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Case Report

A case of lithium toxicity with normal therapeutic level

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Lithium is the mainstay treatment of bipolar affective disorder. However due its narrow therapeutic window, a careful monitoring has been recommended especially in people with risk factors for toxicity. There is a debate about the usefulness of measuring serum lithium concentration to predict toxicity. Here, we are reporting a case of lithium toxicity in 52-year-old female without significant risk factor with normal serum lithium concentration.

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Introduction

Lithium has been a first line medication in the treatment for bipolar affective disorder. [1] Due to narrow therapeutic range (recommended level is 0.6-1.2 mmol/L during initiation and 0.4 -1.0 mmol/L during maintenance).[1] A careful monitoring is required especially for people with risk factor who are at high risk for toxicity. These risk factors include old age, dehydration, impaired renal function, nephrogenic diabetes insipidus, thyroid disease, and concurrent use of certain medications (including NSAIDS, Renin-angiotensin system inhibitors, thiazide diuretics, Spironolactone and Calcium channel blockers). [1] Toxicity can manifest in wide range of symptoms, mainly neurological, gastrointestinal, and cardiac symptoms.[1,2]. Toxicity usually develop with serum level more than 1.5. [2] The pattern toxicity is: acute, acute on chronic and chronic. Despite that Lithium intoxication carries low mortality rate, there is a risk of permanent neurological deficit and treatment of lithium intoxication may require intensive management over several days and treatment decisions can be complex.[1]

Case Description

52-year-old woman with past medical history of bipolar disorder, anxiety and hypothyroidism. Presented to our hospital with Two-week history of nausea, vomiting, weakness, dizziness, blurry vision, gait instability, and tremor. Her medication list includes levothyroxine 112 mcg once daily, alprazolam 1 mg twice daily as needed and lithium 600 mg twice daily. She was managed on lithium 300 mg twice daily for eleven years, with a dose increase to 600 mg twice daily three weeks prior to her presentation by her psychiatrist due to insufficient control of her psychiatric symptoms. Except for gait instability, her physical exam Including neurological exam was normal. Her work up revealed Normal serum lithium level of 1.0 mmol/L, normal thyroid stimulating hormone of 0.77 uIU/mL, normal electrolytes levels, normal renal function, normal hepatic function. Infectious work up that included normal urine analysis did not show any sign of infection. MRI of the brain did not show any abnormalities. her symptoms improved after holding lithium and providing intravenous hydration. On the second day patient was discharged per her wishes after improvement of symptoms. Her previously recorded lithium levels has been always either in the therapeutic or sub therapeutic range as shown in the table 1.

Discussion

There is a debate regarding the usefulness of serum lithium level in predicting the development of toxicity. Reports of patients developing signs of toxicity with

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therapeutic range level. [1,5,6,7] this Lack of relationship can be explained by the discordance between lithium concentrations in plasma and other tissues, including the brain which is the main site of toxicity. Our case demonstrates an example of acute on chronic lithium toxicity despite therapeutic serum level. Her diagnosis was confirmed by the presentation of typical symptoms of lithium toxicity, improvement of symptoms after holding lithium, and exclusion of other possible diagnoses. In addition to that our case stand up unique as our patient did not have significant risk factor to develop lithium toxicity as Her thyroid disease was well controlled. This supports the hypothesis that serum lithium levels do not reflect the intracellular concentration. Furthermore, this draws question to whether the therapeutic range may be too aggressive, considering toxicity reported at the upper end of the normal therapeutic range in some patients.

Table 1: Dosage and serum concentrations of lithium previously recorded in the patient chart.

Date	Lithium dose (mg/day)	Patient lithium level
1/11/2016	600	0.8
11/13/2016	600	0.6
4/10/2017	600	0.1
12/5/2017	600	0.5
2/13/2018	1200	1

Conclusion

To diagnose lithium toxicity, four elements should be considered that include: patient risk factor, does of lithium ingested, time course and serum lithium concentration. We cannot count only on serum lithium concentration for the diagnosis. In addition to that we suggest conservative initiation dose of lithium, slow dose increases, and close monitoring of symptoms in addition to lithium levels. Especially in people who have a predisposing factor. Finally, we believe that data regarding a safer therapeutic range should be studied in a systematic manner.

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Conflict of Interest

None.

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