Case Report

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High-dose levothyroxine for the management of bipolar affective disorder: two case reports

Andy Zamar, Gurvinder Warrya and Christos Kouimtsidis
The London Psychiatry Centre, London W1G 7HG, UK
Corresponding author: Christos Kouimtsidis. Email: drckouimtsidis@hotmail.com

Lesson

In this article, we report two cases from our centre: case A has the longest recovery period and case B is one of the most complex from a diagnostic and management perspective, highlighting how treatment resistance can be overcome depending on patient response and needs.

Keywords

clinical, mood disorders (including depression), psychiatry

Case A

This is a 57-year-old female patient with current diagnosis of severe bipolar affective disorder (unspecified). She was referred in 2008, with the diagnosis of recurrent depressive disorder and a two-month history of two episodes of hypo-mania and five episodes of depression following an admission to hospital due to suicidal ideation. She was on lithium carbonate 1000 mg daily. An electrocardiogram at screening showed first degree AV block and normal QTc.

The patient had experienced multiple episodes of depression alternating with hypo-manic episodes over several years. She has been suicidal on several occasions. She had deteriorated when treated with antidepressants only, marginally improved with courses of electroconvulsive therapy, could not tolerate olanzapine, quetiapine or lamotrigine.

She was prescribed levothyroxine 200 µg/day in addition to lithium carbonate. Within the first month, patient and family reported improved stability of mood. The dose of levothyroxine was increased to 250 µg/day. Following stability for two months, lithium carbonate was gradually reduced and discontinued at month 4. Thyroid function remained abnormal (free T4 was 49.1), with no clinical symptoms of hyperthyroidism other than a mild tremor. Regular reviews by Cardiologist and Endocrinologist with bone densitometry scans were performed. Over the past seven years the patient remains on levothyroxine 250 µg daily and she has not reported any mood instability.

Case B

This is a 23-year-old male patient with 13-year history of increased anxiety, depressive symptoms alternating with periods of flight of ideas, pressured speech, agitation, loss of sleep and total breakdown in social functioning. Previous diagnoses in childhood included depression, Attention Deficit and Hyperactivity Disorder and Asperger's syndrome. A variety of antidepressants and stimulant medication tried with little effect. The diagnosis of bipolar affective disorder was considered at the age of 18. Risperidone, quetiapine alongside sodium valproate were used for short periods and were discontinued on several occasions due to side effects. Family therapy and cognitive behavioural therapy were tried. There was strong family history (mother's side) of bipolar affective disorder.

At the centre, a diagnosis of rapid cycling mood disorder was made. Over the following 12 months, Attention Deficit and Hyperactivity Disorder and antidepressant medication were gradually discontinued and quetiapine XL with sodium valproate (maximum dose of 2000 mg) started with improvement in mood symptoms, reduction in agitation but on-going sedation. Thyroid screening revealed hypothyroidism and sodium valproate levels exceeding normal limits. Sodium valproate dose was reduced to 1500 mg and levothyroxine 100 µg started. Low dose external Trigeminal Nerve Stimulation was started for one week only with increased agitation. Ziprasidone could not be tolerated. Electroconvulsive therapy for eight sessions was used with no effect. Mood fluctuations and agitation have continued.

At month 12, sodium valproate was changed to Epilim maximum dose, levothyroxine dose increased to 300 µg/day and repetitive Transcranial Magnetic Stimulation was started for six weeks. At month 14, levothyroxine was increased to 400 µg. Mood was reported low with anxiety and agitation but reduced fluctuations. Addition of benzodiazepines and/or antipsychotics were not effective; therefore, all

medications but levothyroxine 400 µg were stopped. Regular reviews by Cardiologist and an Endocrinologist with bone densitometry scans were performed. No clinical signs of hyperthyroidism were reported or observed and bone densitometry was normal. Mood became stable and 'best ever' for months 17–20.

Due to re-emergence of anxiety and low mood, repetitive Transcranial Magnetic Stimulation was re-started with levothyroxine 400 µg, with mixed results. During months 21 and 22, levothyroxine was increased to 500 µg and at month 24 to 600 µg. Twelve months since initiation of levothyroxine, mood became stable and continues to be for the past 18 months. Mood is reported as 'far better than ever before'. The patient has recently completed his university degree (1st Class), he is in a relationship, lives independently and travels alone. He also is a regular gym user with a substantial muscle bulk and fitness now. Prior to this, he was mostly bed bound, isolated and living with his parents in need of constant reassurance on many issues. In addition to levothyroxine, maintenance treatment includes repetitive Transcranial Magnetic Stimulation and external Trigeminal Nerve Stimulation once monthly.

Discussion

An extensive literature links mood disorders to disturbances of the hypothalamic–pituitary–thyroid axis. Supra-physiological doses of T4 have been less extensively studied and used compared to physiological doses of T3 in patients with mood disorders.[1,2] Small open studies suggest that supra-physiological doses of T4 (up to 500 µg/day) may offer benefit in the treatment of acute bipolar depression,[3] in rapid cycling bipolar disorder[4] and treatment resistant bipolar affective disorder.[5] This paper discusses the management of two patients: case A supports the role of high-dose levothyroxine into the management of rapid cycling bipolar affective disorder[4] and case B into the treatment resistant bipolar affective disorder.[5]

The observations reported in this paper are based on two cases only, and therefore, could not be generalised to other cases. Case reports though can inform clinical practice and provide guidance until randomised control trials provide the relevant evidence.

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