Hemodialysis Treatment of Monomorphic Ventricular Tachycardia Associated with Chronic Lithium Toxicity

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Abstract

Introduction A patient with chronic lithium toxicity developed a life-threatening ventricular arrhythmia that resolved during removal of lithium by hemodialysis. Chronic lithium toxicity commonly results from diminished elimination and can produce neurotoxicity. Cardiovascular complications have been reported and generally affect the sinoatrial node and produce bradyarrhythmias. The majority of these arrhythmias require no emergent intervention. Ventricular arrhythmias associated with lithium toxicity are occasionally mentioned in the literature, but actual cases are rarely reported.

Case Report A 74-year-old man was brought into the emergency department with a 3-day history of progressive encephalopathy, tremor, and weakness. The lithium level was

elevated at 2.2 mmol/L, with a normal serum potassium. Electrocardiography revealed nonsustained monomorphic ventricular tachycardia (120–130 beats/min) lasting up to 1 min, alternating with sinus bradycardia and wandering atrial pacemaker. Episodes of monomorphic ventricular tachycardia recurred >100 times. The patient required a norepinephrine infusion for hypotension. Emergent hemodialysis was initiated to remove lithium and to treat the monomorphic ventricular tachycardia, which was felt to be secondary to lithium toxicity. Episodes of monomorphic ventricular tachycardia abated as hemodialysis progressed. The episodes resolved completely within 4 h of initiating hemodialysis. The patient was discharged home in sinus rhythm on day 5. Lithium was not reinstated.

Conclusion Monomorphic ventricular tachycardia associated with chronic lithium toxicity is exceptionally rare. Hemodialysis is a treatment option.

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Introduction

Lithium (Li) at therapeutic levels (0.6–1.2 mmol/L) has been associated with electrocardiogram (ECG) changes consistent with sinus node dysfunction [1–6], T wave changes [1–6], QT interval prolongation [1–4], and atrio-ventricular block [1, 6], none of which appear to cause clinically significant illness [1]. Clinical manifestations of chronic Li toxicity are primarily neurological; however, serious cardiac arrhythmias, generally bradyarrhythmias, have been reported [3–8]. Bradyarrhythmias occurring in a patient on Li should prompt testing for Li toxicity and

associated electrolyte abnormalities [4]. Monomorphic ventricular tachycardia (mVT) associated with Li toxicity is exceptionally rare, with only three cases found in the literature [9–11]. We describe the first case of hemodialysis (HD) treatment of mVT associated with chronic Li toxicity.

Case Report

A 74-year-old man presented to the emergency department with a 3-day history of progressive encephalopathy, tremor, weakness, and a 1-day history of diarrhea. Past medical history included bipolar disorder, hypertension, benign prostatic hypertrophy, recent prostate cancer, and undiagnosed chronic kidney disease. Medications included lithium carbonate 300 mg BID, bupropion 150 mg, lisinopril 20 mg, finasteride 5 mg, lovastatin 20 mg, clonazepam 0.5 mg, and tamsulosin 0.4 mg. No medications were taken for 2 days. He denied use of over-the-counter or herbal preparations. Initial vital signs were blood pressure 108/59 mmHg, heart rate 60 beats/min (regular), respiratory rate 18 breaths/min, and oxygen saturation of 100 % (room air). Physical exam revealed lower extremity hyperreflexia and clonus, upper extremity hypertonia and tremor, tongue fasciculations, and garbled speech interspersed with muteness. Initial ECG revealed a junctional rhythm with a heart rate of 51 beats/min, corrected QT interval of 476 ms (prolonged), and multiple premature ventricular and supraventricular complexes (Fig. 1). An ECG obtained 1 month prior, when the serum Li level was 1.2 mmol/L and creatinine was 1.55 mg/dL, had shown first-degree AV block, intraventricular conduction delay (IVCD), T wave flattening, and QT interval prolongation. Magnesium sulfate (2 g) and atropine sulfate (1 mg) were administered for QT interval prolongation and bradycardia in the emergency department. Pertinent initial lab values revealed blood urea nitrogen 93 mg/dL, creatinine 4.79 mg/dL, sodium 143 mmol/L, calcium 9.3 mg/dL, potassium 4.8 mmol/L, chloride 111 mmol/L, carbon dioxide 19 mmol/L, magnesium 2.9 mg/dL

(normal range 1.7–2.4), and Li level 2.2 mmol/L. All other labs including troponin I, thyroid-stimulating hormone, and free T₄ were normal. Arterial blood gas analysis showed a pH 7.35, pCO₂ 34 mmHg, bicarbonate 18.4 mmol/L, and base deficit of 6.3 mmol/L. The patient was bolused 2 L of normal saline for volume resuscitation and clinical signs of dehydration. Foley catheter placement produced over 1 L of dark urine.

During EMS transport to our facility, the patient experienced recurrent runs of a wide complex tachycardia, without hemodynamic compromise. On arrival to the ICU, serial ECGs revealed nonsustained mVT (120–130 beats/min; lasting up to 1 min/run) alternating with sinus bradycardia and wandering atrial pacemaker (34 beats/min) (Fig. 2). Intravenous magnesium sulfate (2 g), sodium bicarbonate (50 mEq), and calcium gluconate (1 g) were promptly given, without effect. Episodes of mVT recurred >100 times, without loss of consciousness. Hypotension (72/31 mmHg) persisted, despite a 1-L saline bolus, and responded to a norepinephrine infusion. A cardiologist and nephrologist were consulted. The cardiologist recommended HD, rather than anti-arrhythmics or transvenous pacemaker, believing that the mVT was secondary to Li toxicity. Episodes of mVT progressively decreased over the first 4 h of HD (F160 dialysis filter, blood flow rate 300 mL/min, dialysate flow rate 500 mL/min) and then abruptly stopped. Hypotension resolved and norepinephrine was discontinued. A Li level after HD was 0.4 mmol/L. There was no significant redistributive increase in Li levels after 10 h of HD. Free digoxin was undetectable. Total bupropion and hydroxybupropion levels, obtained 12 h after admission, were <10 ng/mL (therapeutic 50–100 ng/mL) and 166 ng/mL (therapeutic 600–1,200 ng/mL), respectively.

He had a slight improvement in mental status and tremor by day 2, but he continued to have sinus bradycardia and a junctional escape rhythm. His urine output improved, with a creatinine of 1.26 mg/dL. On day 3, his neurocognition improved and tremor resolved. Electrocardiogram showed normal sinus rhythm with a nonspecific IVCD. Cardiovascular workup included serial troponins

Fig. 1 Initial electrocardiogram in the emergency department showing a junctional rhythm with premature ventricular complexes, supraventricular complexes, and nonspecific intraventricular conduction delay (heart rate 51 beats/min, QRS duration 132 ms) with a prolonged QT interval of 476 ms

Fig. 2 Electrocardiogram showing monomorphic ventricular tachycardia on arrival to the intensive care unit (heart rate 123 beats/min)

(negative $\times 3$), echocardiography (ejection fraction 55–60 %, without wall motion abnormalities), and a lexiscan cardiolute stress test (normal). The patient made a complete recovery and was discharged home on day 5, with a Li level of 0.4 mmol/L. The ECG on discharge revealed resolution of first-degree AV block, QT prolongation, sinus bradycardia, and T wave abnormalities. The patient's chronic kidney disease likely increased his risk of Li toxicity. Lithium therapy was not reinstated.

Discussion

Lithium has a narrow therapeutic range (0.6–1.2 mmol/L). Chronic exposures result in greater tissue loads, which may present with clinical toxicity [7]. Lithium's effect on cardiac conduction is still theoretical. Lithium may interact or compete with other cations, such as sodium, potassium, calcium, and magnesium. Lithium exposure may reveal Brugada syndrome, suggesting that sodium channel blockade may be involved in sinus node dysfunction at toxic levels [7, 12].

Ventricular tachycardia associated with Li toxicity is mentioned in the literature, yet actual case reports are rare and treatment is not established. A literature search utilizing PubMed, Ovid, and Toxline resulted in three cases of Li toxicity-associated mVT. These cases differed from our case in that previous cases were all associated with acute or chronic Li toxicity. Meneguetti et al. [9] reported an acute overdose in a diabetic 61-year-old man with a history of chest pain. Hemodialysis was performed on day 1 to remove Li. On day 3 of hospitalization, the patient developed mVT treated with anti-arrhythmics and transvenous pacing. The Li level at the time of mVT was not reported. Of note, on day 2 of hospitalization, troponin was elevated and the patient was intubated and started on dopamine. The clinical course suggests that mVT was not associated with Li toxicity. Worthley [10] reported a 52-year-old woman with untreated hypothyroidism with a recent increase in her Li dose 10 days prior. She

experienced cardiac arrest followed, 18 h later, by mVT that resolved with intravenous magnesium sulfate. The authors did not claim that Li induced the cardiac arrest or that the cardiac arrest may have lead to the mVT. Francis et al. [11] reported a 10-year-old boy on multiple pro-arrhythmic medications who recently increased his Li dose and presented with mVT. He was treated for 4 days with a procainamide infusion. The pro-arrhythmic medications were methylphenidate, oxcarbazepine, escitalopram, and levothyroxine. This child was discharged with an ECG showing IVCD that had resolved on follow-up. These three cases do not establish a causal association of Li toxicity and mVT. Confounding conditions may have precipitated ventricular tachycardia, independently. In our case the patient had a negative cardiac workup, normal serum potassium, normal thyroid-stimulating hormone, and progressive resolution of mVT during removal of Li by HD. The rapid resolution of mVT in this case may have been secondary to removing free Li from sodium channels, in an individual with pre-existing susceptibility to mVT due to underlying IVCD.

Electrocardiographic changes seen during chronic Li therapy may be influenced by age, pre-existing cardiac disease, and duration of therapy [1]. Our patient was elderly, with pre-existing IVCD and a history of >10 years of Li therapy. The ECG from 1 month prior had revealed first-degree AV block, IVCD, T wave flattening, and QT interval prolongation. At that time, the serum Li level was 1.2 mmol/L, with renal impairment. It is unknown if the patient exhibited clinical evidence of Li toxicity at that time. However, Li therapy likely contributed to these prior ECG abnormalities, since we saw complete resolution by the end of his hospitalization.

Pre-existing IVCD is a risk factor for developing mVT. The possibility that chronic exposure to Li caused or revealed an IVCD is plausible. At high Li levels, IVCDs have been observed previously [2, 4–6, 11]. Intraventricular conduction defects associated with high Li levels have resolved after discontinuation of Li therapy, but the reported time course is vague. Our patient did not have an ECG once the Li level

became undetectable. At the time of our final ECG, Li was likely still present in cardiac cells. Hence, we are unable to determine if the patient had an underlying IVCD, unrelated to chronic Li therapy. While there appears to be an association between chronic Li therapy and abnormal cardiac conduction, the prevalence and clinical significance of these abnormalities remain unknown [6]. Based on the paucity of reported cases of mVT associated with Li toxicity, the development of mVT appears rare. Predisposing risk factors may be essential to developing mVT after Li exposure.

We do not believe bupropion, or its active metabolite hydroxybupropion, contributed to mVT. In renal failure, hydroxybupropion has a half-life >30 h [13]. The levels were drawn 12 h after admission and still would have been less than therapeutic if drawn immediately upon admission. Abnormal potassium concentrations have also been linked to arrhythmias associated with Li toxicity [2, 4, 7–9]. Our patient had normal serum potassium levels throughout hospitalization.

Hemodialysis rapidly removes Li from serum [14], but its use to treat toxicity remains controversial. Based on our patient's critical condition, with acute or chronic renal failure and mVT, we felt HD would rapidly remove Li and potentially cease the mVT. In our patient, the continuous removal of Li by HD correlated temporally with progressively diminishing runs of mVT, suggesting that Li was responsible for the frequently recurrent, nonsustained mVT.

Conclusion

Cardiac arrhythmias associated with Li toxicity may be life threatening and require emergent intervention. Although rare, patients with chronic Li toxicity may present with mVT. Patients with predisposing risk factors for ventricular arrhythmias may develop mVT after Li exposure. Monomorphic ventricular tachycardia associated with chronic Li toxicity may resolve with hemodialysis.

Conflict of Interest The authors have no conflicts of interest to disclose.

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