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증 례

만성 리튬 중독환자의 지연성 정정맥 혈액 투석여과 사례

연세대학교 원주의과대학 응급의학교실

김태수 · 차용성 · 김 현 · 김오현 · 차경철 · 이강현 · 황성오

Delayed Continuous Venovenous Hemodiafiltration in Chronic Lithium Intoxication

Tae Su Kim, M.D., Yong Sung Cha, M.D., Hyun Kim, M.D., Oh Hyun Kim, M.D., Kyoung Chul Cha, M.D., Kang Hyun Lee, M.D., Sung Oh Hwang, M.D.

Department of Emergency Medicine, Wonju College of Medicine, Yonsei University, Korea

A 66-year-old male with chronic alcoholism presented with tremor, gait disturbance, memory impairment, insomnia, decreased appetite, and confusion.

The patient had been taking lithium daily for treatment of bipolar disorder. Brain CT showed no specific abnormality, and serum lithium and ammonia levels were 3.63 mEq/L (therapeutic range, 0.6~1.2 mEq/L) and 85 μg/dL (reference range: 19~54 μg/dL), respectively. Therefore, the initial differential diagnosis included chronic lithium intoxication, hepatic encephalopathy, Wernicke encephalopathy, or alcohol withdrawal syndrome.

Even with the provision of adequate hydration, the patient' s neurologic status did not show improvement, so that lactulose enema, thiamine replacement, and continuous venovenous hemodiafiltration (CVVHDF) were started on the third admission day. By the fifth admission day he had made a rapid neurologic recovery, and was discharged on the 20th admission day.

Therefore, CVVHDF might be a treatment for patients with chronic lithium intoxication, because, even if serum lithium concentration is normal, lithium concentration in the brain may be different from that of the serum.

Key Words: Chronic lithium intoxication, Continuous venovenous hemodiafiltration

Introduction

In the 1970s, lithium carbonate was approved in the United States for the treatment of acute mania and bipolar disorder and it has been in use ever since. However, the narrow therapeutic range of lithium with other well-characterized adverse effects has limited its use. In 2010, there were 6307 cases of lithium intoxication reported to the American Association of Poison Control Centers[1].

Features of chronic lithium toxicity characteristically include sluggishness, ataxia, confusion or agitation, and neuromuscular excitability, which can manifest as irregular coarse tremors. Other recognized effects include T-wave inversion or flattening, prolonged QTc intervals and bradycardia, and development of nephrogenic diabetes insipidus[2].

Lithium is alkali metal that is low molecular weight

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책임저자: 차 용 성
강원도 원주시 일산동 162
연세대학교 원주의과대학 응급의학교실
Tel: 033) 741-1615, Fax: 032) 742-3030
E-mail: zza96@hanmail.net

(6.94 dalton), negligible protein binding, and low volume distribution (0.8 L/kg) and in poisoning, it is known that hemodialysis is effective to eliminate of lithium[3,4]. However, continuous venovenous hemodiafiltration (CVVHDF) is the preferred method for recently because CVVHDF has a better lithium clearance (lithium clearance 38~62 mL/min), and lesser rebound phenomenon[5,6].

We report case that was treated by delayed CVVHDF in chronic lithium intoxication.

Case Report

A 66-year-old man presented to the Emergency Department (ED) with confusion, agitation, insomnia, intentional tremor, and gait disturbance. Family members reported that the patient' s symptoms had been present for over 3 months, and insomnia, agitation, decreased appetite, and confusion, had developed since last week. He had discontinued his habitual daily alcohol consumption 7 days prior to ED presentation.

The patient had suffered from bipolar affective disorder for over 20 years and on continuous lithium therapy. At ED presentation, vital signs were stable. In terms of mental status, patient was drowsy and disorientated however neurological exam revealed no other abnormal findings except for an intermittent tremor with myoclonus-like features in the four extremities.

Results of other laboratory testing were within normal range, such as sodium 138 mmol/L, potassium 4.0 mmol/L, blood urea nitrogen (BUN) 35 mg/dL, creatinine 1.28 mg/dL, and glucose 147 mg/dL, except for ammonia level (85 μg/dL; reference range: 19~54).

Brain computed tomography to evaluate decreased mentation showed no abnormalities. The electrocardiogram showed ST-segment depression and T-wave inversion in leads V2-4, and prolongation of corrected QT interval (529 ms).

Because there had been no abnormal finding in brain image study, abnormal brainstem sign, such as pupil light reflex, corneal reflex, oculocephalic reflex, and gag reflex in neurologic exam, or sign of infection sign, serum lithium levels were assessed (3.63 mEq/L; therapeutic range: 0.6-1.2 mEq/L).

Our initial differential diagnosis included chronic lithium intoxication, hepatic encephalopathy, Wernicke encephalopathy, or alcohol withdrawal syndrome. We initiated intravenous hydration with isotonic saline because the patient had normal renal function and there remained the possibility of mental deterioration causes other than chronic lithium intoxication. By day 3 after hospital admission, although the serum lithium and ammonia levels had decreased to 1.11 mEq/L and 40 μg/dL, the deteriorated neurologic condition had not improved. Therefore, CVVHDF was initiated for management of chronic lithium toxicity despite normal serum lithium level. At five days after hospital admission, the serum lithium level had decreased to less than 0.20 mEq/L and mental status had improved to nearly alert. At nine days after hospital admission, all neurological symptoms had completely resolved and at twenty days after hospital admission, he was discharged.

Discussion

In this case, chronic lithium intoxication may be caused by chronic alcohol consumption and poor oral intake for many days. Although we could have initially instituted CVVHDF to eliminate lithium, we opted for intravenous hydration sufficient to correct dehydration and to promote lithium elimination. To this end, there is no consensus recommendation on the appropriate time to initiate therapy[7,8] and other concomitant metabolic encephalopathy causes may be present such as alcohol withdrawal syndrome, Wernicke encephalopathy and hepatic encephalopathy. Serum ammonia and lithium levels normalized after adequate fluid therapy, lactulose enema, and thiamine replacement; however altered mental status manifested as deep drowsiness persisted. Because of the lack of adequate improvement after correction of other metabolic encephalopathy causes and the fact that serum and brain lithium concentrations are not necessarily correlated[4,9], we decided to initiate CVVHDF though serum lithium concentration was

normal. Neurological symptoms rapidly improved with two days of CVVHDF.

This case illustrates that even if serum lithium concentration is normal, delayed initiation of CVVHDF may help treatment of chronic lithium poisoned patients with neurological sequelae.

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