

# Prolonged delirium caused by lithium poisoning in a cancer patient at progressive stage: A case report

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## Abstract

A patient with schizoaffective disorder and receiving long-term treatment with lithium developed prolonged delirium. She had recently been diagnosed with stage IIIC1 endometrial cancer and presented a deteriorating general condition. Toxic levels of lithium were measured in serum. After hemodialysis, lithium levels gradually decreased and the symptoms disappeared completely.

## Introduction

Lithium remains the drug of choice for the treatment of bipolar disorder<sup>1</sup> and is identified as the first-line agent for this disease in many guidelines<sup>2</sup>. However, due to its narrow therapeutic index, small changes in the serum concentration of lithium can cause toxicity or render the treatment ineffective<sup>3</sup>. The major symptoms of lithium poisoning include tremors, hyperreflexia, gait disturbances, kidney damage, and reduced self-awareness<sup>4</sup>; it can sometimes lead to death of the affected individual. Lithium intoxication has three different courses (acute, acute-chronic, and chronic)<sup>5</sup>. Among these, the chronic course is the most common etiology, usually resulting from an unintentional excess of lithium intake over excretion<sup>6</sup>. Chronic lithium poisoning also presents a higher risk of serious complications than acute poisoning<sup>5</sup>. A retrospective study on the neurotoxicity associated to lithium intake revealed that chronic poisoning mainly occurs in older patients with chronically elevated lithium levels, especially in those with acute kidney injury, and that prolonged delirium can lead to multiple physical complications<sup>7</sup>. In addition, it was found that patients affected by chronic lithium poisoning had a median lithium concentration in serum of 2.2 mmol/L (interquartile range: 1.0–7.1 mmol/L) at presentation and received a median daily dose of 950 mg/day (interquartile range: 250–1350 mg/day). This suggests that even small doses of lithium can lead to poisoning. Here, we report a case of schizoaffective disorder in a patient with cancer at the progressive stage that was being treated with lithium at a low dose of (300 mg/day). In this particular case, the clinical symptoms were masked because of the patient's poor physical status resulting from the progressive stage of cancer disease.

## Case presentation

A 61-year-old Japanese woman was referred to our psychiatric ward due to disturbance of consciousness. She had been diagnosed with schizoaffective disorder at 17 years of age and had been subsequently treated with several antipsychotic drugs, including lithium. Psychiatric symptoms were predominantly negative, and included decreased motivation, emotional flatness, and autism. She visited an outpatient clinic regularly for a long period of time; her last measurement of lithium concentration in serum was 0.51 mmol/L. She had been diagnosed with stage IIIC1 endometrial cancer with lymph node metastases (T2N1M0) at 59 years of age. She underwent total abdominal hysterectomy, bilateral salpingo-oophorectomy, and pelvic lymph node dissection accompanied by adjuvant pelvic radiotherapy. Within the same year, multiple distant metastases were found,

and the patient received chemotherapy consisting of six cycles of docetaxel/carboplatin. Three months after the end of chemotherapy, the cancer recurred in the liver and para-aortic lymph nodes. The patient received six cycles of doxorubicin/cisplatin together with radiotherapy for the metastatic para-aortic lymph node. However, tumor progression could not be controlled, the patient developed ascites and hydronephrosis, and renal function decreased. Although her serum creatinine level was approximately 2.0 mg/dl, she refused the insertion of a ureteral stent. She gradually became unable to walk and suffered from appetite loss. She received palliative care, as her survival time was estimated to be only of several months. Fortunately, she did not suffer from severe cancer pain and did not need to be treated with any non-steroidal anti-inflammatory drugs or opioids. Her physical functions had deteriorated during this period; she developed a gait disturbance and could not maintain a seated position. Subsequently, she became confused. Her consciousness was cloudy and accompanied by dysarthria and myoclonus. At this point the patient was admitted to the Obstetrics and Gynecology ward of our university hospital. She had hypotension, tachycardia, and a mild fever. The patient's laboratory data are presented in **Table 1**. Electrocardiography and head computed tomography revealed no abnormalities. The focus of the infection could not be determined from blood or urine samples, or from a computed tomography scan, and an enhanced inflammatory response due to tumor progression was considered as a possible diagnosis. The reason for the decreased renal function was determined to be the extreme dehydration derived from cancer cachexia. She was referred to the outpatient department of our hospital because of delirium associated to her deteriorating general condition. Her total score on the delirium rating scale-revised-98 (DRS-R-98)<sup>8</sup> was 23 points. Thus, we diagnosed the patient with delirium associated with progressive-stage cancer. Given that she was being treated with several psychotropic drugs (i.e., lithium 300 mg/day, haloperidol 2.25 mg/day, chlorpromazine 25 mg/day, biperiden 6 mg/day, flunitrazepam 2 mg/day, and suvorexant 20 mg/day) and she demonstrated reduced renal function as assessed by the serum creatinine test, her levels of lithium in serum were checked and found to have a value considered toxic (3.02 mEq/L). The patient received hemodialysis immediately; her serum lithium concentration decreased to 1.68 mEq/L after the first session and finally to 0.98 mEq/L after the second session. The clouded consciousness, dysarthria, and myoclonus recovered and eventually disappeared in parallel to the decrease in the serum lithium levels (her DRS-R-98 score decreased to 4 points). Moreover, the gait disturbance and postural retention disorder were completely resolved. Results from the blood tests after the treatment are shown in **Table 1**. There was no further worsening of mental status after lithium treatment was discontinued.

## Discussion

The case presented here taught us two important lessons. First, relatively low doses of lithium could cause toxicity in patients with poor general health, such as those suffering from progressive stage cancer. Second, clinicians often fail to diagnose delirium associated with lithium poisoning. In this particular case, the general condition of the patient was poor and fluid intake was reduced, which led to a decrease in renal function, in turn causing a decrease in excretion. The end result was the appearance of symptoms of poisoning. In addition, the patient was in the terminal stages of cancer and had been treated with anticancer drugs, which may have predisposed her to the observed decline in renal function. Nevertheless, a daily dose of 300 mg/day is considered low according to current literature<sup>7</sup>, which underlines the idea that even low doses of the drug could easily lead to poisoning. Brain metastases, electrolyte abnormalities, and terminal delirium are the most common causes of psychiatric symptoms in cancer patients at the terminal stage<sup>9, 10</sup>. Taking the case presented here into account, lithium intoxication should be considered as a possible diagnosis when myoclonus and gait disturbances are observed. We should also be aware of the fact that serum lithium levels often do not correlate with clinical signs<sup>7</sup>. Lithium poisoning should always be considered as a potential cause for prolonged delirium<sup>7</sup>.

## Conclusion

Clinicians should consider lithium poisoning as a potential cause of prolonged delirium when lithium has been prescribed, even at a low dose. Therapeutic monitoring of lithium levels must be performed regularly, especially when the physical conditions of the patient are poor.

### **Table 1: Summary of blood tests results before and after hemodialysis**

	Before hemodialysis	After hemodialysis
WBC, cells/uL	18400	12900
CRP, mg/dL	10.42	4.51
Na, mmol/L	130	142
K, mmol/L	5.1	4.4
Cl, mmol/L	104	108
BUN, mg/dL	77	21
Cr, mg/dL	4.47	1.42
eGFR, ml/min/1.7m <sup>2</sup>	8.56	30.3
Li, mEq/L	3.02	0.19
NH3, ug/dL	25	-
DRS-R-98, total points	23	4

BUN, Blood urea nitrogen; Cl, Chlorine; Cr, Creatinine; CRP, C-reactive protein; DRS-R-98, Delirium rating scale-revised-98; eGFR, eGFR, B

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None.

### Author Contributions

TN, NO, HA, KH, AI, and RY made substantial contributions to conception and acquisition of data. TN conceived of the study. TN, KH and NO reviewed the literature, analyzed and interpreted the data, drafted and revised the manuscript. NO, KH gave organization support to the study and interpreted the data. All authors read and approved the final version of the manuscript.

### Consent

Written informed consent was obtained from the patient in this case report.

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