DOI: 10.7860/JCDR/2024/73003.20157

Case Report

Psychiatry/Mental Health Section

Thyrotoxicosis Masquerading as Late Onset Mania: A Case Report on Treatment of Mania in Thyroid Storm

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ABSTRACT

Manic episodes, typically associated with Bipolar Affective Disorder (BPAD), can also arise from medical conditions such as thyrotoxicosis, leading to "secondary" or "organic" mania. Thyrotoxicosis, characterised by excessive thyroid hormone levels, can cause neuropsychiatric symptoms and, in severe cases, result in a thyroid storm. Present case is of a middle-aged male patient without a prior psychiatric history who presented with manic symptoms such as overspending, over familiarity, and agitation, alongside physical signs of thyrotoxicosis, including weight loss and tachycardia. He was diagnosed with a thyroid storm secondary to Graves' disease. Despite the rarity of the condition and the absence of established guidelines, management prioritised controlling sympathetic overactivity and restoring euthyroid status. Lithium, along with antipsychotics were chosen for their minimal impact on the QTc interval, was utilised to effectively address the manic symptoms. Aggressive medical management targeting both thyroid function and manic symptoms led to significant improvement. This case highlights the critical need to consider medical aetiologies in psychiatric presentations and underscores the importance of early diagnosis and multidisciplinary management to reduce morbidity. Collaborative efforts among medical specialties are essential to address the complexities of such cases.

Keywords: Bipolar disorder, Graves' disease, Hyperthyroidism

CASE REPORT

A male patient in his late forties, belonging to lower socio-economic status, was brought to the Department of Psychiatry with complaints of overspending, over familiarity, over talkativeness, increased grooming, decreased need for sleep, increased goal-directed activity, expansive ideas, and an elated and labile mood for the past four months. He exhibited frequent anger outbursts, often without provocation, directed both at family members and strangers. Over the past four months, the patient had escalated his daily consumption of smoked tobacco, increasing from initially smoking 2-3 beedis per day to smoking up to 20 beedis per day. He also commenced daily alcohol intake during this period, drinking up to a quarter of whisky per day. Additionally, he experienced significant weight loss, excessive sweating, and hair loss over the last four months, along with visual and auditory hallucinations and fluctuating sensorium for the last three days. The patient did not have any diagnosed medical or psychiatric co-morbidities. There was a family history of tobacco use among multiple first and second-degree relatives, as well as a history of psychosis in a second-degree relative.

On examination, the patient was poorly built (BMI: 17 kg/m^2), tachycardic (HR: 120 bpm), tachypnoeic (RR: 22 breaths/min), febrile (102°F), with no midline neck swelling. He was conscious but disoriented, with increased psychomotor activity, increased speech, and occasional irrelevant remarks. Ward observation revealed visual and auditory hallucinations. Routine investigations on the first day of admission showed significantly elevated fT4, elevated fT3, and low Thyroid Stimulating Hormone (TSH) [Table/Fig-1]. A physician's reference was sought, and the patient was provisionally diagnosed with hyperthyroidism in thyroid storm with bipolar disorder in mania, with a differential diagnosis of multifactorial delirium, including secondary to alcohol withdrawal. Oral carbimazole 10 mg TID, intravenous hydrocortisone 100 mcg TID, and oral propranolol 80 mg were initiated, along with antipyretics. Carbimazole was switched to oral propylthiouracil 200 mg TID on day two as per the physician's advice, as the latter also blocks peripheral conversion of T4 to T3. After three days of treatment, symptoms of thyroid storm and delirium began to show improvement.

Thyroid hormone	Day 1	Day 3	Day 8	Day 13
fT4 (12-22 pmol/L)	100	18.07	24.86	22.7
fT3 (3.1-6.8 pmol/L)	34	1.72	2.80	2.5
TSH (0.27-4.2 µIU/mL)	0.01	0.02	0.01	0.01

[Table/Fig-1]: Serum levels of thyroid hormones of the patient during inpatient admission.
fT3: free Triiodothyronine; fT4: free Tetraiodothyronine; TSH: Thyroid stimulating hormone

The patient was started on divalproex sodium at a dose of 1 gram in divided doses and olanzapine at 10 mg on day 3 due to persistent manic symptoms (Young Mania Rating Scale (YMRS) score: 31) [1]. There was a reduction in aggression and manic symptoms by day 6 of admission.

A repeat thyroid function test on day 3 showed a downward trend in T4 and T3 levels [Table/Fig-1]. Steroids were tapered and discontinued by day 6. An ultrasound of the neck revealed diffuse thyroid disease. Ultrasound-guided Fine Needle Aspiration Cytology (FNAC) showed sections of thyroid tissue with multiple nodules of varying sizes, composed of follicles containing varying amounts of colloid; these features were suggestive of thyroid follicular nodular disease, with no indications of malignancy (Bethesda category II). Autoantibody levels showed significantly elevated levels of antithyroid peroxidase (anti-TPO) antibody at 547 (normal range: 0-35 IU/mL) and antithyroglobulin antibody at 80.47 (normal range: <4.11 IU/mL). Neuroimaging was found to be normal. The patient was diagnosed with Graves' disease based on symptoms of thyrotoxicosis, blood investigations, and the FNAC report, although the patient did not exhibit the typical eye signs characteristic of Graves' disease.

On day 8, the patient began to exhibit increased aggression, disorientation, slurred speech, and gross sleep disturbances. The dose of olanzapine was increased to 20 mg, and intravenous lorazepam 2 mg was administered whenever the patient became aggressive and was unresponsive to verbal de-escalation or oral medication. Blood investigations revealed hyperammonaemia at 143 mg/dL (normal range: 9-30 mg/dL), prompting the decision to discontinue divalproex. Hyperammonaemia was managed with oral lactulose. Despite initial improvement, there was a slight upward trend

in T4 and T3 levels [Table/Fig-1]. Propylthiouracil was stopped, and carbimazole was restarted at 10 mg three times a day, as advised by the physician. Lithium was added at a dose of 600 mg in divided doses and subsequently increased to 900 mg over the course of three days as a mood stabiliser. Both physical and psychiatric symptoms improved, resulting in a reduction in the YMRS score [1] by 14 points within seven days.

The patient was discharged on lithium 900 mg, olanzapine 20 mg, carbimazole 30 mg, and propranolol 60 mg. Over the next four weeks, the dose of carbimazole was reduced to 20 mg, olanzapine to 15 mg, and propranolol to 20 mg, while lithium continued at 900 mg. The patient was under continuous follow-up from the departments of Medicine and Psychiatry.

The patient was diagnosed according to the International Classification of Diseases, 10th edition [2]:

a) Delirium, not induced by alcohol and other psychoactive substances;

b) Organic manic disorder;

c) Thyrotoxicosis secondary to Graves' disease with thyroid storm.

DISCUSSION

As per the natural course, BPAD, characterised by manic, hypomanic, and depressive episodes, typically has its onset in the second or third decade of life. However, new-onset mania in older individuals is not uncommon, though it often requires detailed evaluation to rule out other secondary causes [3]. A review by Sami M et al., of 35 case reports of patients presenting with their first episode of mania or hypomania after the age of 50 years found that the majority (82%) of cases of late-onset mania had an underlying organic cause, such as vascular factors, iatrogenic drug use, electrolyte imbalance, dementia, or thyroid disease [4].

Thyrotoxicosis, characterised by excessive thyroid hormone levels, manifests with symptoms such as tachycardia, sweating, weight loss, heat intolerance, tremors, and neuropsychiatric symptoms including anxiety, emotional instability, cognitive impairment, psychosis, and delirium. Fewer than 2% of patients may present with manic symptoms. It has been proposed that these symptoms could be driven by beta-adrenergic hyperactivity, the influence of thyroid hormones on various neurotransmitters, and autoimmunity [5]. Additionally, it is postulated that the hyperthyroid-induced overactivity of the adrenergic system disrupts the connection between the frontal lobe and the locus coeruleus- a part of the brain that helps control concentration and alertness [6].

The most common cause of thyrotoxicosis is Graves' disease, which is characterised by autoantibodies to the TSH receptor and thyroid peroxidase. It is more common in women (5:1) [7]. Despite the lower prevalence in men, the clinical presentation of this patient led to the suspicion of an underlying thyroid disorder, which was confirmed by investigations.

Thyroid storm is a rare (1-2%), but acute, life-threatening syndrome due to an exacerbation of thyrotoxicosis. Cardinal symptoms include fever, tachycardia, gastrointestinal disturbances, and Central Nervous System (CNS) involvement. It requires prompt and aggressive management. Common triggers for a thyrotoxic storm include infection, diabetic complications, childbirth, trauma, and myocardial infarction, among others [8]. In this patient, the trigger could not be identified; however, it could have been prevented if the thyrotoxic state had been diagnosed and treated earlier. According to a study by Swee D et al., thyroid storm was the first presentation of thyrotoxicosis in nearly half the patients (46.4%), and non compliance with treatment and infection were the major triggers for thyroid storm [9]. Community education initiatives could promote early diagnosis and alleviate stigma, thus narrowing the treatment gap in psychiatry, particularly in regions like India, where it exceeds 80% [10].

The treatment of mania associated with thyrotoxicosis lacks standardised guidelines and often relies on clinical discretion. Few studies suggest that since manic symptoms in thyrotoxicosis are predominantly mediated by sympathetic overactivity, treatment should primarily aim at controlling this and achieving a euthyroid state. According to the study by Chakrabarti S, many patients achieved remission with only beta-blockers and thyroid medication [5]. Among antithyroid medications, propylthiouracil may be preferred, as it not only decreases new hormone synthesis but also blocks the peripheral conversion of T4 to T3 [11]. However, in index patient, propylthiouracil had to be switched back to carbimazole, which is longer-acting [7], due to fluctuating thyroid hormone levels. In the case report by Asif H et al., a 37-year-old male patient diagnosed with Graves' disease, who presented with mania and psychosis, achieved complete remission with methimazole and beta-blockers, without any psychotropics [12]. However, mood stabilisers and antipsychotics may be warranted if symptoms are uncontrollable, as illustrated in the case report published by Adiba A, where a 24-year-old female patient required divalproex sodium 2 g and quetiapine 200 mg, along with antithyroid medication, to achieve a euthymic state [13]. In the present case, divalproex, despite having a rapid onset of action, had to be discontinued due to hyperammonaemia [14]. Previous studies have cautioned against the use of lithium due to the risk of lithium-induced hyperthyroidism [13,15]. However, lithium has also been shown to be efficacious in the treatment of thyrotoxicosis and thyroid storm [16], due to its more common effect of causing hypothyroidism, and was hence considered for this patient due to fluctuating thyroid levels and mood symptoms.

The use of injectable antipsychotics in patients with thyroid storm is risky, as it may prolong the QTc interval and precipitate cardiac arrhythmias. Oral antipsychotics that have minimal effect on the QTc interval, as well as injectable benzodiazepines, can be used for rapid tranquilisation [17]. [Table/Fig-2] shows previous case reports highlighting thyrotoxicosis manifesting as mania [12,13,18,19].

Study title	Author and year of publication	No. of patients	Age of the patient and chief complaint	Important clinical features	Provisional diagnosis	Final diagnosis	Treatment
Association of thyrotoxicosis with mania [13]	Adiba A [13] (2019)	1	24 years/female Manic symptoms, weight loss, alternating between diarrhoea and constipation, and sensitivity to heat	Tachycardia, fine tremors. Thyroid was non tender and not palpable, non pitting oedema in bilateral lower limbs. Low TSH, high FT3 and FT4, elevated thyrotropin receptor antibodies	Thyrotoxicosis without thyroid storm, possibly due to Graves' disease	First episode mania. Thyrotoxicosis without thyroid storm, possibly due to Graves' disease	Tab quetiapine 400 mg T divalproex 2000 mg T methimazole 20 mg T propranolol 60 mg TID
Hyperthyroidism presenting with mania and psychosis: A case report [12]	Asif H et al., 2022	1	37 years/Male Psychotic features, hyperexcitability, excessive agitation, paranoia, insomnia and weight loss	Low TSH, and elevated T3, T4, thyroid-stimulating antibodies, and thyroid peroxidase antibodies	Graves' disease	Graves' disease	Methimazole 30 mg, propranolol 100 mg, and hydrocortisone 100 mg

Recognising thyrotoxicosis in a patient with bipolar mania: A case report. [18]	Lee CSN and Hutto B, 2008	1	59 years/F: Known case of bipolar disorder presented with symptoms of mania	Overweight, fine tremors, mild proptosis, a non tender, non palpable thyroid, non pitting oedema, dry skin. Low TSH, high free T4	Bipolar disorder Hyperthyroidism	Bipolar disorder Hyperthyroidism	T lithium 900 mg T risperidone 3 mg T quetiapine 100 mg T methimazole 10 mg
Graves' disease presenting with hypomania and paranoia to the acute psychiatry service [19]	Bennett B et al., 2021	1	32 years/female, presents with hypomania and paranoia along with weight loss and palpitations	Tachycardia, hypertension, goiter. Low TSH, elevated FT3 and FT4, Technetium scan: graves' disease	Thyrotoxicosis	Graves' disease	Tab carbimazole 40 mg once daily and propranolol 40 mg three times per day
Thyrotoxicosis masquerading as late onset mania: A case report on treatment of mania in thyroid storm	Present study, 2024	1	Male in his late forties, presented with manic symptoms along with weight loss, tachycardia and hair loss	Patient was poorly built with tachycardia, tachypnoea, febrile, in delirium. Elevated anti-TPO and anti-thyroglobulin. FNAC: thyroid follicular nodular disease	Hyperthyroidism in thyroid storm with bipolar disorder in mania	a) Delirium, not induced by alcohol and other psychoactive substances; b) Organic manic disorder; c) Thyrotoxicosis secondary to Graves' disease with thyroid storm	Tab lithium 300 mg 1-1-1, Tab Olanzapine 20 mg, Tab propranolol 60 mg, T carbimazole 30 mg, Inj hydrocortisone 100 mg TID, T divalproex 1000 mg (stopped), Syp Lactulose TID

[Table/Fig-2]: Previous case reports highlighting thyrotoxicosis manifesting as mania [12,13,18,19].

CONCLUSION(S)

Underlying medical conditions can often masquerade as psychiatric symptoms. Maintaining a high index of suspicion, performing a detailed medical examination, and obtaining relevant investigations can lead to early diagnosis and management, significantly reducing morbidity. Lithium can be used in the management of mania associated with thyroid storm, along with adjunct antipsychotics that have minimal effects on the QTc interval. Intravenous antipsychotics should be avoided, as they may precipitate cardiac arrhythmias. Effective liaison among all medical departments is essential to reduce the treatment gap in psychiatry.

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PLAGIARISM CHECKING METHODS: [Jain H et al.]
- Plagiarism X-checker: May 26, 2024
- Manual Googling: Aug 07, 2024
- iThenticate Software: Aug 29, 2024 (7%)

ETYMOLOGY: Author Origin

EMENDATIONS: 6

AUTHOR DECLARATION:
- Financial or Other Competing Interests: None
- Was informed consent obtained from the subjects involved in the study? Yes
- For any images presented appropriate consent has been obtained from the subjects. NA

Date of Submission: **May 25, 2024**
Date of Peer Review: **Aug 08, 2024**
Date of Acceptance: **Aug 30, 2024**
Date of Publishing: **Oct 01, 2024**