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A Case of Lithium Intoxication with Severe Neurological Findings

Ciddi Nörolojik Bulgularla Birlikte Giden Lityum Zehirlenmesi Olgusu

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Abstract

Lithium is used for the treatment of bipolar disorder and some other psychiatric disorders. Due to the narrow therapeutic range, intoxications are common. In this case, chronic lithium intoxication with severe neurological symptoms was discussed in light of the literature. A 72-year-old female patient. The patient had been receiving psychiatric treatment for 7 years with the diagnosis of unipolar depression. In the 6th month of lithium use, she was brought by her relatives with complaints of drowsiness, tremor, muscle twitching, and difficulty walking. On examination, consciousness was confused, there was no cooperation orientation and there was general rigidity, tremor, fasciculations, and ataxic gait. Vital signs; blood pressure 147/92 mmHg, heart rate 69 bpm, SpO2: 94%. The laboratory tests: lithium 2.98 mEq/L, potassium 5.8 mmol/l, sodium 129 mmol/l, creatinine 1.66 mg/dl, urea 166 mg/dl. The patient was transferred to the internal medicine clinic with the diagnosis of lithium intoxication. Lithium treatment was discontinued. On the 7th day, her neurological symptoms improved with supportive treatment, and biochemical parameters returned to normal. A lithium concentration of more than 3.5 mEq/L was defined as severe poisoning. Neurological findings are prominent in severe poisonings. Especially, geriatric population is at greater risk. In our case; age, use of three different groups of diuretics as antihypertensive treatment, and urinary tract infection were defined as factors that predispose to poisoning. In this case, it's emphasized that although the lithium blood level isn't very high, severe neurological symptoms can be seen clinically in the presence of risk factors.

Keywords: Lithium; Lithium Intoxication; Bipolar Disorder; Geriatric.

Özet

Lityum, bipolar bozukluğun ve diğer bazı psikiyatrik bozuklukların tedavisinde kullanılır. Dar terapötik aralık nedeniyle, zehirlenmeler yaygındır. Bu olguda ciddi nörolojik semptomlarla seyreden kronik lityum zehirlenmesi literatür ışığında tartışılmıştır. 72 yaşında, evli, eşiyle beraber yaşayan kadın hasta. Hasta unipolar depresyon tanısıyla 7 yıldır psikiyatrik tedavi alıyordu. Lityum kullanımının 6. ayında, halsizlik, uyku hali, vücutta yaygın titremeler, kas seyirmeleri, yürüme güçlüğü nedeniyle ile yakınları tarafından polikliniğe getirildi. Muayenesinde bilinç konfüzeydi, koopere değildi, oryantasyon bozulmuştu, yaygın rijidite, tremor, fasikülasyonlar ve ataksik yürüyüş mevcuttu. Vital bulgularında tansiyon 147/92 mmHg, nabız 69 atım/dakika, SpO2: %94 idi. Kan gazı normaldi. EKG normal sinüs ritminde idi. Kan tetkiklerinde; lityum 2.98 mmol/l, potasyum 5.8 mmol/l, sodyum 129 mmol/l , kreatinin 1.66 mg/dl, üre 166 mg/dl. Hasta lityum zehirlenmesi ön tanısı ile dahiliye kliniğine sevk edildi. Lityum tedavisi kesildi. 7. gününde destek tedavisi ile nörolojik semptomları düzelen hastanın biyokimyasal parametreleri normale döndü. Lityum konsantrasyonunun 3.5 mEq/L'den fazla olması şiddetli zehirlenme olarak kabul edilir. Klinikte gastrointestinal, kardiyovasküler, endokrin, nörolojik, renal bulgular görülebilir. Şiddetli zehirlenmelerde nörolojik bulgular ön plana çıkar. Özellikle geriatrik popülasyon daha büyük risk altındadır. Olgumuzda; yaşın ileri olması, antihipertansif tedavi olarak 3 farklı grup diüretik kullanılması ve idrar yolu enfeksiyonunun varlığı zehirlenmeyi kolaylaştıran etkenler olarak tanımlanmıştır. Bu olguda lityum kan düzeyi çok yüksek olmamasına rağmen risk faktörlerinin varlığında şiddetli nörolojik belirtilerin klinikte görülebileceğinin akılda tutulması gerektiği vurgulanmaktadır.

Anahtar Kelimeler: Lityum; Lityum Zehirlenmesi; Bipolar Bozukluk; Geriatrik.

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INTRODUCTION

Lithium is a drug that has been widely used in the treatment of bipolar disorder for many years (1). However, it has been frequently used in the treatment of recurrent major depressive disorders and is effective in increasing the treatment response in resistant cases that do not respond to antidepressant treatment (2). However, the potential side effects and risks of lithium treatment can make it difficult to apply in daily practice from time to time (3).

Factors that increase the concentration of lithium in the body include excessive intake and impaired excretion (4). Excessive lithium intake due to suicide attempts or accidental ingestion of excessive amounts of lithium may result in acute overdose (5). Many factors can cause impairment in lithium excretion. Decreased sodium and fluid volume due to any condition such as vomiting, diarrhea, febrile illness, renal failure, excessive exercise, water restriction, excessive sweating, low sodium diet, and congestive heart failure may increase the reabsorption of lithium in the kidneys. In addition, drugs that decrease the glomerular filtration rate (NSAID, ACE inhibitors, thiazides) may cause chronic toxicity (6).

Regarding the subtypes of lithium poisoning, there are acute, chronic over acute and chronic forms, which differ in their symptomatology due to the pharmacokinetics of lithium (7). In acute lithium poisoning and chronic use, gastrointestinal symptoms (nausea, vomiting, diarrhea), cardiotoxic findings (ECG changes, arrhythmias, QT interval prolongation, bradycardia), and late-developing neurological symptoms (Irreversible neurotoxicity syndrome (SILENT)) appear. While the chronic form primarily presents as neurological symptoms including confusion, myoclonus, and seizures, cardiological findings are similar to those seen in acute intoxication, and nephrogenic diabetes insipidus is seen as a renal effect (8). The rationale for clinical differences is compartment saturation. In cases of acute lithium toxicity, lithium concentrations tend to drop rapidly due to distribution in several tissues, while chronic toxicity is faced with lithium-saturated tissues. Therefore, lithium toxicity depends on the exposure pattern, which should be considered in terms of treatment strategy (9).

In this case, we aimed to examine the chronic poisoning in a patient who took lithium for treatment-resistant unipolar depression with the symptoms and findings we found and to present it in the light of the literature.

CASE PRESENTATION

Written and verbal consent was obtained from the patient and her relatives. 72-year-old female patient. She is married, has 2 children, primary school graduate, and lives with her husband. In her story; it was learned that she had a known hypertension disease and that she used the perindopril-amlodipine combination and hydrochlorothiazide-spironolactone combination for this. In her psychiatric history; the patient who started psychiatric follow-up and treatment with complaints of unhappiness, loss of interest, and hopelessness 7 years ago, applied to various centers with the diagnosis of unipolar depression and used various medical treatments. The last hospitalization of the patient was about 1 month in December 2021 in a university hospital, and lithium carbonate 600 mg/day treatment was started at the time of admission. The patient who was admitted to our outpatient clinic 2 months after her discharge due to her depressive symptoms continued, was receiving venlafaxine 225 mg/day, mirtazapine 15 mg/day,

olanzapine 5 mg/day, quetiapine 25 mg/day, and alprazolam 0.5 mg/day in addition to lithium. The results of the patient, whose blood tests (complete blood count, kidney and liver function tests, thyroid hormones, electrolytes) and lithium blood level were checked at her admission, were within the reference ranges.

The patient, whose follow-up was continued, was brought to the polyclinic by her relatives in a wheelchair in the 6th month of lithium use. The general condition of the patient was poor. In the history taken from her relatives, it was learned that she had weakness, sleepiness, widespread tremors in the body, muscle twitches, difficulty in walking and vomiting for the last 2 days.

In her mental examination, was not cooperatively oriented, her consciousness was confused, and her speech was dysarthric. In the physical examination; diffuse tremor, rigidity, and fasciculations were present, and ataxia was present. The patient was referred to the emergency room. Her vital signs were blood pressure 147/92 mmHg, heart rate 69 bpm, SpO2: 94%. As a result of the arterial blood gas test; pH: 7.338, Pco2: 33.1 mmHg, HCO3: 18.5 mmol/L. ECG was in normal sinus rhythm. In blood tests; lithium 2.98 mmol/l, potassium 5.8 mmol/l, sodium 129 mmol/l, creatinine 1.66 mg/dl, eGFR (CKD-EPI) 30.26 (ml/min/1.73 m^2), urea 166 mg/dl, BUN 77.57 mg/dl, TSH 12.79 mIU/L, fT4 0.58 ng/dl, WBC 11.5 (/mm^3) and other blood tests were within reference ranges. The urinary ultrasound of the patient, whose complete urinalysis was evaluated in favor of urinary tract infection, was normal. The patient was followed closely in the emergency department under appropriate hydration and treatment and was hospitalized in the internal medicine clinic with the diagnosis of lithium intoxication/ lithium-related acute renal failure. The patient's lithium treatment was immediately discontinued.

Forced diuresis (furosemide infusion) was applied on the first day, and the patient's clinic improved on the 7th day of hospitalization, creatinine value decreased to 0.98 mg/dl, urea 55 mg/dl, potassium 4.1 mmol/L, TSH 3.56 mIU/L, and lithium blood level to 0.54 mmol/L decreased, sodium level increased to 136 mmol/L. The patient's treatment for urinary tract infection was also completed. The patient was transferred to the psychiatry clinic.

DISCUSSION

Due to a narrow therapeutic range, lithium intoxication is a common clinical problem (10,11). While the effective dose range is 0.6-1.0 mmol/L, 1.2 mmol/L or more can be toxic in long-term use (12). The severity of lithium toxicity is generally divided into three grades; If the serum lithium concentration is between 1.5-2.5 mEq/L, it is considered mild, between 2.5-3.5 mEq/L is moderate, and more than 3.5 mEq/L as severe poisoning (13).
In lithium poisoning; gastrointestinal, cardiovascular, endocrine, neurological, and renal findings may be observed (14,24). These intoxication findings can be seen at high blood concentrations of lithium, as well as at concentrations within the therapeutic dose range in some patients (15). While there were mild gastrointestinal and endocrine findings in our case, cardiovascular findings were absent. Neurological effects and renal dysfunction were present in the foreground.

Especially the geriatric population is vulnerable to chronic poisoning. Most case reports have shown that elderly individuals are at greater risk for lithium-induced neurotoxicity, even in the

presence of lithium serum concentrations within the normal range (16). We think that advanced age was one of the factors that facilitated poisoning in our case.

In a retrospective cohort study of lithium poisoning cases published in 2016, factors associated with intoxication were examined and 9.9% of cases were associated with infections and 12.1% with initiation of interacting drugs. Volume reduction due to diuretics, dehydration, febrile illness, or gastrointestinal losses may cause elevated serum lithium levels (17). Our case was using 3 different groups of diuretics (hydrochlorothiazide, perindopril, and spironolactone) as antihypertensive treatment and had a urinary tract infection.

Although it has been determined in previous studies that lithium causes subclinical or clinical hypothyroidism more frequently, cases with hyperthyroidism and even thyrotoxicosis have also been reported rarely (18-20). Although it is not known for certain whether lithium-related hypothyroidism is reversible, in a retrospective cohort study conducted by Lieber et al., it was found that hypothyroidism resolved in most patients after lithium was discontinued (21). The TSH value of our patient was determined as 12.79 mIU/L and it was associated with lithium use. On the 7th day of the supportive treatment for lithium poisoning, TSH was 3.56 mIU/L, and this value is maintained in the ongoing follow-ups of the patient, and the patient did not receive thyroid replacement therapy. In addition, the incidence of hypercalcemia due to lithium-associated hyperparathyroidism (LIH) was found in a wide range of 3.6-62% (22). In our case, PTH and serum calcium levels were within normal limits.

Neurological manifestations of lithium poisoning are varied. In cases of mild lithium poisoning, symptoms may include a fine tremor, indifference to one's surroundings, fatigue, muscle weakness, and heightened reflexes. In moderate lithium poisoning, individuals may experience more severe neurological side effects such as pronounced tremors, difficulty with speech (dysarthria), ringing in the ears (tinnitus), loss of coordination (ataxia), increased muscle tension (hypertonia), sudden muscle jerks (myoclonus). In cases of severe lithium poisoning, symptoms can progress to include a state of stupor, epileptic seizures, coma, muscle twitching (fasciculation), muscle stiffness (spasticity), involuntary movements (chorea), slow, writhing movements (athetosis), weakness (paresis), and even paralysis(23). While lithium blood concentration was 2.98 mmol/l in our case, there were widespread tremor, rigidity, fatigue, dysarthria, ataxia, and fasciculations. Although neurological symptoms improved with treatment in our patient, tremor continued in the follow-up, and clinical improvement was achieved with propranolol 40 mg/day treatment.

Acute kidney injury was found in 32 of the attacks in a cohort study in which 91 poisoning attacks were examined in the literature (17). The lithium blood concentration level of our patient, who did not exhibit renal dysfunction during routine outpatient follow-ups, measured at 2.98 mmol/L. The creatinine level was 1.66 mg/dl, the estimated glomerular filtration rate (eGFR - CKD-EPI) was 30.26 (ml/min/1.73 m^2), urea was 166 mg/dl, and BUN (blood urea nitrogen) was 77.57 mg/dl. Renal function tests returned within the reference ranges at the end of treatment.

As a result, especially the geriatric population is at greater risk of lithium poisoning. In our case; old age, use of 3 different groups of diuretics as antihypertensive treatment, and the presence of urinary tract infection were defined as factors that facilitate poisoning. In this case, it is emphasized that although the lithium blood level was not very high, it should be kept in mind that severe neurological symptoms can be seen clinically in the presence of risk factors.

Ethical approval and consent to participate
Written informed consent to publish this information was obtained from study participant.

Consent for Publication
Patient included in this case report gave written informed consent to publish the data contained within this study.

Conflict of Interest
The author declare no potential conflicts of interest with respect to the research, authorship and/or publication of this article.

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Authors Contribution
All authors (TT, MŞC, SA and HB) shared the collection of published data, analyzing the results, manuscript writing and final revision. All authors have read and approved the manuscript.

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