

LETTER

Lithium induced neurotoxicity: The SILENT killer

Dear Editor,

The use of lithium dates back to 1949, with primary indication treatment of bipolar disorder. The clinical manifestations of lithium toxicity differ depending on whether it is acute, chronic, or acute on chronic poisoning. Neurological manifestations are the predominant clinical manifestations in chronic intoxication, whereas initially absent in acute poisoning due to the slow distribution of the drug in the central nervous system, but may later progress to neurological. Lithium exhibits a narrow therapeutic range; thus, its serum levels do not necessarily correspond to the clinical manifestations in cases of toxicity. When the neurological manifestations of lithium toxicity persist for more than two months after the discontinuation of the drug, the syndrome of irreversible lithium-effectuated neurotoxicity (SILENT) should be clinically suspected¹, defined by the persistence of neurological or neuropsychiatric symptoms, despite the discontinuation or removal of lithium by hemodialysis.

A 72-year-old woman with an impaired level of consciousness in the context of SILENT was admitted with altered mental status for the preceding few days. Her medical history was remarkable for bipolar disorder treated with lithium carbonate at 600 mg per day for the past 40 years and diabetes mellitus for the past 15 years under treatment with metformin 1,000 mg twice daily and glimepiride 4 mg once daily. No other antipsychotics nor any other mood stabilizers were administered. She was afebrile with normal vital signs on presentation. On clinical assessment, she had mixed non-fluent aphasia, lethargy, spontaneous eye-opening, and was responsive to painful stimuli, while neck stiffness or Babinski signs were absent. Laboratory tests revealed a serum lithium level of 0.9 (normal range 0.5-1.2) mmol/L, WBC: $12 \times 10^9/L$, urea: 62 mmol/L, creatinine: 1.6 mg/dL, glucose: 179 mg/dL, sodium: 138 mmol/L, potassium: 5.4 mmol/L, and CRP: 0.6 mg/L. She underwent brain magnetic resonance imaging showing no acute abnormalities but only age-compatible findings suggestive of microvascular encephalopathy, whereas lumbar puncture findings were normal. Based on her medical history, clinical presentation, and findings, we hypothesized lithium-induced neurotoxicity and decided to discontinue lithium. The given laboratory results indicate a degree of dehydration, which could reduce renal excretion of lithium, a fact usually present and constituting the association reason for chronic cases of poisoning. Apart from dehydration, a decline in renal function and aging remain the main risk factors for the development of SILENT. She received symptomatic treatment with intravenous hydration and nutritional support. Before discharge, the patient regained consciousness; however, she had mild extrapyramidal signs, such as tremors, mild stiffness, and speech and gait disturbances. Four months later, she is partially self-dependent with persistent neurological manifestations.

SILENT, introduced as a term in 1987 by Adityanjee, can occur at any stage of lithium therapy, even when drug serum levels are normal, and in some cases, persists for months or even years after discontinuation. Its predominant clinical manifestation is cerebellar dysfunction, while extrapyramidal symptoms, brainstem manifestations, and dementia often coexist. Typical clinical manifestations include tremor, ataxia, dysarthria, convulsions, and encephalopathy².

The therapeutic approach is typically supportive, with the mainstay of treatment being the discontinuation of lithium. In addition, hydration and nutritional support are suggested, while physiotherapy, speech therapy, and ergotherapy may improve the patient's clinical condition. Hemodialysis may be performed, although its indications are not entirely clear. Hemodialysis is indicated in cases of impaired level of consciousness, epileptic seizures, or potentially life-threatening complications, regardless of serum lithium levels. Lithium exhibits a narrow therapeutic range with therapeutic levels between 0.8-1.2 mEq/L. However, lithium levels are not the ideal diagnostic tool to assess the patient's clinical condition. The persistence of neurological manifestations for longer than two months, especially when cerebellar and extrapyramidal manifestations predominate, should raise the clinical suspicion of SILENT syndrome, which may persist even years after the discontinuation of lithium's administration. Physicians should be aware of this sporadic clinical syndrome, which has appeared in the literature during the past 40 years.

References

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Kounatidis D¹, Chatzieftheriou E¹, Vallianou N²

¹2nd Department of Internal Medicine, Hippokraton General Hospital

²Evangelismos General Hospital

Athens, Greece

Keywords: lithium, neurotoxicity, chronic poisoning

Conflict of Interest

None declared.

Corresponding author: Natalia G. Vallianou, Department of Internal Medicine, Evangelismos General Hospital, Athens, Greece, tel.: +306966592119, e-mail: natalia.vallianou@hotmail.com