Journal of Acute Medicine 11(2): 68-71, 2021
DOI:10.6705/j.jacme.202106_11(2).0004
Case Report

Oral Levothyroxine Treatment in Lithium Intoxication-Induced Myxedema Coma: A Case Report

Po-Hsuan Kao*

Department of Emergency Medicine, National Taiwan University Hospital, Taipei, Taiwan

Lithium intoxication-induced myxedema coma, a rare but dangerous condition of severe hypothyroidism, can be easily misdiagnosed in patients without history of hypothyroidism. The objective of this case report is to describe a lithium-treated patient who presented to emergency department with obtundation and moderate hypothermia and was diagnosed with myxedema coma and lithium toxicity. A 64-year-old female presented to the emergency department with obtundation and hypothermia. The patient had the past history of stage-III chronic kidney disease, bipolar-type schizoaffective disorder, hypertension, and hyperlipidemia, and she had received long-term lithium therapy for the schizoaffective disorder. Bradycardia with hypotension developed after a few hours of admission and thyroid function revealed thyroid-stimulating hormone 53.1 nIU/mL and free T4 (FT4) 0.11 ng/dL, and the serum lithium level was 2.54 mmol/L. Therefore, diagnosis of lithium intoxication-induced myxedema coma was made, and the patient was managed with oral form of levothyroxine (LT4) (loading dose of 400 mcg followed by 100 mcg per day), intensive fluid therapy, empirical antibiotics, mechanical ventilation, and inotropic agents; lithium had been discontinued since admission. The patient weaned from the mechanical ventilation and inotropic support at day 4 of admission and by day 6, the patient's consciousness had fully recovered; on day 9, the serum lithium level was 0.37 mmol/L. The patient's FT4 recovered to the normal range (0.96 ng/dL) on day 15. In patients with no history of hypothyroidism or neck surgery and radiation therapy, lithium intoxication can be the single contributor to myxedema coma, which can be treated with oral form of LT4 as thyroid replacement therapy with instant and intensive supportive care. However, further study is needed to compare the outcomes of the patients with myxedema coma treated by oral and intravenous LT4.

Key words: *lithium intoxication, myxedema coma, oral administration, thyroxine*

Introduction

Myxedema coma is nowadays a rare but still with a high mortality rate medical emergency of hypothyroidism and is easily misinterpreted in lithium-treated patients without previous-diagnosed hypothyroidism. This article describes an elder lithium-treated patient without the past history of hypothyroidism, who presented altered consciousness level and hypothermia and was diagnosed with lithium intoxication and myxedema coma which was managed with oral administration of levothyroxine (LT4).

Case Report

A 64-year-old female presented to the emergency department with obtundation and moderate hypothermia (29.8°C), where atrial fibrillation with slow ventricular response and hypotension were also noted. The patient was a resident in the nursing home with diagnosis of stage-III chronic kidney disease and bipolar-type schizoaffective disorder for which she had been receiving lithium (900 mg/day) and her other medications included Amlodipine, Valsartan, and Atrovastatin for hypertension and hyperlipidemia.

Received: April 8, 2020; Revised: July 8, 2020; Accepted: July 21, 2020.
*Corresponding author: Po-Hsuan Kao, MD, Department of Emergency Medicine, National Taiwan University Hospital, No.7, Zhongshan S. Rd., Zhongzheng Dist., Taipei City 100, Taiwan. E-mail: frankkao66@yahoo.com.tw

Recently, lithium dosage was adjusted to 600 mg daily by her primary psychiatrist.

The patient was obtunded but arousable. Hypothermia (29.8°C), atrial fibrillation with slow ventricular response (ventricular rate: 31 beats per minute), and hypotension with blood pressure of 82/64 mmHg were noted on initial examination. Other physical examination revealed fasciculation over facial muscles and bilateral dilated pupils (pupil size: 5 mm in both eyes) with sluggish pupillary responses to light. The neurologic examinations showed obtundation, Glasgow Coma Scale (GCS) of 11/15 ($E_4V_2M_5$), and there was no significant cranial nerve palsy or focal neurologic deficit noted.

The laboratory examination revealed normocytic anemia (hemoglobin: 9.3 g/dL, mean corpuscular volume: 98.7 fL), creatinine clearance rate of 43 mL/min (creatinine: 1.6 mg/dL), blood glucose of 100 mg/dL, mild elevated liver function (AST: 60 U/L, ALT: 64 U/L) and normal sodium and potassium level. No toxicology screen was arranged. Atrial fibrillation with slow ventricular response and Osborn J wave were shown on electrocardiogram (Fig. 1) and chest X-ray revealed enlarged cardiac silhouette with left costo-phrenic angle blunting.

The patient received passive external rewarming (PER) and active external rewarming (AER) with heat lamp for hypothermia, hydration with crystalloid fluid for hypotension and atropine for unstable bradycardia at the emergency department and then was admitted to the intensive care unit. After a few hours of admission, dopamine was given due to persistent hypotension (blood pressure around 70/40 mmHg) accompanied with bradycardia (heart rate around 30 beats per minute). At day 2 of admission, the patient's level of consciousness stayed obtunded (GCS: $E_4V_2M_5$), and head computed tomography without contrast was arranged, which later revealed only cortical frontal brain atrophy without evidence of acute intracranial abnormality, to rule out intracranial lesion and survey for refractory hypothermia (33°C) under PER and AER management. Dopamine and norepinephrine were both used for refractory hypotension with blood pressure around 70/40 mmHg. Although

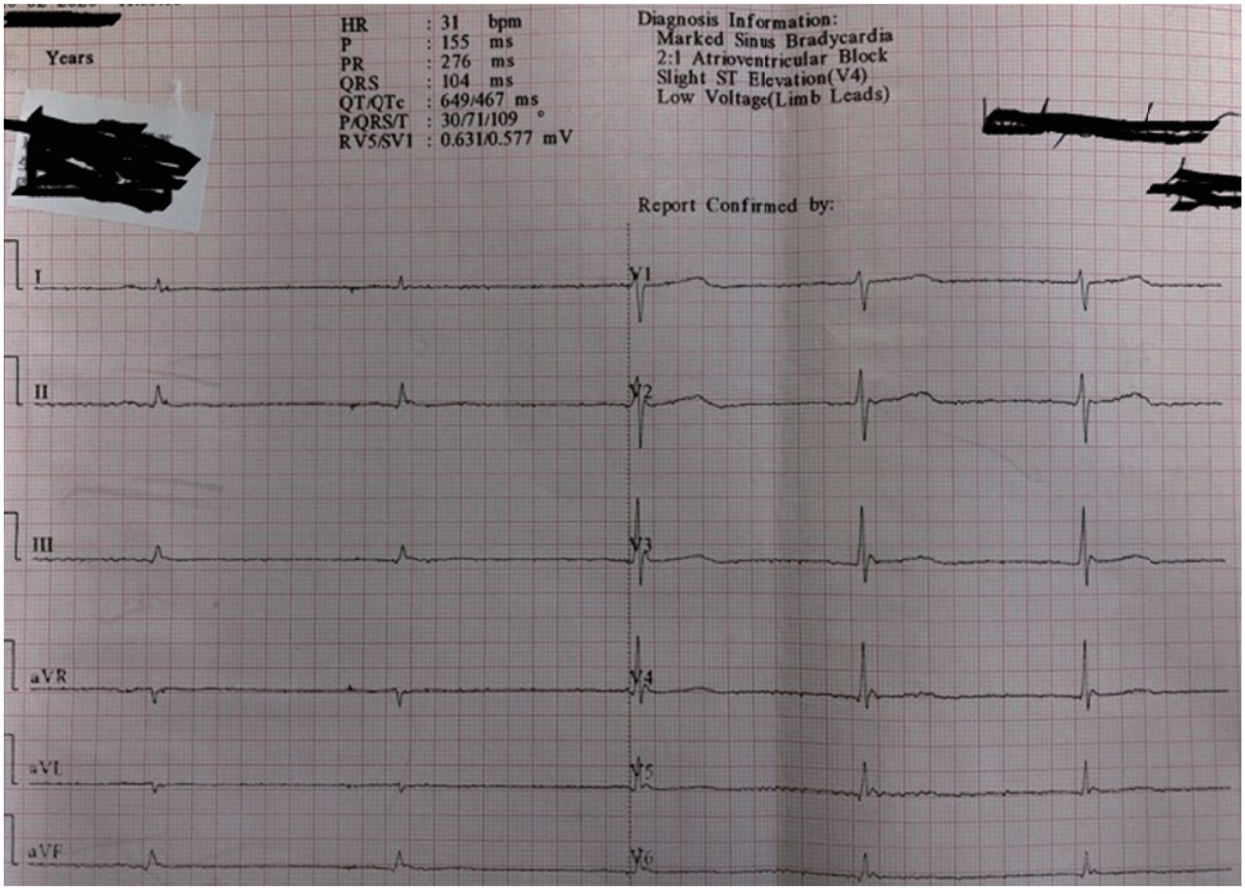

Fig. 1. Electrocardiogram of the patient at emergency department.

respiratory rate and respiratory pattern was normal, elevated oxygen demand was noted and therefore, endotracheal tube as preventive airway was placed with the mechanical ventilator support. Blood gas analysis reported as the following: pH = 7.348, $PaCO_2$ = 42 mmHg, PaO_2 = 131 mmHg, HCO_3^- = 22.6 mEq/L. Lactate level was 1 mmol/L, which remained within normal limits. The significant results of laboratory testing were thyroid-stimulating hormone 53.1 nIU/mL (normal range: 0.27–4.20 nIU/mL) and free T4 (FT4) 0.11 ng/dL (normal range: 0.93–1.70 ng/dL). With the diagnosis of myxedema coma, intravenous hydrocortisone was given initially at 200 mg/day with a loading dose of 0.4 mg oral LT4 followed by a maintenance dose of 0.1 mg/day through nasogastric tube due to unavailability of intravenous LT4. Other managements including intensive fluid therapy, empirical antibiotics, mechanical ventilation, PER, and inotropic agents were kept. On day 3, serum lithium level taken previously reported 2.54 mmol/L, and therefore diagnosis of lithium poisoning with lithium intoxication-induced myxedema coma was made. As to the management of lithium poisoning, intensive fluid therapy had been kept and no more lithium was administered since admission. No hemodialysis was arranged. Vital signs improved within 48 hours after management for myxedema coma initiated and the inotropic agents were gradually tapered off and the endotracheal tube was removed on day 4, when intravenous hydrocortisone was also discontinued due to normal adrenal function reported from the laboratory examination taken at admission. On day 5, the patient could murmur with incomprehensible sound, and on the next day, the level of consciousness improved with coma scale of 13/15 (GCS: $E_4V_4M_5$) and she could communicate with complete sentences, and hence, the patient was transferred to general ward under stable condition. Follow-up FT4 revealed 0.43 ng/dL and 0.65 ng/dL on day 5 and 9, and recovered to the normal range (0.96 ng/dL) on day 15. Follow-up serum lithium level on day 9 dropped to 0.37 mmol/L.

Discussion

Myxedema coma is a nowadays a rare but life-threatening decompensated condition of hypothyroidism. Diagnosis can be challenging especially in patients without history of hypothyroidism or neck surgery and radiation therapy. Lithium intoxication-induced myxedema coma is rare with very few case reported,[1-3] and to our knowledge, this is the second case report of lithium-precipitating myxedema coma treated with oral form of LT4.[3]

Myxedema coma, based on the recommendations of American Thyroid Association,[4] should be treated, as thyroid replacement therapy, with a loading dose of 0.2–0.4 mg intravenous LT4 and then followed by maintenance dose of 0.05–0.10 mg daily, given intravenously or orally. However, as intravenous LT4 is unavailable in Taiwan, 0.4 mg oral LT4 followed by 0.1 mg daily was considered treatment of choice instead. Mir et al.[3] reported a case of myxedema coma precipitated by lithium toxicity, in which the patient was managed with oral LT4 of 0.5 mg loading dose followed by 0.1 mg daily, and the patient gained full recovery of the consciousness by day 10 of treatment. The main considerations of the preference of intravenous LT4 over oral form are the onset of action and the efficacy. However, Yamamoto et al.[5] revealed that among myxedema coma patients treated with LT4 at dose of 0.5 mg/day or more, the outcome of those given LT4 orally appeared more favorable than those treated by intravenous administration, which was probably due to less bioavailability of oral administration (41.3–73.5%), and that lower doses should be considered in elderly patients. Dutta et al.[6] reported that an oral dose of 0.5 mg LT4 as the loading dose followed by the maintenance dose of 0.15 mg/day as the thyroid replacement therapy for patients with myxedema coma, compared with intravenous administration of 0.2 mg loading dose followed by 0.1 mg per day, had no difference in outcome. Still, there is no comparative study of the effect of intravenous LT4 and oral LT4 as the treatment in myxedema coma patients so far.

Our patient's vital sign resumed to her baseline within 48 hours after the management for myxedema coma was initiated and the level of consciousness totally recovered after 4 days of the treatment. Although a relative conservative regimen (0.4 mg LT4 followed by 0.1 mg/day orally) was used in this patient, the clinical course is comparable to that reported by Mir et al.

Although there are several signs and symptoms to differentiate lithium toxicity and hypothyroidism, such as diarrhea, vomiting, coarse tremor, cerebellar disturbances and hyperactive reflexes in lithium intoxication and brittle hair, dry skin, bradycardia and

delayed reflexes in hypothyroidism, the two diseases also shared many non-specific clinical presentations, including dysphonic mood, increased sleeping time, fatigue, and decreased concentration. Especially in lithium-treated patients without history of hypothyroidism, clinical signs of hypothyroidism can be mistaken as the adverse effects of lithium, and hence the diagnosis and treatment is delayed. Furthermore, due to low incidence of lithium intoxication-induced myxedema coma, such patients present with decreased mental status, hypothermia, and other symptoms related to slowing of function in multiple organs can be mistakenly treated only as lithium intoxication rather than lithium intoxication-induced myxedema coma.

Conclusions

This case illustrates that lithium-treated patients with no past history of hypothyroidism or any neck surgery and radiation therapy may develop myxedema coma which can be dangerous, and that with the instant and intensive care, the patients can have good outcomes even though only oral form of LT4 is available. Still, further study is needed to compare the efficacy of the oral form LT4 with the intravenous administration as thyroid replacement therapy in myxedema coma patients.

Authors' Contributions

Po-Hsuan Kao was the primary care of the patient and analyzed and interpreted the patient data and was the only contributor in writing the manuscript.

Availability of Data and Materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Conflicts of Interest Statement

The author declares that he has no competing interests.

Consent for Publication

Written informed consent was obtained from the patient for publication of this case report and any accompanying images.

Ethics Approval and Consent to Participate

The patient, after regaining her consciousness and transferred to general ward, had agreed that her data could be used for related study. There was no ethical review meeting held but the patient's informed consent was provided.

Funding

None declared.

References

1. Waldman SA, Park D. Myxedema coma associated with lithium therapy. *Am J Med* 1989;87:355-356. doi:10.1016/s0002-9343(89)80168-8
2. Santiago R, Rashkin MC. Lithium toxicity and myxedema coma in an elderly woman. *J Emerg Med* 1990;8:63-66. doi:10.1016/0736-4679(90)90390-h
3. Mir SA, Wani AI, Masoodi SR, Bashir MI, Ahmad N. Lithium toxicity and myxedema crisis in an elderly patient. *Indian J Endocrinol Metab* 2013;17(Suppl 3):S654-S656. doi:10.4103/2230-8210.123558
4. Jonklaas J, Bianco AC, Bauer AJ, et al. Guidelines for the treatment of hypothyroidism: prepared by the American Thyroid Association Task Force on Thyroid Hormone Replacement. *Thyroid* 2014;24:1670-1751. doi:10.1089/thy.2014.0028
5. Yamamoto T, Fukuyama J, Fujiyoshi A. Factors associated with mortality of myxedema coma: report of eight cases and literature survey. *Thyroid* 1999;9:1167-1174. doi:10.1089/thy.1999.9.1167
6. Dutta P, Bhansali A, Masoodi SR, Bhadada S, Sharma N, Rajput R. Predictors of outcome in myxoedema coma: a study from a tertiary care centre. *Crit Care* 2008;12:R1. doi:10.1186/cc6211