RESEARCH PAPER

When Silence Persists: Syndrome of Irreversible Lithium-Effectuated Neurotoxicity (SILENT) Following Acute Lithium Overdose

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ABSTRACT

Introduction:Lithium is a cornerstone therapy for bipolar disorder but has a narrow therapeutic index. Although acute lithium toxicity is usually reversible with timely hemodialysis, rare cases may progress to Syndrome of Irreversible Lithium-Effectuated Neurotoxicity (SILENT), characterized by persistent neurological deficits despite normalization of serum lithium levels [1–3].

Case Presentation:A 54-year-old man with bipolar affective disorder ingested approximately 16 g of lithium. Despite early hemodialysis and normalization of serum lithium levels, he developed persistent quadriplegia and mutism. Serial magnetic resonance imaging (MRI) of the brain revealed no lithium-specific structural abnormalities.

Conclusion:This case highlights SILENT syndrome presenting with severe neurological impairment and striking clinical–radiological dissociation. Normal serum lithium levels and unremarkable neuroimaging do not exclude irreversible neurotoxicity, underscoring the need for heightened clinical vigilance

Keywords: Lithium toxicity; SILENT syndrome; irreversible neurotoxicity; clinical–radiological dissociation; hemodialysis; bipolar disorder

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INTRODUCTION

Lithium has been used for more than seven decades as a first-line mood stabilizer in bipolar affective disorder, with well-established efficacy in relapse prevention and suicide risk reduction [1]. However, its narrow therapeutic index and renal elimination predispose patients to toxicity [2]. Acute lithium intoxication is often reversible when promptly managed with supportive care and hemodialysis. Nevertheless, a subset of patients develop persistent neurological sequelae known as Syndrome of Irreversible Lithium-Effectuated Neurotoxicity (SILENT) [3]. This syndrome is defined by neurological deficits persisting for at least two months after lithium discontinuation and normalization of serum lithium concentrations [4]. The pathophysiology of SILENT remains incompletely understood, and diagnosis is primarily clinical after exclusion of alternative etiologies. Neuroimaging findings are variable, and in rare cases, severe neurological manifestations may occur despite normal imaging, resulting in clinical–radiological dissociation [10,11]. We report such a case to add to the limited literature on this devastating condition.

CASE PRESENTATION

Patient Information

A 54-year-old man with a known history of bipolar affective disorder, on lithium carbonate 400 mg/day, presented following intentional ingestion of approximately 40 lithium tablets (~16 g).

CLINICAL FINDINGS

On arrival, the patient was unconscious with frothing of saliva and required immediate endotracheal intubation. Vital signs were stable (blood pressure 130/80 mmHg, heart rate 88/min, oxygen saturation 100% on mechanical

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ventilation). Neurological examination revealed a Glasgow Coma Scale score of E2VtM3 with sluggishly reactive pupils.

DIAGNOSTIC ASSESSMENT

Serum lithium level was markedly elevated at 4.14 mmol/L. Routine laboratory investigations, including complete blood count, renal, liver, thyroid, and electrolyte panels, were largely normal except for hypophosphatemia (1.5 mg/dL), which was corrected. Creatine phosphokinase was elevated at 944 U/L, and serum prolactin was 34.3 ng/mL. Toxicology screening was positive only for benzodiazepines, attributable to hospital administration.

Computed tomography of the brain performed on day 1 was normal. MRI of the brain obtained on day 1 and repeated on day 15 demonstrated no diffusion restriction, cerebellar atrophy, basal ganglia involvement, or brainstem signal abnormalities. Electroencephalography showed diffuse slowing without epileptiform activity. Cerebrospinal fluid analysis and microbiological cultures were unremarkable.

Therapeutic Intervention

The patient underwent one session of hemodialysis followed by five cycles of sustained low-efficiency dialysis, resulting in reduction of serum lithium to 0.6 mmol/L. Supportive intensive care management included tracheostomy and correction of metabolic abnormalities.

Follow-up and Outcomes

Despite normalization of serum lithium levels, the patient showed no meaningful neurological recovery. At two weeks, he demonstrated eye opening but remained quadriplegic. At two months, he was conscious but nonverbal with persistent quadriplegia, fulfilling diagnostic criteria for SILENT syndrome.

DISCUSSION

SILENT syndrome represents a rare but severe complication of lithium toxicity, characterized by irreversible neurological deficits despite appropriate detoxification [3,4]. Reported manifestations most commonly include cerebellar dysfunction, extrapyramidal symptoms, and cognitive impairment; profound motor deficits are less frequently described [3,6]. Several mechanisms have been proposed, including direct lithium-induced neuronal toxicity via disruption of inositol signaling and Na^+/K^+-ATPase inhibition, oxidative stress, demyelination, and selective vulnerability of Purkinje cells [5–7]. Rapid osmotic shifts during aggressive lithium removal by dialysis have also been implicated [8]. Severe neurological disability in the absence of corresponding neuroimaging abnormalities is rare in SILENT syndrome. This phenomenon of **clinical–radiological dissociation** complicates diagnosis and emphasizes the importance of clinical judgment [10,11].

To contextualize our findings, **Table 1 summarizes previously reported cases of SILENT syndrome with minimal or normal neuroimaging abnormalities**. Compared with earlier reports, our patient demonstrated unusually severe manifestations—persistent quadriplegia and mutism—despite timely hemodialysis and repeatedly normal MRI findings. This highlights that normalization of serum lithium levels and unremarkable neuroimaging do not preclude devastating irreversible neurotoxicity.

Table 1. Reported cases of SILENT syndrome with minimal or normal neuroimaging findings

Study	Age/ Sex	Lithium Exposure	Neurological Features	Neuroimaging Findings	Outcome
Schou et al. (1984) [4]	52/F	Chronic	Ataxia, dysarthria	Cerebellar atrophy	Partial recovery
Adityanjee et al. (2005) [3]	48/M	Chronic	Tremor, rigidity	Mild cerebellar changes	Persistent deficits
Tabrizi et al. (2021) [10]	56/F	Acute	Mutism, confusion	Normal MRI	Partial improvement
Lee et al. (2019) [11]	60/M	Acute	Mutism, rigidity	Normal MRI	Persistent disability
Present case	**54/M**	**Acute (~16 g)**	**Quadriplegia, mutism**	**Normal MRI**	**No recovery at 2 months**

Abbreviations: SILENT – Syndrome of Irreversible Lithium-Effectuated Neurotoxicity; MRI – Magnetic resonance imaging.

CONCLUSION

This case demonstrates that SILENT syndrome may develop despite early hemodialysis and normal neuroimaging findings. Clinicians should recognize that normalization of serum lithium levels does not guarantee neurological recovery. Increased awareness of this rare entity is essential to improve patient safety and prevent irreversible outcomes during lithium therapy.

Patient Consent

Written informed consent was obtained from the patient's legally authorized representative for publication of this case report.

Conflicts of Interest

The authors declare no conflicts of interest.

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