

Lithium Toxicity Misdiagnosed and treated as Parkinson's disease

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Received date: January 13, 2018; Accepted date: January 25, 2018; Published date: January 30, 2018

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Abstract

The mechanism of side effect of lithium is poorly understood but probably as a result of excessive effects at therapeutic sites. Tremor is frequently reported to be the most common movement side effects, severe Parkinsonism as a result of neurotoxicity has been reported though rarely.

We present a patient with subacute severe reversible Parkinsonism and acute delirium following long term lithium therapy, misdiagnosed and treated as a case of idiopathic Parkinson's disease. Factors like advanced age and medications all increase the risk of toxicity.

It is pertinent to take this into consideration when prescribing lithium to prevent dangerous interactions as seen in this patient. Also, providers should understand the wide array of presentation of lithium toxicity to prevent misdiagnosis and unnecessary or harmful treatments.

Keywords: Lithium toxicity; Parkinson's disease; Bipolar disorder; delirium

Introduction

Lithium is widely used in the treatment of mood disorders, it is Food and Drug Administration approved for the treatment of manic episodes and maintenance treatment for bipolar patients with a history of mania. Its mechanism of action is complex and poorly understood but believed to act via alteration in sodium transport across cell membranes, the metabolism of serotonin and catecholamines, and intracellular signaling through actions on the second messenger system. Other postulated mechanism of action includes the inhibition of inositol monophosphatase, reduction in protein kinase C activity, increasing cytoprotective proteins, activates certain signalling pathways and possibly increases gray matter. Mechanism of side effects is also poorly understood but probably as a result of excessive effects at therapeutic sites. Notable side effects are ataxia, dysarthria, delirium, tremors, memory issues, diarrhea, nausea, nephrogenic diabetes insipidus, weight gain and cardiovascular changes [1-7]. Though tremor is frequently reported and appears to be the most common movement side effects, severe parkinsonism as a result of neurotoxicity is rarely reported [5,6]. A rare case of combined severe parkinsonism and hypothyroidism due to lithium toxicity have been reported [6], however our patient couldn't relate the timeline and it was not clear which one came first. We present a female patient with subacute severe reversible parkinsonism and acute delirium following long term lithium therapy, misdiagnosed and initially treated as a case of idiopathic Parkinson's disease.

Case Report

Miss E.K. is a 60-year-old female with a history of bipolar admitted for altered mental status, bradykinesia, tremor of the limbs, shuffling gait, frequent falls, and memory issues. Physical examination revealed

rigidity, tremors, cognitive impairment, masked facies, positive cog wheel rigidity, bradykinesia and festinating gait. Symptoms had worsened in the last two [2] months prior to presentation. She was on 600 mg of lithium twice daily for over 10 years and without any history of serum lithium check. She was also on Lisinopril, diclofenac, levothyroxine, atorvastatin, topiramate and trazodone. Hydrochlorothiazide was added to her long list of medications a few weeks prior to onset of symptoms because of poorly controlled hypertension. She also had poor oral intake as cognitive impairment progressed. She was initially seen in a neurology clinic few weeks prior to her inpatient hospitalization, diagnosed as idiopathic Parkinson's disease and treated with carbidopa levodopa and Benzotropine which didn't appear to help, her symptoms continued to worsen. When we saw her on the unit, serum lithium was 2.9mmol/L, creatinine was 1.3, glomerular filtration rate was at the lower limit of normal, all other laboratory findings including computed tomographic scan were within normal limits. Lithium was discontinued and antihypertensive switched to amlodipine, carbidopa levodopa was also discontinued. Patient was adequately rehydrated with serial serum lithium monitoring. Serum lithium level trended down to 0.2mmol/L over a 3-4 days and creatinine level to 0.7mg/dL. Glomerular filtration rate improved and patient's cognition and neurological symptoms abated within 3-4 weeks in the hospital. Patient didn't have any symptom of bipolar so, the resumption of lithium was deferred to her outpatient psychiatrist.

Certain factors like advanced age, infections, dehydration, and other medications like neuroleptics, diuretics, and non-steroidal anti-inflammatory drugs all increase the risk of lithium toxicity [4]. Some or all of which might have played a role in our patient's lithium toxicity. Interaction with Lisinopril and hydrochlorothiazide and possibly Latuda might have played a role. Also important in this patient is the reduced glomerular filtration rate from possibly poor oral intake. We used the drug interaction probability scale and the interaction between lithium and hydrochlorothiazide plus Lisinopril and diclofenac was

probable with a score of 8. In our patient, within a few weeks of adding hydrochlorothiazide [and continued to use her other medications] she began experiencing the symptoms of lithium toxicity and symptoms abated after discontinuing lithium and of course carbidopa levodopa, which wasn't necessary as the working diagnosis was drug induced Parkinsonism. To our knowledge, only very few cases of severe drug induced parkinsonism abated after lithium was discontinued, most required the use of dopaminergic medications [4].

Discussion

It is not completely clear how lithium toxicity causes parkinsonism however, it is speculated to cause a decrease in dopamine levels in the limbic system and the striatum by reducing presynaptic release [2-6]. It is reported that long term use of lithium impairs dopamine transmission with down-regulation of membrane dopamine transporter. It is also believed to increase central cholinergic activity by acting as an anticholinesterase [1]. There are reports of the possibility of lithium induced neurotoxicity resulting from demyelination at various sites of the central nervous system including the cerebellum[2,3]. Genetic predisposition could also play a role in lithium concentration in the neurons and so is a pre-existing damage to the basal ganglia [4]. In drug induced parkinsonism, symptoms start after initiating an offending drug and remit on its withdrawal as seen in our patient [1,6]. A 123I-ioflupane [Dopamine Transporter SPECT] scan would differentiate idiopathic from drug induced Parkinson's disease, this was not done in this case as it wasn't available in the facility [1,3]. Differentiating between the two clinically could be challenging.

In conclusion, it is pertinent to take into consideration other medications a patient is on before prescribing lithium and constantly

ask patients to report new medications to prevent dangerous interactions as seen in this patient. Risk increases in the elderly due to age related decrease in glomerular filtration rate and regular monitoring of lithium levels and adjustment in dose is required [1]. Also, providers should understand the wide array of presentation of lithium toxicity to prevent misdiagnosis and unnecessary or harmful treatments [4].

The authors have no conflict of interest to declare.

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