LETTER

A case of Syndrome of Irreversible Lithium Effectuated Neurotoxicity (SILENT)

N. Vallianou*, F. Konstantinou, V. Gennimata, P. Micha, E. Geladari, D. Kounatidis

*Corresponding author: natalia.vallianou@hotmail.com

Dear Sir,

Herein, we describe a male patient with the Syndrome of Irreversible Lithium Effectuated Neurotoxicity (SILENT), in whom some neurological deficits persisted despite removal of the drug.

A 74-year-old male patient was admitted to the hospital due to dysarthria, agitation, and confusion, which had started five days earlier. His past medical history was remarkable, including bipolar disorder, treated for 37 years with lithium, 900 mg daily; ischaemic heart disease, for which he had been taking imbesartan/hydrochlorotheiazide 300/12 mg daily, betaxolol 10 mg, triflusal 600 mg, ezetimibe/simvastatin 10/40 mg; and hypothyroidism, treated with thyroxin 50 μg daily. On clinical examination, the patient was agitated with sluggishness, coarse tremors, and myoclonus. Eleven years ago, he was admitted to the hospital with the same symptoms and toxic levels of lithium, so lithium intoxication was again suspected. Serum levels of lithium were determined and found elevated (2.03 mEq/l). Notably, the patient did not regularly measure his serum lithium levels. Lithium was immediately discontinued and vigorous hydration introduced, which resulted in subsequent normalisation of serum lithium levels two days later. However, the patient still had ataxia and memory deficits, and nystagmus was still present, together with extra-pyramidal signs. The diagnosis of SILENT was made, after the performance of two computed tomography scans of the brain, since memory deficits and extrapyramidal signs were present for a month after lithium withdrawal; scans were negative for any stroke. Notably, agitation and confusion had passed, after normalisation of serum lithium levels. The patient was discharged with the advice to stop lithium and to take quetiapine 100 mg under the strict supervision of a psychiatrist.

Lithium has a narrow therapeutic index. The therapeutic values range from 0.8 to 1.2 mEq/l. Thus, many patients on chronic lithium therapy experience at least one episode of toxicity during their lifetime.[1] The diagnosis of chronic lithium toxicity is typically made on clinical grounds and confirmed by obtaining serum lithium levels. Mild toxicity usually does not occur until serum lithium levels reache 1.5 mEq/l. Levels ≥ 2.5 mEq/l are considered a medical emergency, even in patients who appear relatively asymptomatic. Drug concentrations correlate more closely with clinical signs in patients with chronic toxicity. Clinical presentation generally involves a patient on chronic lithium therapy who, due to concurrent illness, does not drink enough free water, leading to gradual dehydration and reduced renal excretion of lithium. The initial symptoms and signs of chronic toxicity are often neurological.[1,2]

Medications that cause dehydration or renal impairment can also precipitate lithium toxicity. Examples include diuretics, angiotensin converting enzyme (ACE) inhibitors, and nonsteroidal anti-inflammatory drugs (NSAIDs). Indeed, our patient had been on diuretics (hydrochlorothiazide), angiotensin II receptor blockers (imbesartan), and had a serum creatinine level of 1.8 mg/dl.

Indications for treatment of lithium poisoning with haemodialysis remain controversial. However, it is generally suggested that haemodialysis should be initiated in the following situations: 1) serum lithium concentration is greater than 5 mEq/l; 2) serum lithium concentration is greater than 4 mEq/l in patients with serum creatinine levels > 2.0 mg/dl); and 3) in the presence of decreased level of consciousness, seizure, or life-threatening complications, irrespective of serum lithium concentrations.[2,3]

In some cases, neurologic complications persist despite lithium removal by haemodialysis. SILENT consists of prolonged neurologic and neuropsychiatric symptoms following lithium toxicity. In typical cases, neurologic toxicity develops along with an elevated lithium concentration, but symptoms persist despite successful removal of the drug. Cerebellar dysfunction, extrapyramidal symptoms, brainstem dysfunction, and dementia can develop as part of SILENT.[3]

SILENT can continue for months and in rare cases, may persist for years. Clinicians should keep this in mind, as it is highly avoidable with regularly monitoring of serum lithium and serum creatinine levels, and with enough regular hydration; permanent discontinuation of lithium is mandatory in cases of SILENT. It is noteworthy that lithium is a very efficient drug, which needs close monitoring due to its narrow therapeutic index.

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