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Case Report 1

A 23-year-old woman with a family history of rapid cycling bipolar disorder presented with fatigue, over-eating, over-sleeping, low mood & passive suicidal ideation, alternating with mixed affective episodes, namely, depression with flight of ideas complicated by agitation, irritability and anger.

She also exhibited phases of hypomania (increased energy associated with marked feelings of well-being and happiness).

She was taking high dose Citalopram which is contraindicated. Beck Depression Inventory Score was 38 in keeping with severe depression, Beck anxiety inventory 20 and HCL-32 questionnaire was 29 in keeping with an 80% probability of bipolar depression.

A diagnosis of rapid cycling bipolar disorder (RCBPD) was made.

Comprehensive blood tests excluded an organic cause. She started taking Levothyroxine 50mcg od and increased gradually to supraphysiological doses. Quetiapine, at a licensed dose, was prescribed but discontinued because of weight gain. rTMS was commenced, and she reported significant improvements in her mood but remained symptomatic.

One month later, she had racing thoughts and increased energy levels. The dose of Levothyroxine increased to 400mcg once daily.

Two months later she was in remission and reported feeling the best in a long time. HDL was increased to 500mcg o.d. for minor residual depressive symptoms. She remains in remission over a year later on HDL including maintenance rTMS with no side effects.

Taking Levothyroxine 500mcg o.d., ECG: sinus rhythm, normal QTc. She was clinically euthyroid. Blood tests: TSH < 0.01miu/L (0.27 – 4.2), fT4 37.1pmol/L (12 – 22), fT3 8.4pmol/L (3.1 – 6.8). Reverse T3: 30ng/dL (10 – 24). Genetic analysis: wild type DIO1, heterozygote polymorphism of DIO2 gene (rs225014; T92A).

Discussion

We describe 2 cases of patients with RCBPD, resistant to standard treatments who achieved remission of disease using high dose levothyroxine with rTMS.

There is an association between BPD and dysfunction of the thyroid (HPT) axis.

Thyroid disease is more likely to be present in more resistant and rapid cycling forms of BPD. Contentiously, frank disturbances in the HPT axis are unusual in rapid cycling bipolar disorder. Instead a “latent hypofunction of the thyroid axis” has been suggested as a possible mechanism for the response to high dose Levothyroxine.

Studies have shown that high dose Levothyroxine helped achieve remission in rapid cycling bipolar disorder and was safe with no features of thyrotoxicosis.

Genetic studies have shown that polymorphism of the deiodinase, iodothyronine, type II (DIO2) gene (rs225014; T92A) is associated with depression and the heterozygote polymorphism has been associated with a 1.6-fold increased risk of bipolar disorder. Both our patients had a heterozygote polymorphism of the DIO2 gene and interestingly, an elevated fT4:fT3 ratio.

Case Report 2

A 53-year-old woman presented with a mixed affective state characterised by profound depression and flight of ideas such as relentless racing thoughts, agitation, distress, hopelessness and intense suicidal thoughts.

She was diagnosed with ADHD and bipolar disorder with the latter being poorly treated. Her mood deteriorated substantially following a trip to Australia.

Quetiapine was started, and the dose escalated to 700mg daily which partially helped her mood. Levothyroxine 50mcg once daily was commenced and the dose slowly escalated to 400mcg once daily and her mood stabilised.

ECG showed sinus rhythm, rate 63bpm.

She unfortunately suffered a relapse a few months later taking these 2 medications and so rTMS was commenced.

HDL was eventually increased 750mcg once daily. This, together with rTMS achieved remission, with no side effects.

She has been in complete remission with HDL 750mcgs OD, Quetiapine 700 mgs OD and maintenance rTMS for over a year. She reported no side effects and no symptoms of thyrotoxicosis.

On examination, pulse was 85bpm and regular, weight 71kg (no unintentional weight loss). She is clinically euthyroid.

TSH is suppressed, fT4 77.3pmol/L (12 – 22), fT3 11.7pmol/L (3.1 – 6.8) and reverse T3 elevated: 79ng/dl (10 – 24). Pre-Levo-thyroxine thyroid function was normal: TSH 2.20miu/L (0.27 – 4.2), fT4 12.3pmol/L and fT3 3.6pmol/L (same reference ranges for fT4 and fT3). She had a heterozygote polymorphism of both the DIO2 (rs225014; T92A) and DIO1 gene (rs2235544; 34C>A).

Conclusion

- Rapid cycling bipolar disorder and mixed state affective states are dangerous conditions with high mortality and morbidity rates.
- Standard treatments are often ineffective.
- Data highlights an association between polymorphisms of the DIO2 gene and bipolar disorder and previous studies have highlighted the safety and effectiveness of HDL in achieving remission.
- We speculate that BPD is a form of cerebral hypothyroidism and that HDL helps to overcome the deficit while robust inactivating deiodinases in the periphery protect from systemic thyrotoxicosis.
- This is evidenced by findings of normal clinical examination and elevated rT3.
- rTMS exercises its well established neuroplastic effect, helping to achieve and maintain remission as an adjunct to HDL.

References

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* Declaration of interest: The London Psychiatry Centre has filed a patent application for the above protocol.