



Case Report

Reversible Lithium Toxicity Misdiagnosed as Dementia in an Elderly Patient: A Case Report and Follow-Up to Previous Work on Lithium Sensitivity in Aging

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ABSTRACT

Lithium is a widely used mood stabilizer but requires careful management in the elderly due to altered pharmacokinetics and pharmacodynamics. This case report describes a dramatic reversal of apparent end-stage dementia in an 85-year-old woman after recognition and correction of chronic lithium toxicity. The case is of interest because over a two-year period of the case, the average lithium level, creatinine level, and eGFR remained the same, yet the lithium became toxic. It demonstrates that even though the eGFR remains constant, the dose of lithium may need to be reduced with aging to keep the lithium level therapeutic. It reinforces and expands upon previous findings that therapeutic serum lithium levels can become toxic with aging due to physiological changes, particularly in renal function and neural sensitivity. The woman is in stage four of chronic kidney disease, which means there is a very small therapeutic region for the lithium. The paper also describes how a second, unusual form of dementia, caused by lithium toxicity, was diagnosed and treated.

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Lithium remains a cornerstone in the treatment of bipolar disorder, but its use for elderly patients demands vigilance. Starting with Young [1] in 2005 and Shulman [2] in 2010, there

have been many clinical studies reported that show that the therapeutic range for lithium changes with aging. For the most part, those studies define the toxic level in terms of decades. The main theoretical result was by Burns [3], where he presented an analytic result that can be used to calculate the toxic level of lithium year by year for the patient providing, they do not have Chronic Kidney Disease (CKD). There are no useful papers addressing how to determine the toxic level of lithium for the elderly who have CKD.

Case Presentation

This case concerns an 85-year-old woman who was bipolar and had been on lithium therapy for more than thirty years.

2022-5-11. Over the next 15-month period, she experienced increasing short-term memory loss, long-term memory loss, personality changes (notably irritability and grouchiness), and frequent falls.

2023-11-13. A formal diagnosis was made of vascular dementia, supported by imaging and clinical history. During the previous few years, her average eGFR had been stable at 19.6, and her average lithium level at .49 based on a dose of 150mg a day.

2024-04-19. Her dementia rapidly became worse. Five months after being diagnosed with dementia the following was her state of health:

- She could not find the words to complete a sentence.
- She had a great deal of difficulty making any sentence or carrying on a conversation.
- Her long-term memory was confused. The stories she told were full of errors and had things happening that did not happen.
- She could not make any decision. For example she could not decide between two food choices such as two desserts. She just could not give an answer. She sat there baffled.
- She could not remember where her clothes were. Someone had to get out clothes from the cupboard and dresser drawers for her to wear and help her dress.
- She needed help eating. All her food needed to be cut into bite-sized pieces, and she had to use an electronic spoon that dampens her essential tremor when eating.
- PSW's were needed throughout the day to care for her because of her confusion.

She was completely non-functional and diagnosed with end-stage dementia.

2024-04-11. Her spouse felt that the mental deterioration had occurred too quickly to be caused by dementia. He suspected lithium toxicity might be causing her dementia symptoms. He reduced her lithium from a daily dose of 150mg to an average daily dose of 120mg, using the app MedsReducer, which allows for changing the lithium dose in steps less than 150mg, without cutting the capsule. The goal was to keep her lithium level well below .49, which was now suspected to be the toxic lithium level for her current kidney condition.

2024-05-04. Three weeks after reducing the lithium dose, most of the symptoms of dementia started to go away. Two weeks later, she had fully regained her cognitive abilities, memory, and personality baseline. The diagnosis of irreversible dementia was effectively reversed.

2024-07-05. In a blood test two months later, the lithium level was .45. Since the toxic level was not known precisely, but was known to be at least as low as .49, it was thought that the reading of .45 might be too close to the actual toxic level. A second consideration was that after being stable at 19.6 for two years, the eGFR suddenly dropped to 17. The average daily dose was reduced from 120mg to 112mg. The result was that, for this new maintenance dose, all the symptoms of dementia stayed away and the patient's essential tremor reduced a little so that she could drink from a glass or cup rather than having to use a straw.

Lithium toxicity can display unwanted symptoms in many ways. Fung et al. [4] report that lithium toxicity is often misdiagnosed and attributed to other common conditions in older adults, including gastrointestinal symptoms (diarrhea), urological disorder (polyuria), impaired cognition (dementia) and neurologic symptoms similar to parkinsonism (tremor and rigidity).

2025-03-28. Seven months after the reduction to 112mg a day, the patient started to sleep all the time, day and night. This went on for several weeks. Her lithium dose was reduced to 75mg a day to address the possibility that lithium toxicity had returned. The results were very strange. As desired, she slept less during the daytime and all symptoms of dementia during the daytime were still gone. During the daytime, she led a normal life, looking after herself and having no cognitive problems. However, every evening she had severe sundowner symptoms. She was irritable and argumentative. She often refused to change into night clothes and did not want to get under the covers on her bed. She insisted on sleeping on top of the covers with just a small throw blanket over her. If she was persuaded to go to bed in night clothes, she often woke up in the night, got dressed, and put on her coat, ready to go somewhere. She also had trouble getting dressed in the morning. After breakfast, everything returned to normal behavior. It was decided that the reduction in her daily dose to 75mg was too large a reduction and as a result, lithium displayed the unwanted symptoms just described.

2025-04-05. The average daily dose was increased to 100mg. The effective reduction from 112mg a day to 100mg a day solved the excessive sleeping problem and the occurrence of sundown symptoms. She now leads a normal, healthy life 24 hours a day. The target blood serum level of lithium is less than or equal to .43 and it seems to be working. Monthly blood tests will continue because the average daily dose is so small, and the serum lithium level so low, that the therapeutic region of lithium is very small and needs to be monitored carefully.

Discussion

The average eGFR and the average serum level had been constant for two years during which time the whole incidence of misdiagnosed dementia had occurred. The serum level initially was therapeutic but did not remain so. Even "low" serum levels may become toxic in the elderly due to altered intracellular handling and decreased CNS tolerance.

Changes in the lithium dose for the very elderly need to be by small amounts. This is particularly true for patients with CKD. The eGFR of a patient 85 years old who has CKD may be the same as a person 100 years old who does not have CKD.

When the person on lithium is prescribed many common medications, the blood serum level of lithium can increase by as much as 50% [4]. With the very small therapeutic region of lithium that an elderly person with CKD has, lithium toxicity may happen independent of age or kidney changes.

The patient and her spouse have moved into a Senior's Retirement home that has nurses and PSWs available 24/7 to assist with the care needed. The patient has many of the unwanted long-term side effects of lithium but they are not pertinent to this case.

Conclusion

All the previous papers on the use of lithium as a treatment for bipolar disorder advocate monitoring the lithium level by age groups. They stress that the therapeutic region decreases by age and the research suggests the toxic level for each age group. Such is not the case for those with bipolar disorder who have CKD. Although the eGFR decreases linearly initially [5], the changes can become independent of age for the very elderly.

The change in the blood serum therapeutic region can become independent of the eGFR reduction for those with CKD because serum levels may become toxic in the elderly due to altered intracellular handling and decreased CNS tolerance.

When a person who is elderly, and who has been on lithium for some time, and who has CKD presents to a hospital or doctor with symptoms of a new medical problem, the possibility that lithium toxicity may be causing the symptoms should be considered immediately.

Declarations

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