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

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 After her husband’s demise, she was more withdrawn and depressed.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.10 Asher in 1949 described “myxoedema madness” in his article on the subject, where severe hypothyroidism was implicated in acute psychosis.10 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...
encountered in these patients. Howland, in his meta-
alysis, 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
dehiodinase activity. Animal and human studies suggest
that T3 acts presynaptically in the brainstem to decrease
5-hydroxytryptamine receptor 1A (5-HT1A) receptor
sensitivity, thus stimulating the synthesis and release
of 5HT in the cortex and hippocampus.(5) 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 psychoses. 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 1).(9,10) 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.(9,10) 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.(11) 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.(12) 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.

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