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Case Report / Olgu Sunumu

Seventy-two Months Ongoing Nephrogenic Diabetes Insipidus after Discontinuation of Lithium: A Case Report

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ABSTRACT

Seventy-two months ongoing nephrogenic diabetes insipidus after discontinuation of lithium: a case report

Lithium is a drug commonly used in mood disorders. This common usage has brought with it a better recognition of its common side effects. Side effects of lithium on kidney is one of the most frequent and one of them is nephrogenic diabetes insipidus (NDI). NDI is characterized by polyuria and polydipsia; it develops due to the effect of lithium on sodium and water absorbtion at the level of the collecting tubules causing deterioration in the urinary concentrating ability. Most of NDI cases due to lithium treatment resolve spontaneously after discontinuation of lithium. Recovery of NDI cases due to long-term usage of lithium may take longer. We present a case of nephrogenic diabetes insipidus lasting 72 months after the discontinuation of short term lithium usage and the diagnosis and treatment process of this patient.

Key words: Bipolar disorder, lithium, nephrogenic diabetes insipidus

ÖZET

Lityum kesilmesinden sonra 72 ay devam eden nefrojenik diabetes insipidus: Olgu sunumu

Lityum, duygudurum bozukluklarında sık kullanılan bir ilaçtır. Bu sık kullanım, lityumun yan etkilerinin daha iyi tanınmasını sağlamıştır. Lityumun böbrek üzerindeki yan etkileri en sık karşılaştığımız yan etkilerdendir. Bu yan etkilerden biri de nefrojenik diabetes insipidustur (NDİ). Poliüri ve polidipsi ile karakterize olan NDİ, lityumun toplayıcı tübüller seviyesinde su ve sodyum emilimini etkilemesine bağlı olarak, böbreğin idrarı konsantre etme yeteneğinin bozulması sonucu gelişmektedir. NDİ gözlenen çoğu olgu, lityum tedavisinin kesilmesinin ardından kendiliğinden düzelir. Uzun süre lityum kullanımına bağlı NDİ vakalarının düzelmesi daha uzun süre alabilir. Biz de bu olgu sunumunda, kısa süreli lityum kullanımına bağlı gelişen ve 72 ay boyunca devam eden bir NDİ hastasını, bu hastanın tanı ve tedavi sürecini sunmayı planladık.

Anahtar kelimeler: Bipolar bozukluk, lityum, nefrojenik diabetes insipidus

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INTRODUCTION

Lithium has been used to treat bipolar disorder, recurrent unipolar depression and treatment resistant depression since nineteenth century, its side-effects have been known very well. One of the most common side effects of lithium is impaired renal functions (1). Nephrogenic diabetes insipidus (NDI), which is characterized by polyuria and polydypsia, develops because of impaired renal ability to concentrate urine due to effect of lithium on water and sodium reabsorption at tubular level. NDI associated with lithium use can emerge even in therapeutic dose range (1). Therefore, lithium associated NDI is not directly related with lithium dose or duration of treatment. NDI may be seen in 10-15% of patients who are on lithium for fifteen years or longer (1). Besides, it may be evident after eight weeks of treatment (2). Long-term lithium use may lead to irreversible decrease in urinary concentration while

triggering a partially reversible decrease in glomerular filtration rate (3,4). These complications can be reflected in the clinical picture sometimes as symptoms like polyuria, polydypsia and nocturia, and sometimes as abnormal laboratory results including serum creatinine and urinary density.

Lithium leads to NDI by decreasing renal tubule sensitivity to antidiuretic hormone, aquaporin 2 expression, V2 receptor density and cyclic AMP production and by increasing phophodiesterase actvivity (5). Another mechanism in NDI emergence is impaired function of epithelial sodium channels (ENaC). EnaC is responsible for lithium and sodium reabsorption (6). Biochemical, physiological and histological changes is reversible in 12-30% of patients with NDI. However, in several patients, symptoms can be permanent for several years after cessation of lithium treatment (7,8).

In this case report, a patient with ongoing NDI symptoms after 72 months of stopping lithium treatment, which was continued for three months and stopped for polyuria and polydypsia is presented.

CASE

Thirty-two years old, first-grade graduate, unemployed, divorced, father of one, male patient applied to our outpatient clinic with uneasiness, suspicion, and internal discomfort. Psychiatric examination revealed depressive and restricted affect. Visual hallucinations and persecution delusions were detected. The patient who had poverty of thought and impaired reasoning was hospitalized.

According to information obtained from his files and relatives, he had persecution delusions, auditory hallucinations and episodic mood episodes since 2004. The patient who was incomplient to treatment had almost each year a manic episode lasting an average of one to two months and a depressive episode lasting an average of five to six months and he was hospitalized four times during this period. He was diagnosed with "schizoaffective disorder, depressive period" per DSM-IV criteria (9). Besides, he also had complaints of very frequent urination and drinking too much water. Medical records indicated that lithium treatment was started to the patient 6.5 years ago and he was on 600 mg lithium per day for three months and his frequent urination and drinking too much water complaints begun at that period and treatment was stopped because of these side-effects. Increased water consumption and 8-9 litres daily urination complaints continued after cessation of treatment.

In physical examination, the patient has a favorable general condition, conscious and orientation. Blood pressure was 130/80 mmHg, pulse was 92 beats/min, body temparature was 37.2°C. Mild to moderate dehydration signs were evident. There were no other positive findings in the physical examination. Plasma sodium level was 144 (normal range 135-145 mmol/L), plasma potassium was 4.05 (3.5-5.5 mmol/L), plasma calcium was 8.9 (8.5-11.0 mg/dL), plasma osmolarity was 302 (280-315 mosm/kg), and urine density was 1.001 (normal range 1015-1025). GFR value, which was measured by dynamic renal scintigraphy, using Tc-99m DTPA (diethylene triamine pentaacetic acid), was midly decreased in the patient. Brain magnetic resonance imaging was normal. Thyroid function tests were within normal range. Endocrinological consultation was sought based on clinical and laboratory findings. To diagnose NDI due to lithium use, endocrinology clinic made fluid deprivation test and detected renal impairment in urinary concentration. NDI diagnosis was made after finding that renal impairment in urinary concentration did not improve with desmopression application.

Laboratory values after fluid deprivation were; plasma sodium:134 mmol/lt, plasma osmolarity:282, urine density:1001. After amiloride treatment, daily urination reduced to 4000-4500 mL. Endocrinology considered 50% decrease in urinary output as positive treatment response.

Regarding psychiatric treatment, amisulpride 200 mg/day was started and increased gradually to 1200 mg/day to treat persecution delusions and depressive affect, particuarly. Patient did not respond to amisulpride treatment, and since his medical records indicated that he was not responsive

to several antipsychotics, clozapine was initiated gradually. Clozapine was given 300 mg daily. Amisulpride was gradually tapered. After 36 days of inpatient treatment, the patient was discharged for outpatient follow-up since psychotic symptoms were decreased and his affect was eutymic.

DISCUSSION

Several cases with permanent NDI after long-term lithium use have been reported in the literature (10,11). However, to the best of out knowledge, there have been no previous reports of NDI lasting 72 months after stopping short-term (three months) lithium treatment in the literature. Our patient had polyuria and polydypsia complaints and loboratory evaluations revealed plasma sodium and osmolality levels close to upper limit and low urinary density. Urinary concentration did not increase after fluid deprivation and desmopressin application. NDI was diagnosed by endocrinology. NDI due to lithium use usually recovers after treatment is stopped, but some of the patients may continue to be symptomatic. A patient follow-up by Thompson et al. (12), reported to have polyuria and polydypsia complaints 10 years after stopping lithium, even the patient did not have NDI signs any longer (reversible NDI). In our case, NDI signs continued for 72 months.

World Health Organisation reported 359 patients with drug related diabetes insipidus. Of these patients, 44% (159 patients) were associated with lithium use (1). Lithium impairs protein G activation by depositing on renal tubules. This results in increased water excration and plasma osmolality due to lithium (1,13). It has been recommended that anual measurement of plasma electrolytes, urine volume and osmolality should be ordered by psychiatrist who are using lithium for treatment regarding emergence of NDI in long-term lithium use (8). As evident in our case, NDI can develop even after not long-term use of lithium. We believe that, this must be considered in all patients using lithium.

Lithium associated condition must be known throughly since one in one thousand people in general population use lithium. Lithium can lead to great changes in water equilibrium by causing polyuria and secondary polydypsia. Any fluid restriction, preoperative processes or dehydrating conditions like vomiting and diarrhea and acute diseases can trigger NDI. Patients who are on lithium currently or in the past must be evaluated by keeping this on mind. Fluid loss may cause serious clinical problems including hypotension, hypovolemic shock and death (7).

In our case, polyuria and polydypsia continued for 72 months in spite of stopping lithium treatment which lasted three months, and NDI diagnosis was supported by clinical and laboratory findings. This case informed us that in patients using lithium, cautious follow-up must be made, particularly regarding renal functions, and to keep in mind that symptoms may last for long time and that even short-term lithium use can lead to irreversible side-effects.

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