

# Journal of Atrial Fibrillation



# Acute Atrial Fibrillation as an Unusual Form of Cardiotoxicity in Chronic Lithium Overdose

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#### Abstract

Lithium overdose primarily results in neurologic toxicity; however a number of important cardiac side effects have previously been reported, including nonspecific T-wave changes, ST-segment changes, QTc prolongation, sinus node dysfunction, atrioventricular blocks and ventricular dysrhythmias. Atrial fibrillation due to such toxicity is very uncommon. The current paper describes a patient who developed acute atrial fibrillation due to chronic lithium overdose.

# Introduction

Lithium has been used for many years in the treatment of depression and bipolar disorder.<sup>1</sup> Since it has a narrow therapeutic range<sup>2</sup> and patient population using lithium has a relatively high risk of overdose, lithium toxicity (LT) is still a common entity. Impairment of renal functions may predispose to lithium accumulation because it is mainly excreted by kidneys. Neurologic and gastrointestinal symptoms including nystagmus, ataxia, tremors, nausea, vomiting, and diarrhea predominate in the majority of cases.<sup>2</sup> Serious cardiac toxicity due to LT is uncommon and generally occurs in individuals with underlying heart disease. The exact mechanisms of lithium's cardiac effects are unknown but most probably related to lithium's similarity to sodium and potassium ions, thus affecting intracellular sodium and potassium channels.<sup>3</sup>

# **Case Presentation**

A 68-year old non-diabetic hypertensive man was admitted to our emergency department with altered mental status, ataxia, nausea and vomiting. He had a previous history of bipolar disorder and been taking a combination of lithium carbonate (1200 mg/day) and

# Key Words:

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risperidone (2 mg/day) for 13 years. Two weeks ago, olmesartan (40 mg/day) was prescribed for hypertension. He had no cardiovascular risk factors except hypertension. His vital signs were as follows; blood pressure: 105/65 mmHg, pulse rate: 93 bpm, respiratory rate: 20 bpm, body temperature: 37,3°C and oxygen saturation of 91%. Physical examination was unremarkable. He was confused and unresponsive to verbal stimulation. Intravenous infusion of fluids was started with supplemental oxygen and a cranial computed tomography was performed which excluded a cerebrovascular accident. Chest X-ray was normal and electrocardiography (ECG) showed an atrial fibrillation (Figure 1A) which we considered as acute-onset because his previous ECG at two weeks earlier showed normal sinus rhythm. Transthoracic echocardiography revealed mild left ventricular hypertrophy with a normal ejection fraction (Figure 2A and 2B, Figure 3) and valvular functions. Initial laboratory findings including complete blood count, electrolytes, arterial blood gas, glucose, alkaline phosphatase, aspartate aminotransferase, lactate dehydrogenase, albumin, thyroid function tests and cardiac markers were normal except for serum creatinine levels of 1.7 mg/dL, BUN of 44 mg/dL and toxic lithium levels of 2.1 mEq/L (normal therapeutic range: 0,6-1,2 mEq/L). The patient was admitted for hemodialysis with the diagnosis of possible LT. After hemodialysis lithium levels decreased to 0.8 mEq/L. Spontaneous conversion of atrial fibrillation to normal sinus rhythm (Figure 1B) occurred just 30 minute after the hemodialysis without any antiarrhythmic therapy. Two days later his mental status and general condition improved. Renal arterial Doppler study was performed to rule out any renal arterial stenosis but bilateral renal arterial flows were within normal limits. During

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Figure 1:

Electrocardiography on admission showing an atrial fibrillation with an average ventricular rate of 93/bpm (A) and spontaneous conversion to sinus rhythm after hemodialysis (B).

hospitalization, he was under continuous monitoring and a 48-hours Holter monitor after discharge did not detect any paroxysmal atrial fibrillation. Sinus rhythm was maintained during the following six months. It was considered that the atrial fibrillation episode was probably secondary to LT.

# Discussion

In the early 19th century lithium was used as a treatment for gout, considering high solubility of urate in lithium carbonate-based solutions.<sup>4</sup> It has retained a role in the treatment of depression and bipolar disorder since 1940s.<sup>1</sup> It has a narrow therapeutic window, with therapeutic serum levels ranging from 0.6 to 1.2 mEq/L and toxic effects being seen at levels of 1.5 mEq/L.<sup>2</sup>

LT may occur in three scenarios: 1) acute overdose, when a lithium-naive individual takes an overdose lithium, 2) acute on chronic overdose, when a patient taking lithium acutely overdoses on his/her medication, and 3) chronic overdose, when a patient

taking lithium either takes an increased dosage for a period of time or develops decreased renal elimination of the drug.<sup>5</sup>

In the majority of LT cases, neurologic and gastrointestinal symptoms predominate including nystagmus, ataxia, tremors, nausea, vomiting, and diarrhea.<sup>2</sup> Cardiac toxicity is unusual and generally occurs in individuals with underlying heart disease. Classically, the cardiovascular manifestations of LT may tend to occur later than neurological effects. Important cardiac effects of LT have previously been described, including nonspecific T-wave changes,<sup>6</sup> ST-segment changes,<sup>7</sup> QTc prolongation,<sup>6</sup> sinus node dysfunction,<sup>8</sup> atrioventricular blocks<sup>9</sup> and ventricular dysrhythmias.<sup>10</sup> To our knowledge, this is the first reported case of acute atrial fibrillation which developed due to lithium toxicity.

Chronic lithium toxicity may present with non-specific clinical features, especially in older patients, and the diagnosis requires a high degree of clinical suspicion. In a recent review, the strongest predictors of severe toxicity in chronic lithium poisoning were the



Figure 2:

Two dimensional transthoracic echocardiography apical four chamber view reveals mild left ventricular hypertrophy and normal size of cardiac chambers (A), parasternal long axis view M-mode study confirming normally functioning left ventricle



#### Figure 3:

Two dimensional transthoracic echocardiography parasternal long axis view showing mild left ventricular hypertrophy with a normal ejection fraction and normal atrial dimensions.

presence of diabetes insipidus, age >50 years, hypothyroidism and impaired renal function.<sup>11</sup> In the present case, renal impairment probably predisposed to lithium accumulation and contributed to development of toxicity.

This case highlights that lithium therapy should be used with extreme caution under frequent monitoring, especially in the elderly and in those patients with preexisting cardiac disease. Lithium concentrations and renal function tests should be monitored if the patients start a new medication which may impair renal functions. LT may cause acute atrial fibrillation and should be considered in differential diagnosis. Management of acute atrial fibrillation due to LT may not require specific therapy; discontinuation of lithium and decrement in lithium levels to therapeutic range after hemodialysis may solve the problem.

# **Conclusions:**

Lithium therapy may be associated with development of atrial fibrillation in toxic doses, necessitating extreme caution in patients with older age and underlying cardiac diseases.

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