Lithium-induced Sinus Node Dysfunction: A Case Report

Lithium has been a first-choice medication for bipolar disorder for years. Lithium has some lithium-related toxicities, in cardiac, renal, and endocrine systems [1]. One of the life-threatening side effects is lithium-induced sinus node dysfunction. Previous case reports have been suggested that lithium has the risk with toxic level and in older patients with underlying cardiovascular disease [2]. Here, we report the case of a patient with lithium-induced sinus node dysfunction even within therapeutic levels of lithium on a young male bipolar patient without underlying cardiovascular disease.

Case Report

A 22-year-old male patient did not have a history of any apparent underlying systemic or heart disease. He was admitted to Taipei City Psychiatric Center with a diagnosis of bipolar I disorder, current episode manic, severe, with psychotic features. On admission, the finding of routine electrocardiogram (ECG) examination showed normal sinus rhythm. His drugs were slowly titrated up to lithium to 1,800 mg/day (serum level: 0.72–0.92 mEq/L), combined with valproic acid 1,000 mg/day (serum level: 75 mEq/L), and risperidone 6 mg/day. On day 68, antipsychotic medications were shifted from risperidone to haloperidol 20 mg/day due to persistent mania with severe psychotic symptoms and his good clinical response to haloperidol. On day 87, he had a sudden onset of bradycardia (pulse rate, 44 beats/min) with chief complaints of dizziness and near fainting. The ECG showed the finding of bradycardia with supraventricular premature contraction at that time. For differential diagnosis, he received other laboratory tests such as electrolytes; blood cell counts; cardiac enzymes; and liver, renal, or thyroid function. All tests revealed negative findings, and at the same time, lithium serum levels showed 1.04 mEq/L (with a dosage of 1,800 mg/day).

Considering the rare risk of lithium-induced sinus node dysfunction, we tapered off lithium dose to 1,500 mg/day in the next day (day 88) and rechecked serum levels with 0.96 mEq/L 5 days later. Bradycardia had been persisted from day 87 to day 89, with his pulse rate around 40–50 beats/min without other unstable signs or discomfort, and on day 90, his pulse rate was 62 beats/min with ECG showing normal sinus rhythm. We kept lithium dosage at 1,500 mg/day and followed up his serum lithium level once per month for half a year after this event.

Finally, his manic symptoms subsided with regiments of daily haloperidol 20 mg, lithium 1,500 mg, and valproic acid 1,000 mg. During the following periods, the lithium serum levels were between 0.7 and 1.0 mEq/L, and he had not had any cardiac rhythm abnormalities since.

Comment

The pathophysiology of lithium-induced sinus node dysfunction is hypothetically presumed related to a concentration-dependent block of voltage-gated sodium channels, which is related to sinus node pacemaker activity [3]. Lithium-induced conduction defects usually occur at toxic levels and rarely at serum therapeutic levels (0.6–1.2 mEq/L) [2]. But by observation of high levels of lithium in cardiac tissue of patients died from interstitial myocarditis due to lithium carbonate therapy, it indicated that there may be excessive accumulation in cardiac cells comparing to the peripheral serum levels [4].

A previous review showed that lithium-induced sinus node dysfunction is mostly seen either in older female patients with underlying cardiovascular disease when the serum lithium levels are within therapeutic levels or in younger patients without underlying cardiovascular disease, but under toxic lithium levels [5]. We categorized this case of the patient with lithium-induced sinus node dysfunction as a probable cause using Naranjo Adverse Drug Reaction Probability Scale [6], even the young patient did not have a known previous cardiovascular history and the serum levels of lithium were within normal range. We postulate that maybe the duration of lithium therapy with a relatively high dosage might contribute to one of the risk factors for developing lithium-induced sinus node dysfunction, although no conclusive data exist in previous studies. One previous study further suggested that for patients with long-term treatment of lithium, regular discontinuation intervals (drug holiday) can avoid excessive accumulation of lithium in the heart [7].

Lithium-induced sinus node dysfunction is reversible, but possibly fatal. Clinical attention is warranted to this possibility when prescribing lithium not only to old aged patients with underlying cardiovascular disease but also to those physically well young patients even within therapeutic levels of lithium. (The institutional review board of Taipei City Hospital gave exemption for IRB review in publishing this case report [protocol number = TCHIRB-10812003-W, and date of approval = December 13, 2019]), without the need to obtain written signed consent from the patient).

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Conflicts of Interest

There are no conflicts of interest.

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