Case report
Ενδιαφέρουσα περίπτωση

Glandular cystitis and lithium intoxication in a patient with bipolar disorder

B.J. Havaki-Kontaxaki,[1] P. Ferentinos,[2] D. Karaiskos,[1] D. Pappa,[1] G.N. Papadimitriou[1]

[1]1st Department of Psychiatry, University of Athens, Eginition Hospital, Athens,
[2]2nd Department of Psychiatry, University of Athens, "Attikon" General Hospital, Athens, Greece

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A 42-year-old woman, with a 12-year history of bipolar disorder was referred to our department due to tremor, sedation, dysarthria, polyuria and polydipsia. She had been on lithium monotherapy during the last 3 years. On admission, her cognitive status was intact, and neither depression nor euphoria was reported. Lithium plasma levels were 1.6 mEq/L, whereas creatinine and urea levels were 2.8 IU/L and 110 IU/L, respectively. The patient did not take other medications or misused lithium. Lithium was immediately discontinued. Ultrasound scans of the urinary tract were suggestive of bilateral hydronephrosis secondary to bladder contraction and cystoscopy-guided bladder biopsy revealed glandular cystitis a benign tumour into the bladder's wall, which impeded the bladder's contraction leading to hydronephrosis and subsequent toxic lithium plasma levels. The patient was switched to valproate and was referred for surgical excision of the lesion. One year later, she was in good physical and mental health under treatment with valproate (1000 mg/day). This is the first case report of grandular cystitis leading to lithium intoxication by impairing renal function. Acute renal failure leading to lithium intoxication would be possible. However, a thorough imaging, endoscopical and histological study revealed glandular cystitis as the cause of renal impairment. Although physicians are alert about lithium's toxicity and a monitoring of renal function is routinely prescribed, little focus has been made on the integrity of the urinary tract. We suggest that urinary tract imaging should be part of the routine work-up in patients presenting with symptoms and signs of lithium intoxication, since concomitant urinary tract lesions might occasionally be the cause of renal impairment leading to reduced lithium excretion.

Key words: Glandular cystitis, lithium, intoxication, bipolar disorder.

Introduction

Lithium has been a gold standard in the treatment of bipolar disorder and its efficacy has been documented in numerous trials.[1] However, its use is complicated by low therapeutic index. Dosing must be guided by monitoring of serum levels, so that the risk of severe toxicity is reduced. Potential causes of lithium intoxication include drug overdose, dehydration, a low-sodium diet, interactions with concomitant medications, and renal impairment. In cases of lithium intoxication, immediate discontinuation of the regimen and supporting of renal function is indicated.[2]

We present the case of a female bipolar patient who manifested lithium intoxication which was finally attributed to renal impairment caused by a benign urinary bladder lesion.

Case report

A 42-year-old woman, with a 12-year history of bipolar I disorder was referred to our Department, because she gradually manifested over a period of one week tremor, sedation, dysarthria, polyuria and polydipsia. She had been stabilized on a lithium 660 mg/day regimen during the last 3 years. Lithium plasma levels were routinely monitored and the last plasma level recorded –2 months before the admission– was 0.8 mEq/L. Five years ago, the patient was diagnosed with endometrial cancer which had been successfully treated.

On admission, she was well oriented in time, place and person, and reported no feelings of sadness or euphoria. Lithium plasma levels were found toxic (1.6 mEq/L), whereas creatinine and urea levels were 2.8 IU/L and 110 IU/L, respectively. The rest of serum chemistry assays as well as thyroid function tests were unremarkable. The patient denied taking other medications apart from lithium or ingesting higher doses of lithium. Dehydration (e.g. due to infection, excessive sweating or diarrhoea) was excluded on the basis of serum chemistry and history. Lithium was immediately discontinued. Ultrasound scans of the urinary tract were suggestive of bilateral hydronephrosis. Cystoscopy-guided bladder biopsy finally revealed glandular cystitis, a benign urinary bladder lesion.[3] The patient was switched to valproate and was referred to an urologist for specialist management. One year later, she was in good physical and mental health under treatment with valproate 1000 mg/day (plasma levels 60 μg/mL).

Discussion

The most common renal side effect induced by chronic lithium administration is a defect in urine concentrating ability; patients on long-term therapeutic doses of lithium often complain of polyuria, nocturia and thirst while about 10% may manifest nephrogenic diabetes insipidus.[4] Lithium rarely causes serious but most often reversible glomerular filtration rate reductions and renal failure due to interstitial nephritis acutely or progressively over the years, especially after episodes of lithium intoxication.[5,6] Furthermore, there are occasional reports of usually reversible, lithium-related nephrotic syndrome and incomplete distal renal tubular acidosis.[4,5] In such cases, clinicians usually discontinue lithium, support renal function and switch to another mood stabilizing agent.

Renal impairment was the most probable cause of lithium intoxication in our patient; our first thought was that acute renal failure was induced by chronic lithium treatment per se.[4,5] Our decision to request further evaluation was driven by the patient's history of endometrial cancer and the possibility of secondary metastases. A thorough imaging, endoscopical and histological study finally revealed a benign urinary bladder lesion which had led to hydronephrosis, renal impairment and subsequent toxic lithium plasma levels. Physicians are alert about lithium's toxicity and a monitoring of renal function is routinely prescribed. However, when renal impairment is the suspected cause of lithium intoxication, clinicians usually withdraw lithium while usually omitting an imaging study of the urinary tract. Little focus is made on the integrity of the urinary tract, although obstructions can also impair lithium renal excretion. Moreover, in clinical practice psychiatric patients do not undergo frequent laboratory check-ups although they often suffer from underdiagnosed somatic comorbidities.[7]

Cystitis glandularis is a metaplastic alteration of the urothelium in the urinary bladder that is thought to be induced by chronic inflammation or irritation.[3]

This is the first case report recording an association between chronic lithium administration and cystitis glandularis. This may be a chance finding, given that lithium is not generally considered to be carcinogenic in humans.[8] However, lithium has been reported to promote bladder carcinogenesis in rats.[9]

In conclusion, we suggest that when renal impairment is the suspected cause of lithium intoxication urinary tract imaging should be part of patients' workup, since concomitant urinary tract lesions might occasionally be the cause of renal impairment leading to reduced lithium excretion.

Αδενική-διάμεση κυστίτιδα και τοξίκωση από λίθιο σε ασθενή με διπολική διαταραχή

Μ.Ι. Χαβάκη-Κονταξάκη,[1] Π. Φερεντίνος,[2] Δ. Καραΐσκος,[1] Δ. Παππά,[1] Γ.Ν. Παπαδημητρίου[1]

[1]Α' Ψυχιατρική Κλινική Πανεπιστημίου Αθηνών, Αιγινήτειο Νοσοκομείο, Αθήνα
[2]Β' Ψυχιατρική Κλινική Πανεπιστημίου Αθηνών, «Αττικόν» Νοσοκομείο, Αθήνα

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Γυναίκα 42 ετών με ιστορικό διπολικής διαταραχής από 12 ετίας παραπέμφθηκε στο τμήμα μας, λόγω τρόμου, καταστολής, δυσαρθρίας, πολυουρίας και πολυδιψίας. Βρισκόταν σε μονοθεραπεία με λίθιο κατά τη διάρκεια των 3 τελευταίων ετών. Κατά την εισαγωγή της, οι γνωστικές λειτουργίες ήταν ακέραιες, ενώ δεν ήταν παρούσα σημειολογία κατάθλιψης ή ευφορίας. Τα επίπεδα λιθίου στο πλάσμα ήταν 1,6 mEq/L, και οι τιμές κρεατινίνης και ουρίας 2,8 IU/L και 110 IU/L, αντίστοιχα. Η ασθενής δεν ελάμβανε άλλα φάρμακα ούτε υψηλότερη δόση του λιθίου από τη συνταγογραφούμενη. Η χορήγηση λιθίου διακόπηκε αμέσως. Το υπερηχογράφημα του ουροποιητικού συστήματος ανέδειξε δευτεροπαθή υδρονέφρωση και η καθοδηγούμενη από κυστεοσκόπηση βιοψία της ουροδόχου κύστεως ανέδειξε αδενική-διάμεση κυστίτιδα, καλοήθη νεοπλασματική εξεργασία, στο τοίχωμα της ουροδόχου κύστεως, η οποία οδήγησε σε υδρονέφρωση και στη συνέχεια σε τοξικά επίπεδα του λιθίου στο πλάσμα. Η ασθενής ετέθη σε αγωγή με βαλπροϊκό οξύ και παραπέμφθηκε για χειρουργική εκτομή της βλάβης. Ένα χρόνο αργότερα, η ασθενής ήταν σε καλή σωματική υγεία και σταθεροποιημένη υπό θεραπεία με βαλπροϊκό (1000 mg/ημ). Πρόκειται για την πρώτη περίπτωση που περιγράφεται στη βιβλιογραφία, όπου αδενική-διάμεση κυστίτιδα οδηγεί σε τοξικά επίπεδα λιθίου και νεφρική δυσλειτουργία. Αν και η οξεία νεφρική ανεπάρκεια ως συνεπακόλουθη της δηλητηρίασης από λίθιο θα ήταν δυνατή, μια λεπτομερής απεικονιστική, ενδοσκοπική και ιστολογική μελέτη ανέδειξε ότι η αδενική-διάμεση κυστίτιδα ήταν η αιτία της νεφρικής ανεπάρκειας. Η διενέργεια συμπληρωματικού απεικονιστικού ελέγχου του ουροποιητικού συστήματος σε ασθενείς με συμπτώματα δηλητηρίασης από λίθιο συνιστάται, δεδομένου ότι βλάβες του ουροποιητικού συστήματος μπορεί περιστασιακά να οδηγήσουν σε νεφρική δυσλειτουργία και στη συνέχεια σε μειωμένη απέκκριση λιθίου.

Λέξεις ευρετηρίου: Αδενική-διάμεση κυστίτιδα, λίθιο, τοξίκωση, διπολική διαταραχή.

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Corresponding author: B.J. Havaki-Kontaxaki, Ast. Professor of Psychiatry, University of Athens, Eginition Hospital, 74 Vas. Sofias Ave., GR-115 28 Athens, Greece
Tel: (+30) 210-72 89 257, Fax: (+30) 210-72 42 020
e-mail: bikont@med.uoa.gr