Association of Thyrotoxicosis with Mania: A Case Report and Literature Review

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Case

Ms. F was a 24-year-old African American female who presented to the emergency department with agitation and disorganized behavior. Prior to arrival, she was given haloperidol 10mg, lorazepam 4mg, and diphenhydramine 50mg intramuscularly by first responders. She had been discharged from a psychiatric hospital one week earlier with the diagnosis of Bipolar I Disorder and prescriptions with which she was only partially compliant. She reported no family history of mood disorders; however, she reported thyroid disease in her grandmother. Physical examination was significant for tachycardia, temperature 99.1 °F (37.3 °C), and fine tremors noted bilaterally. Thyroid was non-tender and without palpable abnormality. Skin was dry, and non-pitting edema was noted in her lower extremities. Review of systems was significant for weight loss, anxiety, tremors, emotional lability, alternating bouts of diarrhea and constipation, and heat intolerance. Emergency medicine physicians ordered a psychiatric consult.

On mental status examination, Ms. F reported to "be chosen by God" and "haunted by demons." She was tearful, appropriately groomed, and without acute distress. She had experienced decreased need for sleep and hyper-religiosity. Her speech was spontaneous and of appropriate rate, rhythm, and volume. She was without flight of ideas. She denied suicidal and homicidal ideation. She denied hallucinations and was not internally distracted. Ideas of reference were absent. Her thought process displayed occasional circumstantially. Ms. F was fully oriented, and no deficits were found in her memory testing. Her insight and judgment were impaired.

Table 1

Test	Result
CBC	Unremarkable
BMP	Unremarkable
FLP	Unremarkable
ANA	WNL
B-HCG	Negative
UDS	Negative

Given her physical exam findings, laboratory results (**Table 1**), thyroid tests (**Table 2**), and family history, emergency medicine also consulted the endocrinology service. They noted no history of thyroid-toxic medication exposure including amiodarone and lithium. There was no known exposure to radiation. Endocrinology's diagnosis was thyrotoxicosis without thyroid storm possibly due to Graves' disease. They recommended initiating methimazole 10mg twice daily and propranolol 60mg four times daily for pulse control.

Ms. F was admitted to the psychiatry in-patient unit with a diagnosis of bipolar and related disorder due to thyrotoxicosis and started on lurasidone 40mg daily. After admission, she experienced sleeping impairment and high energy. Her speech became pressured with neologisms. She displayed flight of ideas, tangentiality, grandiosity, hyper-religiosity, and delusional thinking. Her affect was labile. She continued denying auditory and visual hallucinations. Due to a lack of therapeutic response, lurasidone was discontinued.

Table 2

Test	Result	Normal Range
TSH	0.01 mcIU/ml (L)	0.27-4.20 mcIU/ml
FT3	1983 pg/dl (H)	200-440 pg/dl
FT4	5.590 ng/dl (H)	0.930-1.70 ng/dl
TPO Ab	<3.00 IU/ml	≤5.61 IU/ml
Anti-Tg Ab	3.47 IU/ml	≤4.11 IU/ml
TR Ab	11 IU/L (H)	0-1.75 IU/L

Risperidone 2mg nightly and lamotrigine 25mg daily were initiated. She developed a rash leading to the discontinuation of lamotrigine. Subsequently, she was prescribed divalproex sodium 1500mg daily. During the hospital course, risperidone was titrated to 4mg nightly, and divalproex sodium was increased to 2000mg to achieve symptom management. Due to intolerance of risperidone, Ms. F was cross-tapered to quetiapine 200mg every morning and 400mg nightly. With this combination, her sleep improved, speech normalized, and mood became euthymic. Psychotic symptoms abated.

Table 3

Test	Day 12	Day 22
TSH	0.01 mcIU/ml	0.01 mcIU/ml
FT3	593 pg/dl	320 pg/dl
FT4	2.93 ng/dl	0.963 ng/dl

After twenty days of hospitalization, Ms. F met maximum benefit of inpatient treatment. She was discharged on quetiapine 200mg every morning and 400mg nightly, divalproex sodium 2000mg daily, methimazole 10mg twice daily, and propranolol 60mg four times daily. Outpatient endocrinology follow-up revealed continued improvement in thyroid function (**Table 3, Figure 1**).

Discussion

Table 4

Thyrotoxicosis	Mania
Manic excitement	Elevated or irritable mood
Weight loss with increased appetite	Abnormally increased goal-directed activity
Fatigue	Grandiosity
Insomnia	Sleep deficit (decreased need for sleep)
Anxiety	Pressured speech
Tremulousness	Distractibility
Palpitations and/or perspiration	Impulsivity or indiscretion
Generalized weakness	Flight of ideas
Psychosis (delusions or hallucinations)	Psychosis (delusions or hallucinations)

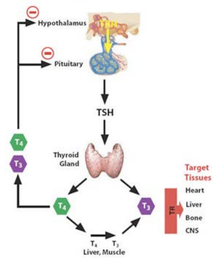
Disturbances in thyroid metabolism significantly alter mental function influencing cognition and emotion (1). The strongest association between thyroid dysfunction and psychopathology has been in the area of mood disorders, particularly between depressive states and hypothyroid conditions (2). Bidirectionally, those with affective disorders have noticeable abnormalities in the hypothalamic-pituitary-thyroid axis (**Figure 2**). Routinely, patients presenting with symptoms of depression undergo a thyroid function workup prior to a primary depressive disorder diagnosis. Although the correlation between depression and hypothyroidism is well established, the relationship between mania and hyperthyroidism is less understood (3). Though severe manic symptoms have been known to occur with hyperthyroidism, it is rare (6). In this case, the possibility of mania presenting as a manifestation of hyperthyroidism is made evident.

Graves' disease is the primary cause in sixty to ninety percent of all thyrotoxicosis cases. This is due to autoantibodies to the thyrotropin receptor causing activation which stimulates thyroid hormone synthesis lowering TSH through negative feedback (4). As seen in Ms. F, resulting symptoms include tachycardia, fine tremors, insomnia, dry skin, elevated mood, grandiosity, pressured speech, distractibility, and increased energy (**Table 4**). Importantly, it is unclear whether the resolution of her manic symptoms occurred from the treatment with mood stabilizers, thyroid hormone inhibitors and beta blockers, or the combination of all.

The *Josephson and Mackenzie* retrospective review of eighteen patients describes an organic affective syndrome of manic symptoms occurring shortly after the initiation of thyroid replacement in hypothyroid patients. Patients were predominantly female, displayed concurrent psychosis, and had a personal or familial history of psychiatric disorders. The authors suggested that rapid administration of thyroxine could abruptly augment catecholamine receptor sensitivity resulting in manic symptoms (8).

Before diagnosis of a primary mania is established, substance-induced and organic causes must first be ruled out (9). Late onset mania is more commonly associated with organic causes (7). The goal of treatment for thyroid-induced depression or mania is restoration of euthyroid states (1,6). Studies investigating the effects of hyperthyroidism on brain function find that psychological symptoms resolve with successful treatment of thyroid hyperactivity (9). *Wallace et al.* determined hyperthyroid-induced effects on the brain return to normal more slowly than systemic effects. Prospective studies suggest that remission of affective and cognitive symptoms usually occurs within a few months of return to a euthyroid state (10). Other studies suggest that a hyperthyroid episode influences affective modulation in a time frame that exceeds the period of thyroid hormone excess (1). Cross-sectional studies report long-term effects on cognitive function and affective modulation following hyperthyroidism (5).

Figure 2

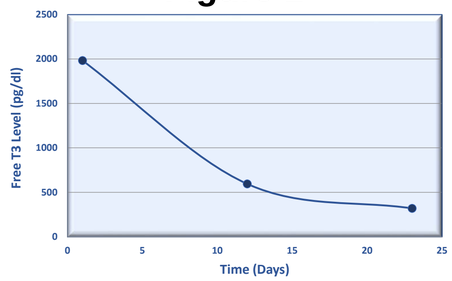


Future research is warranted to elucidate the relationship of affective disorders to central thyroid hormone functioning and pathological processes to best determine clear treatment guidelines.

Clinical Pearls

1. Consider and exclude medical conditions with direct pathophysiological consequences mimicking those found in psychiatric conditions.
2. Thyroid disease can worsen or cause a variety of psychiatric symptoms; Graves' disease induced thyrotoxicosis can mimic mania.
3. Prompt management and treatment of underlying organic causes manifesting as psychiatric symptoms is necessary with utilization of psychotropic medications to minimize concomitant symptoms.
4. Psychotropic medication use should be tailored to the individual with consideration given to potential worsening of the medical co-morbidity.

Figure 1



References

1. Bauer M, Goetz T, Glenn T, Whybrow PC. *The thyroid-brain interaction in thyroid disorders and mood disorders*. Journal of Neuroendocrinology. 2008.
2. Esposito S, Prange Jr. AJ, Golden RN. *The thyroid axis and mood disorders: Overview and future prospects*. Psychopharmacol Bull. 1997.
3. Wysokiński A, Kłoszewska I. *Level of thyroid-stimulating hormone (TSH) in patients with acute schizophrenia, unipolar depression or bipolar disorder*. Neurochem Res. 2014.
4. Smith BR, Hall R. *Thyroid-stimulating Immunoglobulins in Graves' Disease*. Lancet. 1974.
5. Dutra PEP, Gurgel W de S, Higa RA, Costa C. *Where does her mood come from? An organic approach to a once functional patient*. Trends Psychiatry Psychother. 2015.
6. Chakrabarti S. *Thyroid functions and bipolar affective disorder*. Journal of Thyroid Research. 2011.
7. Nath J, Sagar R. *Late-onset bipolar disorder due to hyperthyroidism*. Acta Psychiatr Scand. 2001.
8. Josephson AM, Mackenzie TB. *Thyroid-induced mania in hypothyroid patients*. Br J Psychiatry. 1980.
9. Chang KD, Keck PE, Stanton SP, McElroy SL, Strakowski SM, Geracioti TD. *Differences in thyroid function between bipolar manic and mixed states*. Biol Psychiatry. 1998.
10. Wallace JE, MacCrimmon DJ, Goldberg WM. *Acute hyperthyroidism: Cognitive and emotional correlates*. J Abnorm Psychol. 1980;89(4):519.

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