

## Thyrotoxicosis followed by hypothyroidism in a patient on lithium

Nilamadhab Kar, Surabhi R. Hullumane, Carol Williams

Department of Psychiatry, Black Country Partnership NHS Foundation Trust, Wolverhampton, UK

### Abstract

While hypothyroidism is common in lithium-treated patients, thyrotoxicosis is rarely reported. We present a female patient on lithium for maintenance therapy of bipolar affective disorder, who developed thyrotoxicosis for few months which was followed by hypothyroidism which continued. There was no further thyrotoxicosis episode during a five year follow up period. While she was treated for thyroid dysfunction, lithium was continued. There was no clinical impact on the maintenance of the bipolar affective disorder during the follow up period; she was maintained well in the community.

### Introduction

Thyroid abnormalities have been frequently reported to be associated with treatment with lithium. Hypothyroidism and subclinical hypothyroidism with/without concomitant goiter are commonly observed among patients on lithium therapy, although the frequencies vary widely from 0-52% amongst studies.<sup>1,3</sup> However, lithium induced thyrotoxicosis is very infrequent.<sup>1,3,4</sup> It has been reported that lithium-associated thyrotoxicosis occurred with an incidence rate of approximately 2-7 cases per 1000 person-years, which is higher than the reported incidence rates of thyrotoxicosis (0.8-1.2 cases per 1000 person-years) in the general population.<sup>5</sup> In a retrospective study among 209 patients with affective disorders on long term lithium therapy, post-treatment thyrotoxicosis was noted among 2 patients (1 male and 1 female).<sup>6</sup> In a cross-sectional study, 1.8% of men and 3.9% of women on lithium therapy developed thyrotoxicosis which had an incidence rates of 2.7 and 6.4 per 1000 survivor years respectively.<sup>3</sup> In a prospective study only 1 among 33 women developed hyperthyroidism over the 146 person-years of follow up;<sup>3</sup> while in another report only 1 case of hyperthyroidism among 150 patients on

long-term lithium therapy was observed during a 15-year follow up equivalent to 976 patient-years.<sup>7</sup> These observations suggest that lithium induced hyperthyroidism is extremely rare.

We report here a patient who presented with an episode of thyrotoxicosis followed by prolonged hypothyroidism while on lithium therapy. The nature of the presentation and the follow up information on the maintenance treatment are discussed.

### Case Report

A 61-year-old female patient was suffering bipolar affective disorder for 23 years and was maintained on lithium along with various psychotropic medications over the years. In the past she had comorbid diagnoses of alcohol dependence syndrome, obsessive compulsive disorder, benzodiazepine (temazepam) and nicotine dependence. She also experienced paranoid symptoms secondary to alcohol dependence. She was successfully treated for these conditions. There was history of self-harm attempts by overdose of prescribed medications a few times.

She developed thyrotoxicosis after being on lithium for around 18 years. There was no history of thyroid abnormality in the past and she was maintaining euthyroid state during the course of lithium therapy until she developed thyrotoxicosis. She was compliant to lithium. During thyrotoxicosis, she had many instances of confusion suggestive of delirium.

She was admitted to medicine ward and commenced on carbimazole. Gradually the thyrotoxicosis symptoms became stable. The free T4 levels remained high for about three months at 57, 72, 40 pmol/L (normal range: 12.0-22.0 pmol/L); and the TSH values were 0.01 mU/L (normal range: 0.27-4.20 mU/L). Lithium was continued during the thyrotoxicosis phase. Close monitoring of thyroid status was maintained. After around 5 months of treatment for thyrotoxicosis, the thyroid-stimulating hormone (TSH) level increased beyond the normal range. Consequent to that, the dose of carbimazole was decreased. However TSH level remained high and it was considered that she had developed acquired hypothyroidism possibly due to carbimazole and lithium. Thyroxine was started. The TSH remained high (up to 9.5 mU/L) for around 7 months before becoming normal; although there were a few fluctuations.

The lithium level was within therapeutic range at the onset of thyrotoxicosis. The lithium levels of the patient had fluctuated and she had one recording of lithium level higher than 1.2 mmol/L around 5 months before the onset of thyrotoxicosis; and a few similar recordings around one year following the thyrotoxicosis

Correspondence: Nilamadhab Kar, Black Country Partnership NHS Foundation Trust, Steps to Health, Showell Circus, Low Hill, Wolverhampton, WV10 9TH, United Kingdom.  
Tel.: +44.1902.443.3663 - Fax: +44.1902.444.514.  
E-mail: kar.nilamadhab@yahoo.com

Key words: lithium, thyrotoxicosis, hypothyroidism, bipolar disorder, maintenance.

Acknowledgements: authors wish to thank Quality of Life Research and Development Foundation for the support.

Contributions: NK conceived the idea, followed up, did literature review, wrote the article; SRH helped in data collection, literature review, and wrote the article; CW helped in data collection, management and followed up. All authors read and approved the paper.

Received for publication: 31 March 2014.

Revision received: 11 May 2014.

Accepted for publication: 20 May 2014.

This work is licensed under a Creative Commons Attribution NonCommercial 3.0 License (CC BY-NC 3.0).

©Copyright N. Kar et al., 2014  
Licensee PAGEPress, Italy  
Mental Illness 2014; 6:5415  
doi:10.4081/mi.2014.5415

episode. These were dealt by reducing the lithium dose and repeating the tests. TSH and lithium levels remained within usual range during the follow-up period over 5 years after the described phase of thyroid dysfunction. Besides lithium, she also had olanzapine as another psychotropic medication which was continued during thyrotoxicosis and at follow up. There were no specific episodes of bipolar affective disorder during or following the active phase of thyroid abnormality. Mood symptoms remained under control without any exacerbations. There were occasional obsessive doubts and anxiety symptoms. Her psychiatric treatment continued as usual; and she did not require any additional psychiatric input like crisis intervention, support from home treatment team or admission.

Gradually the thyroid abnormality was contained. The thyroid function tests became normal. During a five year follow up period, she did not have any further episode of thyrotoxicosis. Her thyroid function tests remained mostly within normal range with an occasional brief phase of dysregulation, needing adjustment in thyroxine dose.

## Discussion

The thyroid abnormality in this patient occurred after 18 years of being on lithium at an age of 56. Thyroid abnormality associated with lithium has been reported to be more common in women and increased with age,<sup>3</sup> which fits in to the description of the case described here. It may be highlighted that lithium could be continued while the thyroid dysfunction was treated. Considering the mood symptoms she maintained well in community. In this case the thyrotoxicosis was short lasting; which was followed by a prolonged hypothyroidism. Opposite presentation *i.e.* thyrotoxicosis following hypothyroidism has also been reported in a lithium-treated patient.<sup>8</sup>

The relationship of lithium and hyperthyroidism which occurs rarely seems not to be casual, since hyperthyroidism in these patients occurs three times that of the normal population.<sup>9</sup> There is clearly an increased risk of thyrotoxicosis associated with long-term lithium therapy. Various reasons have been considered for this association *e.g.* diffuse toxic goiter, multinodular toxic goiter,<sup>9</sup> silent/painless thyroiditis have been reported in these subjects.<sup>5,9-11</sup> Autoimmune mechanisms for the thyrotoxicosis have also been suggested.<sup>12,13</sup> The toxic and immunomodulatory roles of lithium and perhaps genetic and dietary factors too have been implicated.<sup>13</sup> According to these reports, it appears that lithium associated thyrotoxicosis is a heterogeneous condition with different kinds of underlying thyroid pathologies and the mechanisms remain uncertain.<sup>10,14</sup>

The initial thyrotoxicosis in this case for few months could possibly due to thyroiditis; while the later acquired hypothyroidism could be due to either carbimazole or lithium, or both. Transient thyrotoxicosis has been reported in lithium-treated patients. It has been postulated that lithium might directly damage thyroid follicular cells and that subsequent release of thyroglobulin into the circulation might be a cause of transient thyrotoxicosis.<sup>15</sup> There is a report where thyroiditis improved after withdrawal of lithium, which is consistent with the theory of lithium's direct toxic effect on thyrocytes.<sup>16</sup> As the patient was euthyroid before the onset of thyrotoxicosis

and was compliant to lithium when the thyrotoxicosis symptoms appeared, probability of latent hyperthyroid was unlikely.

There are reports of unmasking of latent hyperthyroidism when lithium is being completely or partially discontinued.<sup>10,17,18</sup> As lithium suppresses thyroid function, so the early stages of thyrotoxicosis may be clinically undetectable. The symptoms and signs of thyrotoxicosis may be confused with the side effects of lithium and if lithium is withdrawn severe rebound thyrotoxicity may occur.<sup>4</sup>

## Conclusions

In conclusion, the findings suggest that although rare, thyrotoxicosis appears to be associated with long-term lithium therapy and reemphasize periodic clinical evaluation for thyroid dysfunction and thyroid function tests in lithium-treated patients, irrespective of the record of euthyroid state while on lithium. In the presented case, lithium remained effective in its maintenance role for bipolar affective disorder, following the onset of thyroid dysfunction, its course and treatment. There appears no need to discontinue lithium in the presence of thyroid abnormality in well maintained bipolar patients, especially if the thyroid abnormality is controlled.

## References

1. Kibirige D, Luzinda K, Ssekitoleko R. Spectrum of lithium induced thyroid abnormalities: a current perspective. *Thyroid Res* 2013;6:3.
2. Bocchetta A, Bernardi F, Pedditzi M, et al. Thyroid abnormalities during lithium treatment. *Acta Psychiatr Scand* 1991;83:193-8.
3. Kirov G, Tredget J, John R, et al. A cross-sectional and a prospective study of thyroid disorders in lithium-treated patients. *J Affect Disord* 2005;87:313-7.
4. Rosser R. Thyrotoxicosis and lithium. *Br J Psychiatry J Ment Sci* 1976;128:61-6.
5. Miller KK, Daniels GH. Association between lithium use and thyrotoxicosis caused by silent thyroiditis. *Clin Endocrinol (Oxf)* 2001;55:501-8.
6. Kirov G. Thyroid disorders in lithium-treated patients. *J Affect Disord* 1998;50:33-40.
7. Bocchetta A, Cocco F, Velluzzi F, et al. Fifteen-year follow-up of thyroid function in lithium patients. *J Endocrinol Invest* 2007;30:363-6.
8. McDermott MT, Burman KD, Hofeldt FD, Kidd GS. Lithium-associated thyrotoxicosis. *Am J Med* 1986;80:1245-8.
9. Scanelli G. Lithium thyrotoxicosis. Report of a case and review of the literature. *Recent Prog Med* 2002;93:100-3.
10. Dang AH, Hershman JM. Lithium-associated thyroiditis. *Endocr Pract Off J Am Coll Endocrinol Am Assoc Clin Endocrinol* 2002;8:232-6.
11. Pallisgaard G, Frederiksen K. Thyrotoxicosis in a patient treated with lithium carbonate for mental disease. *Acta Med Scand* 1978;204:141-3.
12. Becerra-Fernández A. Autoimmune thyrotoxicosis during lithium therapy in a patient with manic-depressive illness. *Am J Med* 1995;99:575.
13. Chow CC, Lee S, Shek CC, et al. Lithium-associated transient thyrotoxicosis in 4 Chinese women with autoimmune thyroiditis. *Aust N Z J Psychiatry* 1993;27:246-53.
14. Barclay ML, Brownlie BE, Turner JG, Wells JE. Lithium associated thyrotoxicosis: a report of 14 cases, with statistical analysis of incidence. *Clin Endocrinol (Oxf)* 1994;40:759-64.
15. Mizukami Y, Michigishi T, Nonomura A, et al. Histological features of the thyroid gland in a patient with lithium induced thyrotoxicosis. *J Clin Pathol* 1995;48:582-4.
16. Bernstein J, Friedman RA. Lithium-associated hyperthyroidism treated with lithium withdrawal: a case report. *Am J Psychiatry* 2011;168:438-9.
17. Carmaciu CD, Anderson CS, Lawton CA. Thyrotoxicosis after complete or partial lithium withdrawal in two patients with bipolar affective disorder. *Bipolar Disord* 2003;5:381-4.
18. Thompson CJ, Baylis PH. Asymptomatic Graves' disease during lithium therapy. *Postgrad Med J* 1986;62:295-6.