Case Report

**Creutzfeldt-Jakob-like EEG Changes in a Case of Fatal Lithium Toxicity**

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**Abstract**

We present a case of fatal lithium toxicity with EEG changes suggesting Creutzfeldt-Jakob disease. A 52-year-old woman was admitted with declined consciousness, fever, and generalized seizures. She had bipolar affective disorder and was on lithium and chlorpromazine treatment for about three decades. Her family described that she had systemic symptoms of lithium toxicity such as anorexia, nausea, vomiting, diarrhea, and insomnia for one month. Neurological examination disclosed declined consciousness, generalized hypotonia and hyporeflexia. Laboratory examinations revealed leukocytosis, hyperglycemia, and renal and thyroid dysfunction. Cerebrospinal fluid examination and cranial computerized tomography were unremarkable. The EEG demonstrated widespread slow wave activity and runs of periodic sharp waves, some with a triphasic pattern. Blood level of lithium was 1.88 mEq/L. In spite of repeated hemodialyses, she became comatose and died one week after admission. This case represents an uncommon presentation of lithium toxicity with Creutzfeldt-Jakob like EEG changes and fatal outcome inspite of normalization of lithium levels.

**Keywords:** Creutzfeldt-Jakob disease, electroencephalography, lithium toxicity

**INTRODUCTION**

Lithium toxicity causes electroencephalogram (EEG) abnormalities correlated with the degree of neurotoxicity. Disorganization and slowing of background activity are the most common EEG changes, while
periodic complexes of sharp waves may appear in patients with severe neurotoxicity\(^{6,8,21}\). Cases of lithium toxicity with clinical presentation and EEG findings suggestive of Creutzfeldt-Jakob disease have been reported, with complete clinical and EEG recovery\(^{3,4,7,10,12,13,14,17,18,20}\). We report a case of fatal lithium toxicity presented with impaired consciousness, generalized seizures, and Creutzfeldt-Jakob like EEG changes.

**CASE PRESENTATION**

A 52-year-old woman was admitted to the intensive care unit with impaired consciousness, fever, and generalized tonic-clonic seizures. Her first symptoms were anorexia, nausea, vomiting, diarrhea, and fever, that started one month before admission. In the following weeks, she deteriorated continuously, with irritability, insomnia, and speech and gait disturbance. Her consciousness declined gradually and she became lethargic, and had convulsions on admission. The patient had a 27-year history of bipolar affective disorder and was using lithium carbonate (900 mg/odd days of the month – 600 mg/even days of the month) and chlorpromazine (200 mg/day) since the first diagnosis. Almost one week before admission, her daughter noticed that the expiration date of lithium carbonate tablets ended three years ago, and she stopped the treatment. The patient had also been using irbesartane combined with diuretics for hypertension, and insulin glargine for diabetes mellitus, regularly.

On physical examination, she had fever (39°C), tachycardia (104/min), and high blood pressure (160/100 mmHg). She was unresponsive to verbal commands, and inappropriate words, withdrawal response, and eye opening were observed to noxious stimuli (Glasgow coma scale score: 9/15). Meningeal irritation signs were negative. Neurological examination revealed general hypotonia, and decreased deep tendon and superficial reflexes. Abnormal results of laboratory tests were as follows: white blood cell count, 11 600/mm\(^3\); glucose, 148 mg/dl; blood urea nitrogen, 64 mg/dl; creatinine, 1,7 mg/dl; uric acid, 14,5 mg/dl; TSH, < 0,003 mIU/l; free T4, 32,6 pmol/l. Erythrocyte sedimentation rate was 63 mm/h. Electrocardiography showed supraventricular tachycardia. Chest radiography and brain CT on admission were normal. Cerebrospinal fluid (CSF) examination, including CSF pressure, cell count, and biochemistry were unremarkable. The EEG demonstrated widespread slow wave activity and runs of periodic sharp waves, some with a triphasic pattern (Figure 1).

![Figure 1: EEG showing widespread slow wave activity and runs of periodic sharp waves, some with a triphasic pattern.](image)
Blood level of lithium was 1.88 mEq/L (therapeutic levels: 0.6-1.2 mEq/L), although lithium treatment was discontinued by her family a week ago. We started hemodialysis for lithium toxicity, phenytoin 300 mg/d for generalized seizures, dexamethasone 2 mg/d, propylthiouracil 600 mg/d, and propranolol 160 mg/d for hyperthyroidism and supraventricular tachycardia. On the second day of her admission, she became comatose, and required tracheal intubation and mechanical ventilation. Blood level of lithium decreased to 0.14 mEq/L by repeated hemodialyses, but she remained comatose on the following three days and died as a result of respiratory failure caused by aspiration pneumonae and acute respiratory distress syndrome. Cranial MRI and serial EEG recordings could not be performed due to mechanical ventilation and insufficient equipment in the intensive care unit.

**DISCUSSION**

Our patient's EEG demonstrated widespread slow wave activity and runs of periodic sharp waves, some with a triphasic pattern, suggesting Creutzfeldt-Jakob disease. Creutzfeldt- Jakob like EEG changes associated with lithium toxicity were first described in two cases by Smith and Kocen[18], and other cases have been reported subsequently[3,7,10,12,14,17,20]. Most of these cases were admitted with gradually progressive dementia or confusional state, myoclonus, and extrapyramidal signs. Blood lithium levels were either elevated or within the therapeutic ranges. Complete clinical recovery and normalization of EEG were observed in these cases. Fatal outcome due to lithium toxicity is least likely if hemodialysis is undertaken without delay[1,6]. We think that the unfavorable outcome in our patient was associated with the delay of her admission, the severity of toxicity, and pulmonary complications.

The most common signs of lithium neurotoxicity are generalized hypertonia and hyperreflexia, tremor, muscle fasciculations, myoclonus, ataxia, and dysarthria[6]. Our patient had hypotonia and hyporeflexia which are not usual findings. A similar clinical presentation of lithium toxicity with general hypotonia, hyporeflexia, and convulsions was previously reported by Kikyo and Furukawa[10]. Our patient had several systemic symptoms of lithium toxicity such as diarrhea, nausea, vomiting, anorexia, and fever. These symptoms were defined as the indicators of impending lithium neurotoxicity[6]. They may also precipitate neurotoxicity by causing dehydration and sodium depletion. Combined therapy of lithium with other agents such as diuretics and psychotropic agents may be another precipitating factor for lithium intoxication[10,15]. Our patient was using both chlorpromazine and an antihypertensive agent combined with diuretic. Phenothiazines increase intracellular lithium accumulation, thus providing much more neurotoxicity[15]. Although serum lithium decreased to the level of 0.14 mEq/L in our patient, she did not regain consciousness, and died due to respiratory failure. A previously reported case of acute lithium toxicity remained comatose and died, despite the serum level of lithium has decreased from 3.2 mEq/l to 0.4 mEq/l after repeated hemodialyses[11]. It has been speculated that lithium accumulates in the cells and has longer effects on the central nervous system, so serum lithium level does not reflect intracellular lithium level and correlate with severity of side effects[1,8,21]. Herpes encephalitis and other central nervous system infections were excluded by subacute generation of the symptoms, normal CSF findings, and imaging of the brain in this case. Prolonged coma in our patient despite repeated hemodialyses and
normalizing lithium level in plasma may be secondary to accumulation of lithium in central nervous system and/or metabolic disturbances and pulmonary infection superposed on lithium toxicity.

Lithium has relatively narrow therapeutic ranges and may therefore cause toxic effects on maintenance treatment. Central nervous system is the organ system most commonly affected by toxicity, followed by renal, gastrointestinal, endocrine, and cardiovascular systems(9). Metabolic disturbances, such as renal failure, dehydration and thyroid dysfunction are well-known systemic complications of lithium toxicity, which were also present in our patient(9). We think that delayed admission to the Emergency, severity of toxicity, metabolic disturbances and pulmonary complications were the main causes of progressing deterioration. Acute respiratory distress syndrome due to pulmonary infection was the diagnosis leading to respiratory failure and death in this case.

Hashimato encephalopathy, metabolic encephalopathy, neuroleptic malignant and serotonin syndromes, and intoxications with several drugs may also cause EEG abnormality characterized with generalized slowing and high voltage biphasic or triphasic waves(2,5,19). Intoxication with several types of drugs has been associated with triphasic waves(2). The most notable is valproate-induced hyperammonemic encephalopathy(16). Other drugs producing this association are baclofen, levodopa, monoamine oxidase inhibitors, L-tryptophan and pentobarbital(2,5).

CONCLUSION

We suggest that lithium intoxication may be fatal in cases presenting with Creutzfeldt-Jakob like periodic EEG discharges. Concomitant psychotropic medication may increase lithium neurotoxicity, which may lead to death in a case of severe toxicity and delayed treatment. The outcome may be fatal even if the serum concentration of lithium decreases to therapeutic levels. Precipitating factors such as gastrointestinal disorders, and concomitant medication should be considered in patients who are prone to be affected by lithium toxicity.

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