

Acute mania after thyroxine supplementation in hypothyroid state

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ABSTRACT

The current literature variedly ascribes depressive and manic symptoms to hypo- and hyperthyroid state, respectively, reporting mania in hypothyroidism as an unusual entity. More unusual is precipitation of manic state in hypothyroid subjects after thyroxine supplementation for which studies report otherwise treating manic symptoms in hypothyroid state with thyroxine. We report a case of a patient whose acute mania appears to have been precipitated by thyroxine supplementation in hypothyroidism state. This case underscores the importance of thyroid screening in patients with mood and psychotic disorders, as well as the potency of thyroxine in producing manic symptoms.

Key words: Hypothyroidism, mania, thyroxine supplementation

INTRODUCTION

Thyroid dysfunction has been associated with numerous neuropsychiatric manifestations of which depression, apathy, disturbances in cognition, psychosis, and affective disorders are common.^[1] Although depressive and manic symptoms have been well described with hypo- and hyperthyroidism, respectively, mania in the setting of hypothyroidism is unusual.^[2]

We present the case of a patient whose acute mania is probably due to the administration of levothyroxine in hypothyroid state.

CASE REPORT

A right-handed 27-year-old unmarried Indian male nondiabetic, normotensive, vegetarian was diagnosed with

hyperthyroidism 7 months earlier [antithyroid peroxidase antibody: 16.1 (reference range: 0–65) IU/mL, T3: 5.59 (reference range: 0.92–2.33) nmol/L, T4: 207.30 (reference range: 60–120) nmol/L, thyroid stimulating hormone (TSH): 0.05 (reference range: 0.35–5.5) IU/mL, ^{99m}Tc-pertechnetate thyroid scan suggestive of thyroiditis] and started on medications (neomercozole 30 mg/day) by an endocrinologist. Three months later he started complaining of weakness and lethargy and upon investigating his TSH levels were raised significantly [TSH: 32.7 IU/mL, T4: 8.6 (reference range: 12–22) pm/L, ultrasonography thyroid—both lobes mildly hyperechoic and heterogenous in pattern with no definite nodule or calcification seen] and he was shifted to thyroxine 25 µg per day in view of hypothyroidism. Subsequently, after about a week of treatment, he developed manic symptoms (euphoria, increased talkativeness, over familiarity, over religiosity, increased energy levels, reduced need for sleep, abusive and violent behavior with socio-occupational dysfunction). He presented to psychiatry department with 2 months history of such symptoms and was admitted. Upon investigating, TSH levels were found to be within normal limits with increased T3 [T3: 5.48 (reference range: 2–4) pg/dL, T4: 1.30 (reference range: 0.6–2) ng/dL, TSH: 3.74 IU/mL]. His manic symptoms remitted within 5 days of stopping

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thyroxine and initiating valproate 800 mg/day and olanzapine 20 mg/day. His Young Mania Rating Scale^[3] scores (to assess improvement in mood symptoms) reduced from 28 to 11 in 5 days and thyroid hormone levels normalized within 20 days.

Patient was euthymic with normal thyroid hormone levels after 2 months of followup wherein his medications were tapered off and did not show mood symptoms when seen 2 months later.

DISCUSSION

Our case reports that manic symptoms were precipitated during hypothyroid state when the patient was treated with thyroxine. Only a few cases of mania or hypomania associated with hypothyroidism have been reported in the literature.^[2,4,5] While most of these cases have reported improvement in manic symptoms after initiating thyroid replacement therapy, occurrence of mania with psychotic features has also been reported following abrupt normalization of thyroid status, both in Grave's disease and in hypothyroid states.^[6]

Josephson and MacKenzie^[7] 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, attributing symptom production to past history of personal or familial psychiatric disorder and high normal dosage initiation of levothyroxine (150 µg/day), which could abruptly augment catecholamine receptor sensitivity, thereby precipitating a hypercatecholaminergic state and subsequent manic symptoms. Our case neither had a past personal or family history of any psychiatric illness, nor was not exposed to abrupt high initial dosage of thyroxine.

Similar instances of T3-induced mania in patients with bipolar depression have also been reported.^[8] It has been speculated that thyroid hormone–catecholamine receptor interactions might underlie these T3-associated clinical manifestations as well.^[8]

With previous literature reports, rapidity and concurrent initiation as well as resolution of manic symptoms with thyroxine, supported by serum thyroid hormone levels, lack of previous or family psychiatric history and, Naranjo adverse drug reaction probability scale^[9] score of 5, led to our conclusion that the manic symptoms were probably

secondary to thyroxine supplementation.

Whybrow and Prange^[10] proposed the hypothesis that interactions between thyroid and neurotransmitter systems may have a causal role in the pathophysiology of mood disorders. They suggested that the antidepressant properties of T3 could be explained by its augmentation of postsynaptic beta-adrenergic activity. Hypothyroidism was, thus, believed to cause depression by producing a functional decrease in noradrenergic transmission. The obverse of this would be mania caused by a hyperadrenergic state, which may be the case in our patient.

With literature supporting thyroxine induction as well as attenuation of manic symptoms,^[2,5,6] we suggest that a subset of thyroid dysfunction patients exists with a potential for producing manic-like symptom after thyroid replacement in hypothyroid state. Further large scale prospective case-control studies are needed to confirm this.

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