Reprinted from the German Journal of Psychiatry · http://www.gjpsy.uni-goettingen.de · ISSN 1433-1055

CASE REPORT

Pitting Type Pedal Edema With Lithium: A Case Report

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Abstract

Lithium is widely used in psychiatry because of its mood stabilizing properties. Although it is considered a relatively safe mood stabilizer, occasionally, it can lead to atypical and uncommon adverse effects. We describe here a case of a patient of bipolar affective disorder, who developed pitting type of edema of both his legs and feet, while being on lithium therapy. Edema of the peripheries is a seldom reported side effect of lithium (German J Psychiatry 2008; 11: 76-78).

Keywords: Edema, lithium, bipolar, side effects.

Received: 8.1.2008
Revised version: 29.1.2008
Published: 6.6.2008

Introduction

Lithium is widely used in the management of patients with affective and other behavioral disorders (Bilanakis & Gibiriti, 2004). Lithium salts, used for the first time in 1949, had proved to be a highly effective preventive measure in bipolar illness (Pieri-Balandraud et al., 2001). In addition to its therapeutic role, it is equally important to recognize its occasional severe side effects like ataxia, tremor, muscle hyperirritability, blurring of vision, blackout spells, seizures, cranial nerve involvement, toxic confusional states, arrhythmias, cardiac collapse and dehydration. We report a patient who developed bilateral, pitting type of pedal edema associated with lithium therapy, with absolutely normal plasma lithium levels. Pedal edema is a rarely reported side effect of lithium. In fact, after widespread search of literature and of Cochrane and Pubmed databases, we came across only one article mentioning 'peripheral edema' as an uncommon side effect of lithium (Long, 2005). The case demonstrates a rare but significant side effect of lithium and emphasizes that regular clinical assessment of the patient rather than serum lithium levels or laboratory investigation reports, is more relevant.

Case Report

A 30-year-old, un-married male, a known case of bipolar affective disorder, was admitted to the psychiatry ward of Government Medical College & Hospital, Sector 32, Chandigarh, India in manic state. This was his third admission in ward in last three years.

His psychiatric illness began 8 years back with abrupt onset of a manic episode in form of elated mood, pressure of speech, flight of ideas, insomnia, hyperactivity, violence at home and grandiosity. At that time, he was admitted to another hospital, recovered and was doing well with maintenance treatment with sodium valproate (1000 mg/day) until 2004 when sodium valproate was discontinued because the patient developed signs of toxicity (sodium valproate levels = 114.75 µg/ml). He was admitted to the psychiatry ward of Government Medical College & Hospital, Sector 32, Chandigarh, India for the first time then in October, 2004. His physical examination, Complete Blood Counts, urinalysis, thyroid function tests, renal function tests, liver function tests, chest film, ECG, and EEG, all were normal. He was given olanzapine 20 mg/d, lithium carbonate 300 mg q.i.d., resulting in a serum lithium level of 1 .2 mEq/l. He improved gradually and was discharged four weeks later. Subsequently, the lithium dose was stabilized at 600 mg b.i.d.

He was again admitted in psychiatry ward in August 2005, 9 months after discharge, due to poor compliance with treatment with the resultant relapse of manic symptoms. This time, he was again stabilized on the same drugs, with a lesser dosage of lithium (900 mg/day) with serum lithium levels of 0.9 mEq/l. Patient gradually improved and dose of olanzapine was then slowly tapered off. After that, patient maintained compliance with the treatment and was regular in outdoor follow-ups till the current admission.

During this admission, all the routine hematological and radiological investigations were conducted and all were found to be normal. The dose of lithium was increased to 1200 mg/day (with serum lithium levels = 1.1 mEq/l), and olanzapine (20 mg/day) was added. The patient gradually improved, his manic symptoms disappeared over next 3 weeks and therefore, olanzapine was gradually tapered off. Meanwhile, patient developed swelling of both the feet, which was slowly increasing upwards. It was examined to be pitting type of edema. It was initially expected that with the stoppage of olanzapine, the edema would disappear, but, rather it increased. The edema was quite discomforting to the patient, who would repeatedly complain to the doctors about it. Medicine consultation was sought. On physical and neurological examination, there was no muscle weakness, rigidity, or sensory loss. Coordination was fair and the sensory examination had normal results. The patient was advised repeat Chest X-ray, Complete Blood Counts, ECG, renal & liver function tests which were all found to be normal again. The patient was prescribed 12. 5 mg/ day of hydrochlorothiazide (a thiazide diuretic), but the edema persisted and even increased in volume with patient complaining of difficulty in lifting his legs and also, pain in legs. Serum lithium levels were again assessed which were within normal range (1.1 mEq/l). There were no other early symptoms of lithium toxicity like abdominal cramps, polyuria, polydipsia, nausea, vomiting, and diarrhea.

As there was no benefit of the medical intervention and the patient's distress further increased with increasing pedal edema, it was decided to stop lithium altogether and shift the patient onto quetiapine as maintenance therapy for prophylaxis of bipolar disorder. To our surprise, within 4 days of stopping lithium, the edema disappeared completely from both his lower legs and feet. The patient was ecstatic about his recovery. Subsequently, the dosage of quetiapine was slowly built up to 1000 mg/ day and patient was discharged in normal mental state, a week later. The patient has been symptom free since then (around six months) and has been maintaining proper compliance with treatment till now.

Discussion

Lithium has a narrow therapeutic/ toxic ratio - serum lithium concentrations must be measured regularly. Mild adverse effects can occur even if serum lithium levels are 1 mmol/L. Initial post-absorptive symptoms include gastrointestinal discomfort, nausea, vertigo, muscle weakness, which frequently disappear after stabilization of therapy. More common and persistent side effects are fine hand tremors, fatigue, thirst, polyuria. Mild to moderate toxic reactions occur at lithium levels of 1.5 to 2 mmol/L; moderate to severe reactions at levels > 2 mmol/L. Progressive intoxication may be manifested by confusion, increasing disorientation, muscle twitchings, hyper-reflexia, nystagmus, seizures, diarrhea, vomiting, and eventually coma and death (Long, 2005). Thiazide diuretics, furosemide, spironolactone, methyldopa, indomethacin, phenylbutazone and piroxicam can increase lithium concentrations. Acetazolamide, sodium bicarbonate, sodium chloride, theophylline and mannitol can decrease lithium concentrations. Neurotoxicity may be increased by concomitant use of haloperidol, phenothiazines, carbamazepine or phenytoin (Jefferson & Greist, 1999).

The current available literature on lithium does not report 'edema' as an adverse effect. No case report pertaining to any type of lithium induced edema was found by us despite extensive search. In the absence of any research findings in this aspect, it would be difficult to comment on pathophysiology of lithium induced pedal edema, but, at the same time, it would be interesting to find out whether this edema involves the cardiovascular, endocrine or the renal system, the three most affected systems of the body by lithium.

The most prevalent renal effect of lithium is impairment of concentrating ability and reduced GFR and long-term lithium therapy may induce a progressive and partly irreversible defect in concentrating ability leading to potential risk for dehydration associated with lithium-induced polyuria (nephrogenic diabetes insipidus) (Gabutti et al., 1998). The conventional treatment of lithium induced nephrogenic diabetes insipidus is thiazide diuretics. The thiazide diuretics lead to natriuresis and hypokalemia which can rapidly precipitate neurotoxicity (Boton et al., 1987). In this case also, a conventional diuretic was prescribed by the medical specialist, which could have lead to a dangerous interaction with lithium, increasing its plasma levels and leading to life-threatening lithium toxicity. But, luckily, wisdom prevailed in time and nothing of this sort happened. There were no physiologic, or electrolyte abnormalities and treatment by discontinuing oral lithium was successful.

This case highlights the need for the treating doctors to be aware of exact nature and dosage of the drug, its indications, drug interactions, dietary restrictions, and the nature of adverse side-effects. It also demands paying attention towards uncommon and atypical side effects of commonly used drugs.

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The German Journal of Psychiatry · ISSN 1433-1055 · http:/www. gjpsy.uni-goettingen.de
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