Very Severe Self-Poisoning Lithium Carbonate Intoxication Causing a Myocardial Infarction*

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A case of severe lithium carbonate self-poisoning is described, presenting with a very high serum lithium level (14.6 mmol/L) on admission. Lengthy and repeated hemodialyses were required to lower lithium to nontoxic ranges. As is usually reported, our patient had prolonged neurologic manifestations (coma, hyperreflexia, fluctuating focal signs) and developed hypotension, cardiovascular collapse, nephrogenic diabetes insipidus, and diarrhea. Other less common features were the occurrence of acute myocardial infarction without coronary artery lesions and thrombocytopenia. The possible pathogenic mechanisms are discussed. Hemodialysis and supportive intensive care treatment are commented upon. The final outcome was favorable, and the patient recovered completely.

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Since its first utilization by CADE in 1949, lithium has been widely recognized as a potent and effective therapeutic agent in manic-depressive illness, both for treating acute manic phases and for the prevention of recurrences. Lithium is thus a frequently prescribed drug, despite its common neurologic and renal side effects, sometimes occurring at therapeutic serum levels, and its narrow therapeutic margin. Acute lithium intoxication is relatively rare, considering the widespread utilization of this drug, but is a life-threatening occurrence which may result in permanent neurologic and renal sequelae.

We herein report a patient with very severe lithium intoxication who presented with one of the highest plasma lithium levels ever reported on admission. Characteristic neurologic, gastrointestinal, and renal complications were present, but unusual cardiovascular and hematologic manifestations also appeared. Both features are discussed, with reference to their possible pathogenic mechanisms, and a brief discussion of hemodialysis and supportive intensive care treatment follows.

CASE REPORT

A 46-year-old white man, who had been receiving lithium carbonate therapy for ten years because of manic-depressive disease, was found comatose and was admitted to our hospital on Feb 17, 1989. On physical examination the pulse was 84 beats per minute, and the blood pressure was 100/60 mm Hg. Neurologic examination disclosed ocular incoordination, diffuse hypertonia, and increased deep tendon reflexes. No Babinski sign or clonus was noted. Voluntary lithium intoxication was confirmed by a high lithium plasma level of 14.6 mmol/L.

Laboratory values were as follows: hemoglobin, 16.2 g/dL; hematocrit, 49.2 percent; white blood cell count, 25 × 10^9/L, with 5 percent band forms; platelets, 254 × 10^9/L; serum sodium, 135 mmol/L; potassium, 6.4 mmol/L; chloride, 101 mmol/L; CO2, 16.4 mmol/L; glucose, 5.4 mmol/L; calculated anion gap, 17.6 mmol/L; protein, 92 g/L; urea, 15.6 mmol/L; creatinine, 344 μmol/L; calcium, 3.77 mmol/L; and CPK, 308 units/L, with an MB fraction of 91 units/L. The peak CPK value was 449 units/L, with an MB fraction of 90 units/L, 8 hours after admission. Arterial blood gas levels were pH of 7.24, PaCO2 of 4.4 kPa, and PaO2 of 10.2 kPa. Urinalysis after rehydration showed the following: sodium, 112 mmol/L; potassium, 80 mmol/L; and osmolality, 440 mmol/kg. The ECG showed a striking ST-segment elevation in leads V1 and V2.

Intubation and gastric lavage were performed, hypovolemia was corrected with isotonic saline solution, intravenous nitroglycerin was started, and the patient was admitted to the intensive care unit. Despite lengthy hemodialysis (first course, 17.5 hours [Fig 1]), lithium remained stable at a very high average level of 6 mmol/L for 48 hours. Four courses were required to lower lithium to 1.5 mmol/L with a rebound after each course (Fig 1). On the second day the patient developed watery diarrhea which resolved spontaneously. On the third day, brisk hypotension appeared, which was unresponsive to 4,000 ml of isotonic saline, dopamine, and dobutamine, with subsequent gradual correction by continuous intravenous infusion of norepinephrine. There was no evidence favoring hypovolemic, cardiogenic, or septic shock. The patient remained comatose with fluctuating focal neurologic signs (right deviation of the head and gaze) and displayed coarse tremor with bouts of myoclonus. A cerebral CT scan was normal. The clinical course was rapidly satisfactory, and the patient could be weaned from norepinephrine 24 hours later. A peripheral thrombocytopenia appeared gradually, reaching a nadir of 20 × 10^9/L, with complete resolution by the tenth day. No specific etiology was found. On the fifth day of hospitalization, daily urinary output increased rapidly to 7,800 ml (Fig 1), with a urinary osmolality of 224 mmol/kg. Nephrogenic diabetes insipidus was diagnosed. Despite volume compensation with an increasing proportion of saline-free solution, hyponatremia (serum sodium level of 156 mmol/L) was observed on the sixth day, prompting diuretic therapy with thiazides. Serum sodium levels were normal by the 11th day. The patient remained comatose for a total of seven days, even though the lithium was continuously under 2 mmol/L.

On the 12th day the patient was discharged from the intensive care unit. He was still confused and disoriented, and neurologic examination disclosed coarse tremor, bilateral upper limb rigidity, and hyperreflexia. These signs disappeared gradually over a period of three weeks. Polyuria persisted until the patient left the hospital and subsided only one month after discharge. In addition, myocardial infarction was suspected because of signs of transmural ischemia on the admission ECG accompanied by moderate CPK elevation. A myocardial scintigram with 2-methoxyisobutyl isonitrile-technetium-99m indicated decreased uptake in the anterolateral and high septal region, indicating hyperperfusion of this area. A left ventricular angiogram showed moderate anterior hypokinesia, confirming myocardial infarction. A coronary angiogram displayed normal coronary arteries (Fig 2). The patient has now completely recovered.

DISCUSSION

The main features of this case report, ie, (1) the occurrence of a myocardial infarction, (2) the thrombocytopenia, and (3) the problems related to hemodialysis, are most probably related to the unusually high plasma lithium levels. Serious cardiovascular toxicity resulting from lithium salts is rare when the therapeutic drug level is well monitored and adjusted. Electrocardiographic alterations appear to be very common: T-wave depression may occur in up to 20

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percent of the patients adequately treated with lithium. This pattern appears to be benign and is probably related to a partial intracellular displacement of potassium. ST-segment elevation or depression, either at rest or during exercise, has not been described in lithium-treated patients without a previous cardiovascular history; however, cardiac conduction can be altered by lithium salts: reversible atrioventricular block (first degree), sinoatrial dysfunction, bradycardia, and sinus pauses have been observed, even within the therapeutic serum level range, mostly in elderly patients. Finally, severe ventricular arrhythmias have been reported, but almost exclusively in acute intoxications. Cardiomyopathy is poorly documented in lithium-treated patients: it may represent either a rare form of toxicity or be just a coincidental finding; however, cardiovascular collapse has been reported in acute lithium intoxications with severe neurologic symptoms. Our patient fits this description, but fortunately, and unlike previous observations, recovered from this shock state.

We were unable to find any other convincing description of myocardial infarction clearly associated with lithium intoxication in the literature. We found only three case reports apparently linking lithium and myocardial damage. The first is that of an elderly lithium-treated patient who developed profound bradycardia soon followed by myocardial infarction. Two important points are worth mentioning here: first, this patient was not intoxicated by lithium salts but only on maintenance therapy; and, secondly, myocardial infarction was probably related, according to the authors, to an interaction between propranolol and verapamil. The second case was that of a 52-year-old woman who suffered from severe neurologic symptoms and cardiovascular collapse during "mild" lithium intoxication; recent myocardial infarction was found at autopsy, but so were numerous atheromatous plaques. Despite the absence of a detailed clinical description, it can thus be fairly assumed that severe arterial hypotension in a patient with coronary disease was a much more likely cause than the direct toxic effect of

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**Figure 1.** Upper tracing, Serial plasma lithium (Li⁺) levels; note "rebound effect" after each course of hemodialysis. Middle tracing, Plasma sodium (Na⁺) level, illustrating occurrence of diabetes insipidus on fifth day. Lower tracing, Daily water and electrolyte balance.

**Figure 2.** Coronary angiogram (day 13), showing normal coronary arteries, particularly in anteroseptal region.
lithium on the myocardium, as postulated by the authors. Finally, the third case is no more convincing: there were fluctuating ECG abnormalities but no definite evidence favoring acute myocardial infarction. Also, no coronary angiogram or isotopic studies were performed, contrary to our case. Therefore, to our knowledge, we are reporting the first case of myocardial infarction undoubtedly associated with a severe lithium intoxication; the normal coronary angiogram (Fig 2) supports our hypothesis. Because of a lack of experimental evidence, no clear pathogenetic mechanism for myocardial damage due to lithium toxicity can be proposed; however, the fact that the myocardial injury was segmental suggests a vascular etiology, such as a prolonged coronary artery spasm, for example, rather than a direct toxic effect of lithium on myocardial cells.

Lithium salts are known to increase platelet counts in vivo. In contrast, thrombocytopenia has only been reported once as a feature of lithium intoxication. No etiology other than lithium toxicity could be found for this patient’s thrombocytopenia. Thus, we cannot rule out an unusual side effect of this drug.

Finally, we would like to comment on the therapeutic problems related to severe lithium intoxication. Lithium salts are eliminated almost exclusively by the kidneys. With normal renal function, this clearance amounts to 20 to 30 ml/min, with a fractional excretion of 25 to 35 percent. Hence, lithium clearance is directly correlated with urinary flow, and the first approach to treatment, beyond gastric lavage, is rehydration to reestablish normal renal function. In severe intoxications (plasma lithium levels over 3.5 to 4.0 mmol/L), hemodialysis should be undertaken. The main limitation of hemodialytic efficacy is the extravascular accumulation of lithium. Our case demonstrates these problems very well: plasma lithium levels decreased very slowly despite five prolonged dialyses (totaling approximately 36 hours), with several “rebound effects” after hemodialysis (see Fig 1). Therefore, on theoretical grounds, lengthy hemodialysis periods are probably less useful than shorter but more often repeated procedures.

In conclusion, we present one of the most severe lithium intoxications reported to date in the literature; this is also the first well-documented case of myocardial infarction due to lithium salts. Thrombocytopenia may be a side effect of very severe lithium intoxication. Repeated short-lasting sessions of hemodialysis could be more useful than prolonged procedures.

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Bronchoalveolar Lavage Neutrophilia Seen in Pneumocystis Pneumonia Presenting with Pneumothorax

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Spontaneous pneumothorax is a known complication of Pneumocystis carinii pneumonia (PCP) in patients with acquired immunodeficiency syndrome. From a series of 61 patients with PCP, we identified two cases, not associated with aerosolized pentamidine, that presented with spontaneous pneumothorax and cystic changes seen on chest radiographs. Bronchoalveolar lavage cell findings were remarkable for very elevated neutrophil counts in both

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