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Syndrome of irreversible lithium induced neurotoxicity due to chronic lithium use (SILENT)-Effect on functional status-a case report

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Research

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Abstract

Background
Lithium has been used as a mood stabilizer for over a century, it is still the first-line agent for bipolar disorder. A Large proportion of patients on chronic lithium therapy experience at least one episode of toxicity during treatment given its narrow therapeutic window.

Case Presentation
This is a case report of a 50 year-old female with bipolar affective disorder who developed the Syndrome of Irreversible Lithium Effectuated Neurotoxicity (SILENT). The case presentation covers the clinical symptoms and signs of SILENT causing functional impairment which effects their mobility and activities of daily living.

Conclusion
Given its rare presentation, it is important for clinicians to be aware of this syndrome and its devastating effects. Early rehabilitation measures may help with achieving some functional independence but would assist with community reintegration and quality of life, long term.

Key Words: Lithium induced Neurotoxicity.

Introduction

Lithium toxicity was first described in 1898, and the extent of its toxic effects was recognized in 1949 when lithium chloride was used as a salt substitute in patients with heart failure[1]. In the 1970s, lithium carbonate was approved in the United States for the treatment of acute mania and bipolar disorder after appropriate serum monitoring became readily available [2,3]. Lithium toxicity often occurs in vulnerable populations, such as patients with mental illness and poor living conditions. Chronic lithium toxicity presents with early and predominate neurologic signs and symptoms. The clinical manifestations of toxicity (eg, agitation, confusion, slurred speech) are often superimposed on complications from chronic use (eg, neuromuscular irritability, tremor). Cerebellar dysfunction, extrapyramidal symptoms, brainstem dysfunction, and dementia can develop as part of SILENT [4]. Other neurologic sequelae may include nystagmus, choreoathetoid movements, myopathy, and blindness. SILENT can persist for months and, in rare cases, for years [5].Serum lithium concentrations often do not correlate with clinical signs in acute toxicity because they do not necessarily reflect Central Nervous System (CNS) concentrations of lithium. Patients with therapeutic lithium concentrations can develop severe clinical toxicity [6-8]. Thus, treatment should be based upon clinical manifestations and not solely upon serum concentrations. Patients on chronic lithium therapy are at risk for developing AVP-R, caused by a concentrating defect in the kidneys, resulting in the excretion of dilute urine [9]. Normally, the resulting thirst and increased intake of free water compensate for these fluid losses. Thus, many patients on chronic lithium therapy have polyuria and polydipsia without hypernatremia.

Case Presentation

Mrs. N is a 50 year old lady, married with 2 children, previously worked as bar tender. She was diagnosed with Bipolar Affective Disorder in 2011 and was managing well on lithium tablets in doses ranging from 500mg – 900mg since 2010. She had regular Lithium levels checked with her GP.

She presented to hospital in August 2023 with recurrent falls and a decline in her mobility for a few months. She was initially admitted to the General Medical ward for work up and investigation for her falls, and later referred to rehabilitation ward for reconditioning.

Lithium levels at the initial time of presentation was 1.0 mmol/L. Lithium was stopped temporarily and recommenced on 450mg OD as her repeat serial serum

lithium levels were between 0.4-0.6 mmol/L. Following this she developed Nephrogenic DI and eventually her lithium was stopped. Despite stopping lithium, it was noted that she developed constant jerky movements initially in her upper limbs and gradually progressed to lower limbs. It was choreiform in nature. She had reduced power in both upper and lower limbs, with loss of proprioception too. She was noted to have peripheral neuropathy affecting both arms and legs at this stage.

Her case was discussed with Neurologist, and she was extensively and thoroughly investigated. Investigations included- EEG, NCS, MRI brain and spine and extended blood work up including Huntington's panel. NCS showed electrophysiological evidence of moderately severe length dependent sensory motor peripheral neuropathy. EEG showed moderately severe diffuse encephalopathy with evidence of cortical dysfunction in left hemisphere. MRI brain showed chronic small vessel ischemic disease (Figure 1).

Collateral history was obtained from her husband, who mentioned Mrs N had long standing history of bowel and bladder incontinence. She had multiple falls in the last 6months leading to the current admission. She had reduced mobility requiring her husband to carry her up the stairs. Collateral history from GP was obtained, as per her GP Mrs N was diagnosed with bipolar affective disorder in 2010 and had been on lithium since. Her serial serum lithium levels in the community were in the normal range.

On admission to the rehabilitation ward Mrs N had trouble in managing her daily activities of living, requiring assistance for majority of activities including mobilising and feeding herself. She additionally had trouble with severe neuropathic pain and flare ups of her bipolar affective disorder. She was commenced on regular sodium valproate and olanzapine for her bipolar affective disorder management as per psychiatrist. Based on extensive investigations and significant collateral history from husband and GP, and excluding alternative diagnoses, the diagnosis of SILENT was made.

Following her admission to the rehabilitation ward, she was re-assessed for severity and progression of symptoms. She had ongoing less intense choreiform movements, permanent peripheral sensory neuropathy, associated neuropathic pain and no change in power in upper and lower limbs. This significantly affected her mobility and pADL's. She required assistance of two people for her pADL's and wheelchair for mobility. The diagnosis of SILENT in this patient has proven significant with regards to the impact on her functional status and mental wellbeing. She was discharged home with NDIS support.

Discussion

Severe lithium neurotoxicity occurs almost exclusively in the context of chronic therapeutic administration of lithium, and rarely results from acute ingestion of lithium, even in patients currently taking lithium . Serum lithium concentrations often do not correlate with clinical signs in acute toxicity because they do not necessarily reflect Central Nervous System (CNS) concentrations of lithium. Patients with acute ingestions may be relatively asymptomatic despite serum concentrations above 4 mEq/L (4 mmol/L) due to slow distribution into the CNS. Conversely, patients with therapeutic lithium concentrations can develop severe clinical toxicity. Thus, treatment should be based upon clinical manifestations and not solely upon serum concentrations. Chronic pharmacotherapy with lithium often causes increased levels in the brain because of physiological accumulation over time leading to demyelination, which causes encephalopathy as presented. The syndrome can also present with other symptoms like persistent cerebellar dysfunction, persistent extrapyramidal syndrome, persistent brainstem dysfunction, or dementia with varying organic mental syndromes [10, 11]. It also sometimes presents in an atypical manner which includes downbeat nystagmus, retrobulbar optic neuritis, persistent papilledema, choreoathetosis movements, peripheral neuropathy, myopathy, and blindness[12].

This case report supports the assertion that syndrome of irreversible lithium effectuated neurotoxicity almost invariably develops in the context of chronic use of lithium. This has debilitating implications on the functional status in a previously independent individual, eventually impacting their mental health and quality of life.

Conclusion

Lithium is the most common first line choice of medication for management of bipolar effective disorder. Serum lithium concentrations often do not correlate with clinical signs in acute toxicity because they do not necessarily reflect Central Nervous System (CNS) concentrations of lithium. Patients with therapeutic lithium concentrations can develop severe clinical toxicity. Close monitoring of clinical symptoms in chronic lithium users is highly recommended and it is important to raise the awareness of permanent sequelae of SILENT impacting the functional quality of life.

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ABBREVIATIONS

- SILENT- syndrome of irreversible lithium effectuated neurotoxicity.
- CNS- Central nervous system
- AVP-R-Arginine vasopressin resistance
- DI – diabetes Insipidus
- EEG- Electroencephalogram
- NCS- Nerve conduction studies
- MRI- Magnetic resonance imaging
- pADLS- Personal Activities of Daily Living
- NDIS- National Disability Insurance Scheme

Figures

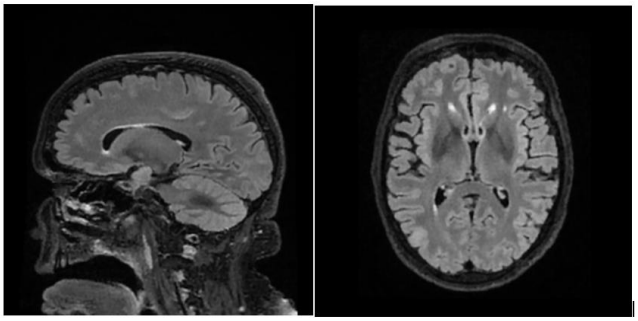

Figure 1: Sagittal and Axial T2 Flair sequence image of MRI brain showed hyperintense foci in deep white matter and periventricular areas.

ETHICS APPROVAL

Was reviewed by Ethics and Governance team of West Moreton Health and is compliant with the NHMRC guidance "Ethical Consideration in Quality Assurance and Evaluation Activities" 2014.

CONSENT

Patient has given her consent to be included in the case report. The patient has agreed to provide her clinical details and for the same to be reported in the journal. The patient understands that her name and personal details will not be divulged, and her identity will be concealed.

CONFLICTS OF INTEREST

The Author Declares no Conflict of Interest.

AUTHOR'S CONTRIBUTIONS

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Data Curation: Dr. Bhanu Motru, Dr. Deepa Iyer
Formal analysis: Dr. Bhanu Motru, Dr.Deepa Iyer
Funding acquisition: Dr.Bhanu Motru, Dr.Deepa Iyer
Methodology: Dr. Bhanu Motru, Dr.Deepa Iyer
Supervision: Dr. Deepa Iyer
Writing – original draft: Dr. Bhanu Motru
Writing – review & editing: Dr. Deepa Iyer

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