

Severe Hypothyroidism Presenting with Acute Mania and Psychosis: A Case Report and Literature Review

Nicole Giunio-Zorkin¹, Mariana Golts^{2,3} and Virginia C Fernandes^{1,4*}

¹Leslie Dan Faculty of Pharmacy, University of Toronto, Toronto, ON, Canada

²Department of Psychiatry, Mount Sinai Hospital, 600 University Avenue, Toronto, ON, Canada

³Department of Psychiatry, Faculty of Medicine, University of Toronto, Toronto, ON, Canada

⁴Department of Pharmacy, Mount Sinai Hospital, 600 University Avenue, Toronto, ON, Canada

Abstract

Introduction: In patients presenting with acute mania and psychosis, it is important to rule out organic causes of their symptoms. Patients with severe hypothyroidism may present with psychosis and less commonly with symptoms of mania. We report a case of a 40 year old male presenting with acute mania and psychosis, in the context of severe hypothyroidism.

Case presentation: A 40 year old Caucasian male presented to the emergency department with acute onset mania, and delusions of grandeur. One week prior to presentation, he demonstrated bizarre behavior and hyperactivity. On the day of admission, he sustained a self-inflicted burn on his left arm and left leg causing partial thickness burns. Blood work demonstrated elevated creatine kinase and creatinine, as well as profoundly high TSH (>100 uIU/L) and low thyroid hormones (T4=2 pmol/L, T3 1.9=pmol/L). He was medically diagnosed with rhabdomyolysis with acute kidney injury and severe hypothyroidism. He was started on antipsychotic medication (loxapine), a mood stabilizer (divalproex sodium) and levothyroxine. His psychosis and mania resolved after 2 weeks in hospital and TSH trended down (84.10 mIU/L) and free T4 (9 pmol/L) and free T3 (3.8 pmol) trended upwards.

Conclusion: In patients presenting with severe hypothyroidism and acute mania with psychosis, treatment should include thyroid hormone replacement in addition to psychotropic medications.

Keywords: Hypothyroidism; Mania; Psychosis; Bipolar disorder; Levothyroxine

Introduction

Thyroid dysfunction is known to have a significant impact on mental health [1]. Hypothyroidism, in particular, has been linked to mood disorders and acute psychosis. Though most commonly associated with depression, hypothyroidism has been linked to psychosis since the late 1800s, in reports of delusions and hallucinations in patients with myxedema [2]. In 1949, Asher coined the term “myxoedematous madness” to identify the psychotic manifestations of hypothyroidism, reporting 14 cases of psychosis with hypothyroidism [3]. More recent literature highlights the incidence and coexistence of hypothyroidism and psychiatric disorders, describing possible mechanisms contributing to the pathophysiology of these disorders [1,4]. The link between hypothyroidism and mania, however, is less clear, with few reports in the literature [5]. We present a case report of a 40 year old Caucasian male presenting with acute onset mania with psychosis and previously undiagnosed severe hypothyroidism.

Case Report

AB is a 40 year old Caucasian male who presented with acute onset mania including grandiose delusions, and self-inflicted partial thickness burns on his left arm and left leg. One week prior to admission AB demonstrated bizarre and self-injurious behaviour. AB's neighbors reported flooding in his apartment, and he was found screaming and dancing by his landlord. AB began fasting by not eating or drinking to prove he could become a 'spiritual advisor'. One week later his neighbors called 911 after they heard cries from his apartment. He was found naked in a tub with burns on his arm and leg. His brother indicated that AB wanted to see how acid would feel on his skin. AB told the psych team after admission that he poured acid on his arm as he wanted to be “disconnected from the universe so he could connect himself

spiritually”. In the emergency room he was agitated and aggressive with ongoing grandiose delusions. Initial assessment noted grandiose ideas, racing thoughts, rapid and pressured speech, and distractibility. His past medical history was significant for depression and ADHD.

Blood work indicated thyroid-stimulating hormone (TSH)>100.00 mIU/L (reference range 0.40-3.80 mIU/L), free triiodothyronine (T3) 1.9 pmol/L (reference range 4.0-6.8 pmol/L), and free thyroxine (T4) of 2 pmol/L (reference range 12-21 pmol/L). In addition, elevated creatine kinase plasma 4490 unit/L (reference range 0-240 unit/L) and creatinine 210 umol/L (reference range 55-105 umol/L) were present. He was diagnosed with rhabdomyolysis with acute kidney injury and severe hypothyroidism. He was started on levothyroxine and loxapine and his burns and acute kidney injury were medically managed. One week later, he was deemed medically stable and transferred to the inpatient psychiatry unit for diagnostic workup and management of acute mania and psychosis.

AB stated he experienced manic and depressive episodes starting in his teenage years. He recalls 3-4 depressive episodes over his lifetime, and countless hypomanic episodes. He first sought treatment for depression 6 years prior to this episode and was treated with paroxetine

***Corresponding author:** Virginia C Fernandes, Department of Pharmacy, Mount Sinai Hospital, 600 University Avenue, Toronto, ON, Canada, Tel: 416 586 4800; E-mail: Virginia.fernandes@sinaihhealthsystem.ca

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and quetiapine. Both medications were stopped abruptly after an incident resulting in his incarceration and were not restarted after his release. In a manic episode, he stole his employer's vehicle and attempted to cross the border illegally, leading to brief incarceration and then hospitalization. At that time, he had ingested alcohol, marijuana, and Adderall, and his episode was attributed to substance use. He was not diagnosed with a psychiatric disorder and not started on medications. AB reports no other hospitalizations for psychiatric illness.

AB's past management of ADHD included Adderall XL 60 mg daily, which he discontinued one year prior to presentation due to sleep disturbances.

AB denied previous diagnosis of hypothyroidism or ever having thyroid hormone levels checked. His mother had hypothyroidism managed with levothyroxine. Physical symptoms of hypothyroidism were not apparent and he denied physical symptoms in the past.

His social history included poly-substance use. He endorsed recent use of alcohol, and marijuana, as well as past use of cocaine, LSD, mushrooms and MDMA, which he had not used for many years. AB stated he coped with manic symptoms by smoking 1 g marijuana daily, drinking small amounts of alcohol and practicing meditation. Three days prior to admission he stopped all substances (marijuana and alcohol) and stopped meditation. This was his first episode manifesting with psychotic symptoms. Toxicology screen was negative except for cannabinoids >300 mcg/L and benzodiazepine 165 mcg/L (lorazepam 2 mg oral tablet was given in the emergency department).

In this admission AB was started on loxapine 25 mg and levothyroxine 100 mcg. He became more goal directed and less grandiose. He continued, however, to have poor sleep and restlessness. Loxapine was increased to 50 mg daily and divalproex sodium was initiated. The endocrinology team increased levothyroxine to 112 mcg daily. On this combination, his sleep and restlessness stabilized. Psychosis and mania resolved after 2 weeks in hospital, and TSH trended down (84.10 mIU/L) and free T4 (9 pmol/L) and free T3 (3.8 pmol) trended upwards. He was discharged on loxapine 50 mg daily, divalproex sodium 1000 mg daily and levothyroxine 112 mcg daily with no residual psychotic or manic symptoms.

Discussion

Assessment of thyroid function is a common practice in the differential diagnosis in patients presenting with psychiatric illness. The coexistence of hypothyroidism with depression, bipolar disorder and psychosis has been reported, dating back to the late 1800s. In 1949, Asher reported 14 cases of psychosis with hypothyroidism, 9 of which recovered with thyroid hormone treatment alone [2]. Numerous cases have since linked psychosis to hypothyroidism [2,6-12]. The majority of these cases were managed with a combination of antipsychotic medication and thyroid replacement, however in some cases maintenance therapy included thyroid replacement alone. There was no correlation between the degree of hypothyroidism and the severity of psychiatric symptoms [2]. Psychosis usually remits after 1 week of thyroid replacement, with earlier resolution with the addition of antipsychotic medications [2]. Although psychosis is less commonly associated with hypothyroidism than depression, it is a possible manifestation of the disorder.

Hypothyroidism is a common comorbidity in bipolar disorder. Patients with rapid cycling or treatment-resistant bipolar disorder, have higher incidence of hypothyroidism [4]. The association between hypothyroidism and mania is less clear. Mania with concomitant

hypothyroidism has been reported in patients previously undiagnosed with psychiatric illness [13,14]. Patients presenting with acute manic episodes and hypothyroidism have improved clinically with a combination of psychotropic medications and thyroid hormone [5]. In some cases, patients presenting with new onset mania and hypothyroidism have clinically improved with thyroid hormone replacement alone [5]. The mechanism of hypothyroidism-induced mania remains to be elucidated, however it is postulated that low thyroid hormone increases cerebral dopamine activity [1,5]. The difficulty in managing patients presenting with new onset mania and hypothyroidism lies in identifying the etiology of manic symptoms. Further research is required to determine the relationship between hypothyroidism and bipolar disorder.

Delineating etiology of psychiatric symptoms in our patient is a challenge. AB's description of depressive and manic episodes in the past supports an underlying untreated bipolar illness. However, previous thyroid function tests were not performed, and the duration of hypothyroidism is, therefore, unclear. Furthermore, AB's history of substance use further complicates his case. It is possible that hypothyroidism aggravated an underlying psychiatric illness or induced a manic episode with psychotic features. Nevertheless, treatment with levothyroxine alone was not considered for this patient as his recent severe self-harm behavior and lack of insight on admission establishes him as high risk. It is possible that levothyroxine contributed to improvement of AB's psychotic and manic symptoms; however the thyroid hormone levels, though improved, were still below the reference range. It is likely that the antipsychotic medication and mood stabilizer were critical to the rapid resolution of AB's psychotic and manic symptoms.

Conclusion

Thyroid function should be investigated in all patients presenting with mania or psychotic symptoms. Without an underlying psychiatric illness, thyroid hormone replacement may suffice in the treatment of acute onset psychosis in the context of severe hypothyroidism. However, during an acute manic episode, treatment with thyroid hormone therapy alone is insufficient, and likely requires concomitant therapy with an antipsychotic or mood stabilizer. Further research is required to investigate hypothyroidism-induced mania in order to aid clinicians in long term management of patients with new onset mania with or without psychosis in the context of severe hypothyroidism.

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