CASE REPORT

Unusual Cause of Syncope in a Patient with Ischemic Heart Disease

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Lithium is a commonly used drug for bipolar mood disorder. Though effective, it has a narrow therapeutic range and has potentially life-threatening effects at higher serum levels. Lithium toxicity can be precipitated by several drug interactions. Many commonly used cardiac drugs have serious drug interaction with lithium which is not commonly known in clinical practice. We present a case where a patient on lithium therapy since 15 years, presented with sinus arrest and syncope due to lithium toxicity, within 2 weeks of initiation of low dose angiotensin converting enzyme (ACE) inhibitor. The patient however needed temporary pacemaker support and had an uneventful recovery, without the need for a permanent pacemaker, once the lithium levels fell down to normal.

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INTRODUCTION

Lithium is a commonly used drug for bipolar mood disorder.¹ Lithium toxicity can be precipitated by several drug interactions. Many commonly used cardiac drugs have serious drug interaction with lithium which is not commonly known in clinical practice.² We present a case where a patient on lithium therapy since 15 years, presented with sinus arrest and syncope due to lithium toxicity precipitated by an unusual interaction.

CASE REPORT

A 55-year-old man, presented with two episodes of dizziness and vomiting followed by syncope. On presentation his heart rate was 40/minute and blood pressure was 105/65 mmHg. The electrocardiogram showed sinus arrest (Fig. 1, Panel A) with a junctional escape rhythm of 35–40 beats/minute (Fig. 1, Panel B), which did

not show any change with intravenous atropine. In view of symptomatic sinus arrest, temporary pacemaker implantation was done. Two weeks prior to this episode, patient had undergone a percutaneous coronary intervention (PCI) to obtuse marginal branch for recent onset angina. A check coronary angiogram showed normal instant flow. Patient was on dual antiplatelet therapy, statin and Angiotensin converting enzyme (ACE) inhibitor (Ramipril) therapy. He was not taking any atrioventricular (AV) node-blocking drugs. Patient revealed that he was a case of bipolar disorder for 15 years and was taking 450 mg of lithium carbonate and carbamazepine 1000 mg daily. He has been on this dose for a long time with periodic monitoring of serum lithium levels which were always in the therapeutic range. However, the present serum lithium level was raised to 2.1 mM (normal 0.40–1.20), and serum carbamazepine level was 5.84 µg/mL (normal 5.0–15.0). Levels of serum electrolytes, plasma creatine

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Figure 1. Panel A and B: electrocardiogram with rhythm strip showing sinus arrest with heart rate varying from 35 to 40 per minute.

kinase (muscle-brain), troponin I, as well as renal function, were within normal limits. Thyroid function tests showed normal thyroid-stimulating hormone levels and free triiodothyronine and L-thyroxine levels. A diagnosis of lithium induced sinus node dysfunction was made and patient was monitored for spontaneous sinus node recovery failing which dialysis was planned. Both lithium and ramipril administration were stopped. After 36 hours, there was acceleration of idioventricular rhythm to a rate of 60–65 beats/minute. After 60 hours, normal sinus rhythm returned at a rate of 70–80 beats/minute. A diagnosis of lithium-induced sinus node dysfunction was made based on the absence of other competing diagnosis. Given the high likelihood of a recurrence of the bradyarrhythmia, lithium carbonate was restarted at a lower dose, carbamazepine was continued, ramipril was stopped and patient was discharged after a week.

DISCUSSION

Lithium is a common and effective drug used in psychiatric practice. It has a very narrow therapeutic range and has serious toxic effects at

higher levels. Lithium induced conduction defects include sinus node dysfunction, atrioventricular blocks, right bundle branch block, and left anterior hemiblock.¹ These defects have been described at therapeutic levels and at toxic serum levels.¹ Sinus node dysfunction due to lithium may manifest as sinus bradycardia, sinoatrial block, sinus pauses with junctional escape rhythm, and sinus node arrest with idioventricular escape rhythm.¹ In the present case, patient presented with sinus node arrest and syncope. Bradyarrhythmias due to lithium have often been attributed to associated hypercalcemia and hypothyroidism. However, serum calcium levels and thyroid profile was normal in the present case. Mechanism of lithium induced sinus node dysfunction is complex. Sinus nodal pacemaker activity is governed by interaction between pacemaker (HCN2/4) channels, L-type calcium and acetylcholine-gated potassium channels, and sodium-calcium channel exchanger.² Lithium has been shown to alter the sinus node pacing function by interacting with pacemaker (HCN) channels and/or the sodium channel exchanger.² However, the need for pacemaker implantation in patients on lithium is rare and most of these effects are either reversible or clinically not significant.³ Interesting observation in the present case was

that a patient who had stable therapeutic serum lithium levels since last 15 years, developed lithium toxicity with sinus arrest within 2 weeks of initiation of cardiac drugs including statins, antiplatelet agents and ACE inhibitors. While statins and antiplatelet agents have no known interactions with lithium, ACE inhibitors can cause lithium toxicity. Lithium is not metabolized and removed, almost exclusively, by the kidneys from the body. The blood levels are hence dependent greatly on the kidney function, age, and the volume status. Any drug affecting the renal physiology can potentially affect the lithium concentration in the body. Drug interactions are a very important cause of lithium toxicity as seen in this patient. A significant number of the commonly used cardiac drugs have potentially serious drug interaction with lithium. The most pronounced of these is the thiazide diuretics which, owing to their distal renal tubular action, promote sodium and lithium reabsorption in the proximal tubule. The lithium levels can rise by as high as 40% with their use.⁴ ACE inhibitors have also been reported to increase the serum lithium levels. One study showed that after initiation of ACE inhibitor, steady-state lithium concentrations increased by 36%, lithium clearance was reduced by 26%, and four patients presented with symptoms suggestive of lithium toxicity.⁵ Considering that both these drugs are very commonly used in general practice, being used in hypertension and a lot of cardiac ailments, knowledge of their interaction with lithium is very important in general practice. Our patient was

prescribed ramipril after PCI which precipitated lithium toxicity leading to sinus arrest and syncope. Studies have shown that there is no effect of aspirin on lithium levels while loop diuretics and calcium channel blockers have an unpredictable effect and the lithium levels need to be carefully monitored.⁴

This case reminds us of an unusual interaction of two commonly used drugs for cardiac disorders (ACE inhibitor) and for bipolar depression (lithium). This also highlights the fact that lithium has potentially serious drug interactions with many commonly prescribed cardiac medications and before prescribing any drugs to a patient on lithium it will be prudent to check the possible drug interactions and then monitor the serum lithium levels carefully. Also, the need for pacemaker implantation in patients on lithium is uncommon and the conduction anomalies are reversible once the lithium levels fall back to normal.

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