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Hemodynamic, Electrocardiographic, Metabolic, and Hematologic Abnormalities Resulting from Lithium Intoxication

A Case Report

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ABSTRACT

The authors report a unique case that presented with hemodynamic abnormalities and severe bradycardia, necessitating the insertion of a temporary pacemaker, as well as metabolic disturbances, hematologic changes, and hepatic and renal dysfunction in an elderly individual owing to lithium intoxication. This case also demonstrates that these various serious side effects of lithium resolved with prompt recognition and discontinuation of lithium. Lithium should be used with extreme caution and frequent monitoring especially in the elderly.

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Introduction

Lithium carbonate has been the mainstay for the treatment of manic depressive disorders for many years.[1] It also appears promising in a variety of other psychiatric and nonpsychiatric conditions.[2] The widespread use of lithium salts compromises a certain number of side effects in patients. The increasing use of lithium salts underscores the need for clinicians to understand the risks as well as benefits associated with this therapy. We report a very unusual case of a patient with a history of atrial fibrillation who developed hemodynamic abnormalities with severe bradycardia necessitating temporary pacemaker insertion, as well as metabolic and hematologic disturbances, hepatic dysfunction, and renal insufficiency as results of lithium intoxication.

Case Report

An eighty-one-year old woman with a history of paroxysmal atrial fibrillation and manic depressive illness previously well controlled with oral lithium carbonate (300 mg po qd) was admitted to our hospital, because she was found on the floor at home. She had had a recent decline in memory and decreased functioning a few days prior to this admission, though she had continued to live alone. There was no history of fever, alcoholism, or smoking. The patient was taking no other medication. She had no complaints or any history of cardiopulmonary problems prior to this episode and presented to our hospital with severe bradycardia and hypotension.

The patient was found to be in sinus bradycardia with a heart rate of 34–40 beats/minute (bpm), blood pressure of 85/50 mmHg, and respiratory rate of 20/minute and was afebrile and very confused. She had dry mucous membranes. Initial laboratory examination revealed white blood cells, 12.5 x 1000; neutrophils, 91.3%; hemoglobin, 13.3 g/dL; hematocrit, 40.8%; sodium, 132 mmol/L; potassium, 3.0 mmol/L; chloride, 104 mmol/L; carbon dioxide, 25 mmol/L; blood urea nitrogen, 38 mg/dL; creatinine, 1.6 mg/dL; calcium, 11.2 mg/dL; albumin, 4.1 g/dL; bilirubin-T, 1.7 mg/dL; alkaline phosphatase, 140 mu/mL; lactate dehydrogenase, 250 mu/mL; aspartate aminotransferase, 20 mu/mL; glucose, 162 mg/dL, T_4, 8.2 μg/mL, thyrotropin, 6.6 μIU/mL. Lithium concentration was found to be in the severe toxic range of 2.7 mmol/L (normal 0–1.3 mmol/L). An electrocardiogram showed marked sinus bradycardia with occasional premature ventricular complexes that converted to atrial fibrillation the following day along with inverted T waves in anterior leads. A temporary pacemaker was inserted and digoxin and quinidine were administered. The patient stayed in atrial fibrillation and eventually went back into sinus rhythm. Her heart rate increased above 50 bpm with hemodynamic improvement when her lithium concentration decreased to nontoxic levels (1.2 mmol/L). The temporary pacemaker was then removed. It was felt that the patient's bradycardia and other abnormalities were probably secondary to lithium toxicity. In addition to a temporary pacemaker insertion and discontinuation of lithium, management consisted of administration of intravenous fluids with potassium supplementation. Her blood chemistries returned to normal levels, her mental status and general condition improved, and she was then discharged home on a regimen of valproic acid.

Discussion

This patient presented with hemodynamic abnormalities along with severe bradycardia, multiple metabolic abnormalities (hyponatremia, hypokalemia, hypercalcemia, and hyperglycemia), hematologic changes (granulocytosis), and hepatic and renal dysfunction resulting from lithium toxicity. This case report has several points of major interest. A large number of patients managed by lithium have side effects, which may not be apparent initially, may be neglected, or may be attributed to psychiatric illness. The recent decline in memory and decreased functioning a few days prior to admission in our patient suggests that lithium intoxication should be considered in the differential diagnosis when there is a new change in clinical status, and such a change should not be attributed to the underlying psychiatric disorder without investigation.

Lithium has been reported to cause T wave flattening or inversion on the electrocardiogram, resembling changes seen with hypokalemia and symptomatic sinus node dysfunction.[3] In most cases, including ours, adverse effects of lithium are reversible when the lithium is discontinued, but some patients require a permanent pacemaker.[4] The effect of lithium on the sinus node seems to be intrinsic. First-degree atrioventricular block, premature ventricular contractions,[5] and even

sinus arrest with asystole[6] have been reported. Because symptoms of syncope, dizziness, and confusion are difficult to evaluate in patients with prexisting psychiatric illness, as in our case, they may be overlooked, and episodes of significant bradycardia induced by lithium may be underestimated.

The risk of lithium intoxication is increased in the presence of hyponatremia,[7] which can lead to increased reabsorption of lithium and subsequent intoxication, because the proximal transport system does not adequately differentiate between sodium and lithium.[8] Patients taking lithium are generally not sodium depleted, though mild hyponatremia was the presenting feature in our case. Excretion of lithium is directly related to the glomerular filtration rate, so factors that decrease glomerular filtration (eg, aging in our case) will have a similar effect on lithium excretion. In turn, glomerular filtration rate may decrease during lithium intoxication.[9] This case also calls attention to the risk of lithium toxicity in the face of unexpected renal impairment. While lithium may be continued even when treatment puts renal function at risk, lithium levels must be closely observed. Unlike many psychotropic medications, lithium has little potential for hepatotoxicity,[10] and was the probable cause of the mild liver function abnormalities seen on presentation in our patient. Lithium itself on rare occasions causes clinical hypercalcemia with documented increased levels of parathyroid hormone[11] with decreased calcium excretion and increased fractional tubular calcium reabsorption. The finding of hypercalcemia in our patient is consistent with the data in the literature.[11] In addition, our patient's blood chemistry also demonstrated a slightly elevated level of thyrotropin, which was normalized after the lithium concentration was restored to the therapeutic range.

Lithium intoxication was the probable cause of our patient's leukocytosis. Mild to moderate granulocytosis, characterized primarily by mature neutrophils, is a frequent side effect of lithium.[12] Lithium has been administered with significant increase in granulocyte counts during anticipated chemotherapy-induced nadir periods.[13] It reduces infections, length of hospitalization, and antibiotic use[14] and reverses azidothymidine-induced neutropenia in patients with acquired immunodeficiency syndrome.[15] However, lithium is not generally used in treating granulocytopenia.

Conclusion

The major interest of this unique observation resides in the clinical symptomatology—the hemodynamic, electrocardiographic, metabolic, and hematologic changes and the liver and renal dysfunction in an individual resulting from lithium intoxication. This case also demonstrates that the various serious side effects of lithium may resolve with prompt recognition and discontinuation of the lithium. Several recommendations can be made based on the case report presented here. This case demonstrates that lithium therapy should be used with extreme caution with frequent monitoring, especially in the elderly as well as in those patients with preexisting cardiac arrhythmias. Lithium concentrations should be monitored if the patients experience any significant change of mental status. Immediate work-up should include complete blood count, electrolyte values, fasting glucose, renal function assessment, liver function tests, thyroid function studies, 12-lead electrocardiogram, and electrocardiographic monitoring. For proper management of patients, physicians should be aware of different hemodynamic, electrocardiographic, metabolic, and hematologic abnormalities seen in lithium intoxication.

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