personal or family history. He talked rapidly and often repeated the words spoken to him. He would be extremely restless during interviews and mimic his examiner's behavior. He displayed a labile affect and claimed to have supernatural powers. All routine haematological investigations were within normal range.

Therapeutic intervention

The patient was started on Lithium optimized up to 900 mg/d and Thioridazine optimized up to 600 mg/d and showed minimal improvement; hence, MECT was started and a total of 8 sessions were administered, to which he showed a good response, with a reduction in the YMRS score from 44 to 11. Later, Lurasidone was started, which was optimized up to 160 mg/d; and Sodium Valproate, optimized up to 1,000 mg/d.

Follow-up and outcomes

The patient was discharged with significant improvement.

Cases summary

The cases presented in this study are summarized in Table 1.

DISCUSSION

This case report adds to the available medical literature on the clinical features, risk factors, investigations to be ordered, and treatment of DM. This information will be of help to clinicians in improving their knowledge and modifying their treatment methods in order to achieve a faster response. This is extremely important as patients with DM present extreme hyperactivity and might pose an imminent threat of harm to themselves or others. However, this study is a case series and the documentation of such case reports dates back to the 19th century. There exist no diagnostic guidelines for this condition and no higher level of evidence available for this condition. This saps interest among researchers who want to analyze such cases. However, every mental health institution providing treatment to a large number of patients often faces challenges in the identification and adequate treatment of this condition: hence, such studies should continue in order to help upgrade clinicians' knowledge and skills, with a view to alleviating the distress of patients and their caregivers. The onset of DM usually happens in early adulthood. It is characterized by disorientation, extreme psychomotor activity, emotional lability, delusions, and hallucinations [8, 9]. After recovery, patients are unable to recall the events that occurred during their episode of illness. The clinical picture might indicate an exploration of the differentials of drug toxicity, metabolic disorders, and central nervous system infections. Electroconvulsive therapy and high-dose benzodiazepines provide effective management of DM [10, 11]. Putative aetiologies of DM include the following:

- Klerman described DM as a variant of classical bipolar disorder [12];
- Mann et al. defined Delirious mania to have resulted from underlying medical and neuropsychiatric aetiologies [13];

Table 1. Summary of clinical cases

Parameter	Case 1	Case 2	Case 3	Case 4
Patient age	40	22	35	38
Patient gender	M	F	M	M
Family history of bipolar disorder	-	-	-	-
Past history of manic episode	+	+	+	+
Onset of symptoms	Acute	Acute	Acute	Acute
Progress of symptoms	Rapid	Rapid	Rapid	Rapid
Manic symptoms	↑Talk, ↑PMA, ↓need for sleep, ↑libido, ↑appetite, ↓self-care. Aggressive and violent behavior. Del. of grandiosity.	Hyperactivity, flight of ideas. Abusive and agitated behavior. Hypersexuality-disrobing self-sexual gestures disrobing. Sleep disruption. Emotional lability.	↑Talk, ↑PMA, ↓need for sleep, ↑libido, ↑appetite, ↓self-care. Aggressive and violent behavior. ↑Goal directed activity (overspending). Del. of grandiosity.	↑Talk, ↓need for sleep, ↓self-care, ↑PMA. Aggression, over religiosity, disrobing self. Del. of grandiosity. Emotional lability.
Delirium signs	Disoriented to time and place. Impaired memory of recent events. Impaired attention span with fluctuating course.	Disoriented to time and place. Impaired memory of recent events. Impaired attention span. Floccillation with fluctuating course.	Disoriented to time, place and person. Impaired memory of recent events. Impaired attention span with fluctuating course.	Disoriented to time, impaired memory of recent events. Impaired attention span, floccillation with fluctuating course.
Catatonic signs	Negativism Echolalia Echopraxia	Echolalia Echopraxia Negativism	Echolalia Echopraxia	Echolalia Echopraxia
Treatment given	No response to intramuscular antipsychotics. Thioridazine 500 mg/d. Lithium 900 mg/d. LZM 8 mg/d intravenously till Day 6 of admission with 50% remission.	No response to intravenous Lorazepam 12 mg/d. Good response with MECT-6 sessions, delirium resolved by 2nd MECT. D/C on Lithium 900 mg/d. Risperidone 8 mg/d. THP 2 mg/d.	Good response to intravenous Lorazepam 6 mg/d. D/C on Valproate 1,500 mg/d. Lithium 900 mg/d. Risperidone 8 mg/d.	No response to intramuscular antipsychotics and Lithium 900 mg/d. Thioridazine 600 mg/d. Good response with MECT-8 sessions. D/C on Lurasidone 160 mg/d. Valproate 1,000 mg/d.
Haematological findings	↑TLC, ↑ANC, ↑SGOT, ↑SGPT with fever	Haematological, Neuroimaging-WNL	Haematological, Neuroimaging-WNL	Haematological, Neuroimaging-WNL
YMRS score	36 to 20	48 to 8	32 to 6	44 to 11
Course	Referred to GHPU, diagnosed with Pulm. TB with PE	D/C with significant improvement	D/C with significant improvement	D/C with significant improvement

Note: PMA — Psychomotor Activity, LZM — Lorazepam, D/C — Discharged, MECT — Modified Electric Convulsive Treatment, THP — Trihexyphenidyl, TLC — Total Leucocyte Count, ANC — Absolute Neutrophil Count, SGOT — Serum Glutamic Oxaloacetic Transaminase, SGPT — Serum Glutamic Pyruvic Transaminase, WNL — Within Normal Limits, YMRS — Young Mania Rating Scale, GHPU — General Hospital Psychiatry Unit, TB — Tuberculosis, PE — Pleural Effusion. The arrows (↑) show the increase in level, the arrows (↓) show the drop in level.

- Taylor and Fink described DM as a variant of catatonia (i.e., excited catatonia) [14];
- Dunayevich and Keck stated that DM is similar to schizophrenia [15].

Bond has defined the criteria for a diagnosis of DM [4, 16], which include the following:

- acute onset with or without premonitory signs of irritability, insomnia or emotional withdrawal;
- the presence of the hypomanic or manic syndrome (as defined by DSM-III criteria) at some point in the illness;
- development of signs and symptoms of delirium;

Table 2. Pathophysiology of DM

Pathophysiology of delirium	Pathophysiology of catatonia	Pathophysiology of mania
↓Acetylcholine — leads to decreased awareness	↓GABA binding in the lateral orbitofrontalcortex — leads to echolalia/echopraxia	↓Prefrontal cortex activity — leads to socially inappropriate behaviour
↑Dopamine — leads to perceptual disturbance	Aberrations in glutamate signaling at posterior parietal cortex — leads to posturing	↑Dopamine — leads to manic symptoms of elevated mood, increased energy and psychosis
↑GABA — leads to sleep disturbance	Abnormal dopamine signaling in corticothalamic loops — leads to autonomic dysregulation of malignant catatonia	
↑Serotonin — leads to confusion	The increase in glutamate at NMDA-receptors in frontal lobe leads to inhibition of GABA. Therefore, NMDA-receptor antagonists may lead to treatment of catatonia by inhibiting glutamate and increasing GABA	

Note: The arrows (↑) show the increase in level, the arrows (↓) show the drop in level.

- a personal history of either mania or depression;
- a family history of major affective disorder;
- responsivity to standard treatments for mania.

Research does not offer comments on any specific pathophysiology of DM. However, its pathophysiology can be hypothesized on the basis of the known neuropathophysiology of its three principal clinical features as stated below (Table 2) [10].

In all 4 cases, a past history of manic episode was present [17]. The patient's presentation in hospital during the episode had an acute onset, and the symptoms had a rapid progression. The common clinical features included:

- manic symptoms — decreased need for sleep, irritability/aggression, increased PMA, increased talkativeness, increased goal directed behaviour-hyper-religiosity, hypersexuality, emotional lability, grandiosity;
- delirium signs-disorientation to time/place/person, impaired recall of recent events, impaired attention;
- catatonic signs of negativism/echopraxia/echolalia.

The haematological and neuroimaging findings were within normal range, except in one case, where there was comorbidity of pulmonary tuberculosis. There was a good response to intravenous Lorazepam or MECT in all cases, similarly to that found in other studies [17, 18]. MECT yielded drastic improvement whenever used. There was a good response to antipsychotics and mood stabilizers upon stabilization of the acute stage with intravenous Lorazepam or MECT. In all the cases, patients had followed up in OPD post discharge, with continuous remission of symptoms. The patients were prescribed oral antipsychotics and/or mood stabilizers, and/or benzodiazepines.

A clinician should strongly consider the diagnosis of Delirious mania whenever delirium, mania, and psychosis are present concurrently; the additional presence of catatonia further bolsters the confirmation of DM [19]. In cases where the risk of harm to self or others is high, benzodiazepines and/or MECT may provide immediate relief [3, 18].

CONCLUSION

DM can be rightfully called a severe, but rare condition that involves severe incessant agitation. This leads to the referring of cases to emergency. Misdiagnosis is likely in such cases, with the most common differential being the manic episode. Ignorance of this condition and its different modalities of treatment can turn into an ordeal for the treating clinicians, leading to mismanagement and morbidity, or mortality.

Our current classificatory system does not mention DM under a major heading due to its complex symptomatology. In all cases of DM, all potential underlying etiologies must be investigated. Atypical antipsychotics and mood stabilizers may be used to treat less severe forms of DM. Early recognition and definitive treatment of DM in an acute setting can be life-saving. This case series will be of help to clinicians in identifying cases of DM and providing treatment at the early stages, leading to a faster response and minimized morbidity.

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