Rapid Response to Loading Dose Levothyroxine in Myxedema Psychosis

To the Editor: Hypothyroidism associated psychosis is a relatively rare clinical event that has been well described in the literature.[1,2] The usual treatment is to initiate levothyroxine starting with a low dose, ie, 25–75 µg/d, before achieving the maintenance dose of 1.6 µg/kg,[3] or before commencing antipsychotic medication. However, this approach generally takes several weeks for psychosis to resolve.[1,4] We present a report discussing the specific benefits of using loading dose levothyroxine combined with antipsychotic medication to treat myxedema psychosis rapidly.

Case report. Ms A is a 44-year-old woman who presented with *DSM-5* first-episode psychosis of 3 weeks' duration, characterized by referential and persecutory delusions. She had no past psychiatric or medical history of note, particularly none of ischemic heart disease. She demonstrated minimal clinical evidence of hypothyroidism, with no symptoms such as of fatigue, constipation, or weight gain and only subtle signs of dry hands and alopecia in the lateral third of her eyebrows. However, a baseline thyroid function test showed her free T_3 level was 1.7 pmol/L (normal: 3.1–5.4 pmol/L), free T_4 was < 5 pmol/L (normal: 10–20 pmol/L), and thyroid-stimulating hormone (TSH) was > 100 mIU/L (normal 0.5–4.5 mIU/L). Other tests were unremarkable, with no biochemical complications of hypothyroidism in lipid, lipase, or cortisol values and no evidence of cardiac dysfunction on her electrocardiogram and chest x-ray. Ms A had no cardiac symptoms and was euvolemic on examination.

Olanzapine 10 mg daily was initiated, and the consulting endocrinologist recommended a loading dose of levothyroxine 300 µg daily for 1 week and 100 µg thereafter. (The consulting endocrinologist recommends a loading dose for patients who present with severe hypothyroidism [ie, TSH > 80 mIU/L] to enable a therapeutic drug level over a few days prior to continuing with maintenance dosing. However, this recommendation precludes patients with ischemic heart disease, as the increased myocardial oxygen demand that levothyroxine stimulates may trigger myocardial infarction, arrhythmias, or heart failure.[3]) In our patient, given the magnitude of morbidity caused by psychosis attributable to severe hypothyroidism, loading dose levothyroxine was recommended because her cardiac status was within normal limits. Within 4 days, her psychotic symptoms had completely resolved, which also correlated (day 4) with a reduction in TSH to 62 mIU/L (> 100 mIU/L at admission) and normalization of free T_4 to 13 pmol/L (< 5 pmol/L on admission). Electrocardiogram and echocardiogram results on day 4 were unremarkable. Thyroid peroxidase antibodies were revealed to be 235 IU/mL (normal: < 50 IU/mL) consistent with autoimmune hypothyroidism. Ms A was prescribed olanzapine 10 mg for 4 weeks (after her admission), which was then ceased, and she maintained subsequent clinical and biochemical remission by taking levothyroxine 100 µg daily.

Our case is unusual in describing psychotic symptoms without obvious preceding clinical signs of hypothyroidism and reinforces the importance of thyroid function tests as a screening tool for first-episode psychosis. This report is also unique in the literature to describe the specific benefits of using loading dose levothyroxine for myxedema psychosis, because traditionally, loading doses were mainly used in the setting of myxedema coma[3] when there is a need for a rapid response within days. The use of loading dose levothyroxine combined with antipsychotic medication resulted in rapid improvement of psychotic symptoms within 4 days. Only 2 other reports[4] describe a faster response (36 and 48 hours) for myxedema psychosis. However, in these 2 cases, triiodothyronine was used rather than levothyroxine. In our case, it is not entirely possible to determine if levothyroxine, olanzapine, or combination therapy was responsible for the rapid resolution of this patient's psychosis. We suggest that, in non-elderly patients without history or evidence of cardiac compromise, loading dose levothyroxine could be considered by clinicians for the treatment of myxedema psychosis, particularly if the initial period of antipsychotic treatment is unsuccessful.

References

1. Asher R. Myxoedematous madness. *BMJ*. 1949;2(4627):555–562.
2. Heinrich TW, Grahm G. Hypothyroidism presenting as psychosis: myxedema madness revisited. *Prim Care Companion J Clin Psychiatry*. 2003;5(6):260–266.
3. Khandelwal D, Tandon N. Overt and subclinical hypothyroidism: who to treat and how. *Drugs*. 2012;72(1):17–33.
4. Cook DM, Boyle PJ. Rapid reversal of myxedema madness with triiodothyronine. *Ann Intern Med*. 1986;104(6):893–894.

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