Brief Communication

Lithium toxicity and myxedema crisis in an elderly patient

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ABSTRACT

While thyroid dysfunction is a frequent complication of lithium treatment, myxedema crisis is a rare occurrence with a handful of cases described. Here, we describe a patient receiving lithium for about a decade for bipolar disorder, who presented with myxedema crisis and lithium toxicity. In this patient, myxedema crisis was likely precipitated by lithium toxicity and community acquired pneumonia. The effects of lithium on thyroid are briefly reviewed. **Objective:** To describe an elderly male who was diagnosed with myxedema crisis and lithium toxicity. **Case Report:** A 70-year-old male was admitted in our hospital with history of gradual onset progressive decrease in level of consciousness and altered behavior for last 1 month. Patient also had history of respiratory tract symptoms for 1 week. Patient was a known case of diabetes and bipolar affective disorder for which he had been receiving insulin and lithium for 10 years. One year earlier, patient was admitted in our ward for glycemic control and evaluation of complications and was found to be clinically and biochemically euthyroid; he never returned for follow up until the present admission. On examination patient had incoherent speech, hypothermia, and bradycardia. Thyroid function showed thyroid-stimulating hormone >150 IU/ml, Tetraiodothyronine (T4) <1 μg/dl, anti-thyroid peroxidase titer of 60 IU/ml. The serum lithium level was 2.9 nmol/L (therapeutic level 0.2-1.2 nmol/L). He was managed with levothyroxine, starting with a loading oral dose of 500 μg through ryles tube followed by 100 μg daily, IV antibiotics and fluids; lithium was stopped after consultation with a psychiatrist. From day 5, patient started showing progressive improvement and by day 10, he had a Glasgow Coma Scale of 15/15, normal electrolyte, serum creatinine of 1.8 mg/dl and serum lithium level of 0.5 nmol/L. **Conclusion:** Lithium-induced hypothyroidism may be life-threatening, thyroid function should be monitored before and during lithium therapy and drug should be discontinued and appropriate therapy instituted if hypothyroidism develops.

Key words: Bipolar disorder, lithium, myxedema crisis

Introduction

Thyroid dysfunction spanning abnormalities on thyroid function testing, subclinical hypothyroidism, hypothyroidism, aggravation of existing thyroid autoimmunity and rarely hyperthyroidism are well known undesirable effects of lithium treatment; lithium treatment is reported to cause hypothyroidism in 20% and goiter in 40% of recipients.[1] These thyroid abnormalities are usually mild. Lithium causing myxedema crisis is very rare and usually occurs in context of lithium intoxication. We describe an elderly patient with bipolar affective disorder who was admitted with lithium intoxication and myxedema crisis. This case underscores the fact that severe and dangerous hypothyroidism can develop in some patients who take lithium for prolonged periods.

Access this article online	
Quick Response Code:	Website: www.ijem.in
	DOI: 10.4103/2230-8210.123558

Case Report

A 70-year-old male was admitted in our hospital with history of gradual onset progressive decrease in level of consciousness and altered behavior for last 1 month. He also developed cough, coryza, and fever for last 7 days. He was known to have insulin-requiring type 2 diabetes mellitus for which he was receiving insulin, and bipolar affective disorder for which he had been receiving lithium (300 mg

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twice a day) for about 10 years; his other medications included atorvastatin for dyslipidemia and losartan for hypertension. One year earlier, he had been admitted in our ward for glycemic control and evaluation of complications and found to be clinically and biochemically euthyroid; he never returned for follow up until the present admission.

On initial examination, he was drowsy with incoherent speech. Patient had hypothermia (94º F), bradycardia with heart rate of 52 beats per minute and stable blood pressure. Patient's respiratory rate was 12 per minute. He had features of hypothyroidism including a slow husky voice, a small goiter, a thick, dry, and cold skin, pouting lips, and profoundly delayed deep tendon jerks. The systemic examination revealed crepitations in the right infrascapular region, normal cardiac examination, other than bradycardia, and unremarkable abdominal examination. The neurological examination revealed drowsiness, incoherence (a glasgow coma scale (GCS) of 13/15), no apparent cranial nerve palsy or focal motor weakness, and markedly delayed deep tendon reflexes.

The routine laboratory evaluation showed macrocytic anemia (Hb 10.2, MCV103), azotemia (urea 76 and creatinine 2.6 mg/dl), fasting blood glucose of 141 mg/dl, mild hypernatremia and hypokalemia, and normal liver function test results. Electrocardiogram revealed bradycardia and chest X-ray showed infiltrates in right mammary region.

Thyroid function showed thyroid stimulating hormone (TSH) >150 IU/ml, Tetraiodothyronine (T_4) <1 μg/dl, anti-thyroid peroxidase (TPO) titer of 60 IU/ml. The serum lithium level was 2.9 nmol/L (therapeutic level 0.8-1.2 nmol/L) [Table 1]. He was managed with levothyroxine, starting with a loading oral dose of 500 μg through ryles tube followed by 100 μg daily, IV antibiotics and IV fluids; lithium was stopped after consultation with a psychiatrist. From day 5, patient started showing progressive improvement and by day 10, he had a GCS of 15/15, normal electrolyte, serum creatinine of 1.8 mg/dl and serum lithium level of 0.5 nmol/L.

Table 1: Thyroid function and lithium level at presentation

Investigation	Patient value	Normal value
Serum T_3 (ng/dL)	<15	>75
Serum T_4 (μg/dl)	<1	>4.5
Serum TSH (mIU/L)	>150	0.5–6.5
Serum Anti TPO (U/L)	60	3–12
Serum lithium (U/L)	2.9	0.2–1.2
Cortisol (μg/dl)	38	>33

TSH: Thyroid stimulating hormone, T3: Triiodothyronine, T4: Tetraiodothyronine, anti-TPO: Anti-thyroid peroxidase

Discussion

Myxedema crisis, potentially a fatal disorder with high mortality, usually occurs in long standing untreated hypothyroidism. Myxedema coma caused by lithium is rare with very few case reports in literature.[2,3] Lithium is very potent drug commonly used for treatment of bipolar disorders. It has multiple effects on thyroid function, including inhibition of thyroid hormone release, effects on the hypothalamic pituitary axis, and effect on the thyroid autoimmunity. Lithium is preferentially concentrated in brain and thyroid where it may reach levels 4 times that of plasma. The most important effect of lithium is inhibition of thyroid hormone release from thyroid gland by alteration in tubulin polymerization and inhibition of TSH action on cyclic adenosine monophosphate (cAMP).[4] Lithium is concentrated in pituitary hypothalamic area. A study showed that about half of the patients receiving lithium had exaggerated TSH response to thyrotropin-releasing hormone (TRH).[5] Lithium also exacerbate autoimmune thyroid disease by accelerating the increase in thyroid antibody titer.[6]

Differential diagnosis of our patient was hyperglycemic hyperosmolar nonketotic coma, sepsis due to any infections, and hypoventilation syndrome. Our patient had many features of myxedema crisis, in the form of decreased respiratory rate, increased partial pressure of carbon dioxide (pCO_2), low body temperature, and altered sensorium. There were many contributing factors in development of myxedema coma in this patient. Firstly, the patient was on lithium which is known to have effect on thyroid function, as already discussed. Serum lithium level (2.9 nmol/L) was in toxic range, which was exacerbated because of renal failure and severe hypothyroidism. Hypothyroidism decreases glomerular filtration rate (GFR) because of decrease in cardiac output. So lithium intoxication occurs when lithium renal excretion decreases because of decrease in GFR.[7,8] Probably a vicious cycle sets in with hypothyroidism causing decrease in renal perfusion that leads to retention of lithium, which in turn causes inhibition of thyroid hormone release from thyroid gland exacerbating hypothyroidism. The other major risk factor that contributed in myxedema coma was community-acquired pneumonia.

Lithium toxicity in the elderly may be misattributed to the underlying bipolar disorder for which lithium is being given or to advancing age. The common symptoms of lithium toxicity are nausea, vomiting, ataxia, confusion, seizures and coma. Our patient had many features of chronic lithium intoxication, including vomiting, dysarthria, confusion and coma. The polyuria and hypernatermia reflect lithium

induced impairment of antidiuretic hormone effect on kidney. This case illustrates that lithium-induced thyroid dysfunction, though usually mild, can be severe and dangerous and underscores the need for monitoring thyroid function in patients receiving lithium and withdrawing lithium or instituting appropriate replacement therapy should hypothyroidism develop.

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Cite this article as: Mir SA, Wani AI, Masoodi SR, Bashir MI, Ahmad N. Lithium toxicity and myxedema crisis in an elderly patient. Indian J Endocr Metab 2013;17:S654-6.

Source of Support: Nil, **Conflict of Interest:** None declared.