

Mania as a presentation of primary hypothyroidism

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ABSTRACT

Hypothyroidism is a common problem in clinical practice, with diverse manifestations. Neuropsychiatric problems include affective disorders, disturbances in cognition and psychosis. Mania is commonly associated with hyperthyroidism. Only a few selected case reports mention mania as a presenting feature of hypothyroidism. We report a case of mania with psychotic symptoms in a 47-year-old woman who had no previous history of psychiatric disorder. She had signs of florid hypothyroidism. She required both antipsychotic drugs and thyroxine replacement for the amelioration of her symptoms. The report is followed by a brief review of the literature on mania as a clinical presentation of hypothyroidism and its probable pathogenesis. One has to have a high index of suspicion of underlying organic causes in patients presenting with depression, psychosis or cognitive disorders.

Keywords: hypothyroidism, mania, psychosis

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INTRODUCTION

Hypothyroidism presents with numerous neuropsychiatric manifestations of which depression, apathy, disturbances in cognition, psychosis and affective disorders are common.⁽¹⁾ The association between mania and hyperthyroidism is known but the occurrence of the same in hypothyroidism is rare. We report a patient who presented with features of acute manic psychosis precipitated by severe hypothyroidism.

CASE REPORT

A 47-year-old woman with no significant past medical history was brought to the emergency room with symptoms of inappropriate talk, bizarre behaviour, hyperactivity, sleeplessness and symptoms suggestive of acute psychosis of three days' duration. She was three years post-menopausal and had no previous psychiatric ailments or history of substance abuse. After her husband's demise, she was more withdrawn and depressed. She had auditory and visual hallucinations, and had grandiose delusions of the goddess having entered her. She was

restless, and became aggressive towards her family members. She had spent sleepless nights prior to these symptoms for a few weeks, according to her relatives. On examination, she was conscious but restless, agitated and inattentive. She had facial puffiness, dry skin, a hoarse voice but no goitre. Her body temperature was 37.4°C, heart rate 60/min, respiratory rate 19/min and blood pressure 150/90 mmHg. Examination of her cardiovascular and respiratory systems was unremarkable. Her formal neurological examination did not reveal any focal findings except for a delay in the relaxation time of the deep tendon reflexes.

The laboratory evaluation revealed a haemoglobin level of 10.4 g/dL, normal total and differential counts and a peripheral blood smear indicative of a normochromic, normocytic anaemia. The blood glucose, renal function and the liver function tests were also normal. Serum sodium and potassium was normal (138 mmol/L and 3.8 mmol/L, respectively). Urine analysis did not show any active sediment. Chest radiograph and electrocardiography were normal. The thyroid functions revealed a thyroid-stimulating hormone (TSH) level of 63.7 (reference range 0.3–5.0) mIU/ml, free thyroxine of 0.1 (reference range: 0.8–1.8) ng/dL, and the thyroid peroxidase antibody titre was negative. Computed tomography of the brain was normal. The patient was started on parenteral haloperidol, low-dose thyroxine replacement therapy (25 mcg/day), which was increased subsequently to 100 mcg/day over the ensuing weeks. Her auditory and visual hallucinations disappeared within a week. However, she continued to require haloperidol for a month after discharge.

DISCUSSION

Primary hypothyroidism, a common clinical problem with diverse physical manifestations, was first linked to psychosis in 1888, by the Committee on Myxoedema of the Clinical Society of London.⁽¹⁾ Asher in 1949 described "myxoedema madness" in his article on the subject, where severe hypothyroidism was implicated in acute psychosis.⁽²⁾ Common symptoms of psychological dysfunction encountered in hypothyroidism include forgetfulness, mental slowness, lethargy and emotional lability. Cognitive changes with alterations in attention, concentration, perception and speed of thought are common. Depression is the commonest affective disorder

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Table I. Case reports of mania as a clinical presentation of hypothyroidism.

Author	Age at presentation (years)	Primary diagnosis	Duration of manic symptoms	Baseline TSH (mIU/ml)	Concurrent therapy	Time to recovery
Mahendran ⁽⁹⁾	25	Congenital hypothyroidism	1 month	85.7	Antipsychotics	2 weeks
Heinrich and Graham ⁽¹⁰⁾	73	Postpartum thyroiditis	2 weeks	43.79	Antipsychotics	3 weeks
Stowell and Barnhill ⁽¹¹⁾	35	Postpartum thyroiditis	2 weeks	> 150	Antipsychotics	1 week
Levitte ⁽¹²⁾	40	Manic depressive psychosis	2 years	64	Lithium	2 months

encountered in these patients. Howland, in his meta-analysis, found that approximately 50% of patients with refractory depression have subclinical hypothyroidism.⁽³⁾ The response to conventional antidepressants is sub-optimal if this is untreated. As many as 20% of the patients with depression have detectable antithyroid antibodies.⁽⁴⁾ Suicidal ideations, delusions and hallucinations are seen in advanced disease.

T3 receptors have been demonstrated in high concentrations in the hippocampus and the amygdala – regions of importance in mood regulation but low in the brainstem and the cerebellum. In hypothyroidism, as serum T4 levels decline, intracerebral generation of T3 from T4 increases due to an increase in Type 2 deiodinase activity. Animal and human studies suggest that T3 acts presynaptically in the brainstem to decrease 5-hydroxytryptamine receptor 1A (5-HT_{1A}) receptor sensitivity, thus stimulating the synthesis and release of 5HT in the cortex and hippocampus.⁽¹⁾ The tyrosine hydroxylase activity in the brain is increased, leading to an increase in the dopamine levels. Serotonin levels are low, which positively correlates with the T3 levels.⁽¹⁾

The basis for the occurrence of mania in hyperthyroidism is that thyroid hormones increase the beta adrenergic receptor sensitivity, thus leading to increased catecholamine action and further to mania.⁽⁵⁾ The exact mechanism of the same in hypothyroidism is still unknown. In addition, as in any mental illness, premorbid personality, family history and social factors can precipitate a psychotic illness in a patient with hypothyroidism. Psychoses that are seen in patients with hypothyroidism may mimic schizophrenic, paranoid and affective psychosis. Cognitive disturbances or visual hallucinations that are commonly seen in hypothyroidism are not seen in schizophrenia. The symptoms can include delusions, visual/auditory hallucinations, loose associations and paranoia. Cognitive deficits like memory lapses, psychomotor slowing and perceptual skills have also been described. Electroencephalography shows a reduction in alpha activity with low voltage theta and delta waves predominating. PET scan shows a generalised decrease in cerebral blood flow and glucose uptake.⁽¹⁾

An association between subclinical and clinical hypothyroidism and bipolar disorders has been proposed.

Kupka et al found a higher rate of the presence of thyroid peroxidase antibodies in patients with bipolar disorder.⁽⁶⁾ The rapid cycling form of bipolar disorder with more than four episodes of bipolar illness per year has a much higher incidence of hypothyroidism (25%) than depressed patients in general (2%–5%) or those taking lithium carbonate (9%).⁽⁷⁾ Thyroxine replacement has been shown to reduce the severity and frequency of manic and depressive episodes in otherwise refractory bipolar disorder and high dose thyroxine therapy has been used successfully to treat refractory rapid cycling in the absence of hypothyroidism.⁽⁸⁾ Mania is commonly seen in hyperthyroid states, but selected case reports also mention the occurrence of the same in severe hypothyroidism (Table I).^(9–12) Our patient had a lack of sleep and appetite, hyper-religiosity, increased goal-directed activity, auditory and visual hallucinations and depressive thoughts, all consistent with mania with depressive psychosis.

The occurrence of mania with psychotic features has been reported following abrupt normalisation, both in Grave's disease and in hypothyroid states.^(13,14) Josephson and Mackenzie reviewed 18 case reports of patients with hypothyroidism developing mania soon after the initiation of replacement therapy, but concluded that 15 of them had psychosis prior to the treatment.⁽¹⁵⁾ Significant changes in the thyroid indices indicative of hypothyroidism were consistently associated with longer illness duration in lithium-free manic patients, but with greater severity of mania and more mood episodes in their lithium-treated counterparts.⁽¹⁶⁾ To conclude, the neuropsychiatric manifestations of hypothyroidism are very diverse and have much in common with other organic syndromes of brain dysfunction. One has to have a high index of suspicion, as failure to recognise the endocrinopathy may cause difficulties in recovery.

REFERENCES

1. Whybrow PC, Bauer M. Behavioral and psychiatric aspects in hypothyroidism. In: Braverman LE, Utiger RD, eds. *Werner & Ingbar's The Thyroid: A Fundamental and Clinical Text*, 9th ed. Philadelphia: Lippincott Williams & Wilkins, 2005: 842-50.
2. Asher R. Myxoedematous madness. *Br Med J* 1949; 2:555-62.
3. Howland RH. Thyroid dysfunction in refractory depression: implications for pathophysiology and treatment. *J Clin Psychiatry* 1993; 54:47-54.
4. Nemeroff CB, Simon JS, Haggerty JJ Jr, Evans DL.

- Antithyroid antibodies in depressed patients. *Am J Psychiatry* 1985;142:840-3.
5. Whybrow PC, Prange AJ Jr. A hypothesis of thyroid-catecholamine-receptor interaction. Its relevance to affective illness. *Arch Gen Psychiatry* 1981; 38:106-13.
 6. Kupka RW, Nolen WA, Post RM, et al. High rate of autoimmune thyroiditis in bipolar disorder: lack of association with lithium exposure. *Biol Psychiatry* 2002; 51:305-11.
 7. Bauer MS, Whybrow PC, Winokur A. Rapid cycling bipolar affective disorder. I. Association with grade I hypothyroidism. *Arch Gen Psychiatry* 1990; 47:427-32.
 8. Bauer MS, Whybrow PC. Rapid cycling bipolar affective disorder. II. Treatment of refractory rapid cycling with high-dose levothyroxine: a preliminary study. *Arch Gen Psychiatry* 1990; 47:435-40.
 9. Mahendran R. Hypomania in a patient with congenital familial hypothyroidism and mild mental retardation. *Singapore Med J* 1999; 40:425-7.
 10. Heinrich TW, Grahm G. Hypothyroidism presenting as psychosis: Myxedema madness revisited. *Prim Care Companion J Clin Psychiatry* 2003; 5:260-6.
 11. Stowell CP, Barnhill JW. Acute mania in the setting of severe hypothyroidism. *Psychosomatics* 2005; 46:259-61.
 12. Levitte SS. Coexistent hypomania and severe hypothyroidism. *Psychosomatics* 1993; 34:96-7.
 13. Irwin R, Ellis PM, Delahunt J. Psychosis following acute alteration of thyroid status. *Aust N Z J Psychiatry* 1997; 31:762-4.
 14. El-Kaissi S, Kotowicz MA, Berk M, Wall JR. Acute delirium in the setting of primary hypothyroidism: The role of thyroid hormone replacement therapy. *Thyroid* 2005; 15:1099-101.
 15. Josephson AM, Mackenzie TB. Thyroid-induced mania in hypothyroid patients. *Br J Psychiatry* 1980; 137:222-8.
 16. Zhang ZJ, Qiang Li, Kang WH, et al. Differences in hypothyroidism between lithium-free and -treated patients with bipolar disorders. *Life Sci* 2006; 78:771-6.