A CASE REPORT OF RAPID CYCLING BIPOLAR DISORDER AND MULTIPLE SCLEROSIS

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Background

Multiple sclerosis (MS) is a common, chronic and often disabling central nervous system (CNS) disorder which has been associated with higher prevalence of psychiatric symptoms and disorders. The incidence of bipolar disorder can be as high as 13% in MS patients compared with 1–6% in the general population and often presents later in the course of the illness.[1] Rapid cycling affects 13-30% of bipolar patients and can be associated with greater illness burden and treatment resistance.[2] Also, major depression is common with MS, with lifetime prevalence as high as 50%.[3] The co-morbidity of the two disorders can be challenging to identify and tricky to manage. This is a case report of a 68 years old female who presented to our service with the coexistent conditions.

Case presentation

Objective:
This case report aims to improve the knowledge of Rapid Cycling Bipolar Disorder (RCB) management particularly in a patient with demyelinating disorder such as MS. Stabilizing mood in a patient with MS can be challenging requiring successive medication trials. It also explores the current recommended guidelines for managing RCB disorder.

Methods:
This is a retrospective case report of a patient who attends the Psychiatry of Later Life service. The information was obtained through several clinical interviews with the individual. Written consent was obtained from the patient for this case report.

Case presentation:
68-year-old, married woman, with a history (hx) of unspecified mood disorder, an organic mixed affective disorder and MS. She was voluntarily admitted for the treatment of a depressive episode. Notably, a rapid cycling pattern was described during previous admissions (2 manic and 2 depressive episodes in the year of admission). She reported feeling low mood mood for 7-8 weeks and complained of associated somatic symptoms and poor concentration for 3 weeks. No psychotic features or suicidal ideation were elicited. Patient was compliant with her medications.

Collateral History:
Husband reported the last period of elevated mood was around 2 months ago, possibly triggered by stressful family circumstances.

Psychiatric History:
Diagnosed as Unspecified mood [affective] disorder and organic mixed affective disorder. She had three psychiatric admissions between 2009-2010.

Family History:
No family history of mental illness.

Medical History:
She was diagnosed with MS in 2010 and later developed Lithium toxicity in 2018. She also has a history of degenerating fibroadenoma and hysterectomy, bladder carcinoma (under surveillance), thyroid nodule (incidental finding in 2018), CKD and recurrent cystitis with suprapubic catheter in-situ. She also has had recurrent falls and requires a walking aid.

Social History:
No history of substance misuse was identified. She worked as a canteen manager and retired in 2001. She lives with her husband who is very supportive and attends the local day centre once a week. She also has 3 hours of home help daily.

Timeline

2008
GP started **Escitalopram** due to depressive symptoms, was switched in 3 months to **Sertraline** which was adjusted due to cyclical mood changes.

2009
Sertraline was switched in 2009 to **Venlafaxine** and **Aripiprazole** under the supervision of Psychiatry services. Later in the year she was switched from **Aripiprazole** to **Lamotrigine** due to the ongoing mood fluctuation, and **Olanzapine** was added, which was stopped subsequently as it was not tolerated with the heightened falls risk. She had 1 admission in SJOGH, and was discharged on **Venlafaxine** and **Lamotrigine.**

2010
Two admissions to SJOGH. She was maintained on **Venlafaxine** and **Lamotrigine** in the 2nd admission. In her 3rd admission MRI scan was organized, which showed changes consistent with demyelination and she was linked in with Neurology and a subsequent diagnosis of Multiple Sclerosis was made. Both the psychotropic medications were discontinued gradually.

2011
Ongoing follow up with local psychiatry services, maintained on **Quetiapine** and **Venlafaxine** with limited efficacy.

2012
Epilim Chrono was added and dose was optimized during this year

2016
Lithium was started around this year, and titrated up to 800 mg nocte. Despite this her mood continued to fluctuate.

2017
A trial of **Escitalopram** to manage the depressive features was discontinued due to limited efficacy.

2018
Lithium toxicity (Level 1.31) admitted to regional hospital and Lithium discontinued. Epilim Chrono was charted as the main mood stabilizer. Citalopram was also introduced and was later changed to Mirtazapine. She continued to present with rapid cycling pattern.

Investigations

Physical Exam:
Physical Examination revealed nil of note except for decreased power in upper limbs (4/5) and lower limbs (4/5) and ataxia.

Neuroimaging & EEG:
Previous MRI brain showed bi-hemispheric, periventricular, lesions suggestive of demyelination plaques, slight involvement of the right cerebellar peduncle. DAT Scan did not pick up any abnormalities. Previous EEGs showed intermittent dysfunction affecting the left temporal region. No epileptiform discharges were noted.

Lab results:
Abnormal lab results included Valproic acid level of 21.7mg/L (Therapeutic Range 50 - 100 mg/L), Creatinine was 114 umol/L (44-80) and Urea was 11.2 (2.7 – 8.0). FBC, LFTs, TFTs, B12, and Folate levels showed no clinical concerns.

Cognitive Testing

She scored 76/100 on the Addenbrookes Cognitive Examination III (ACE) conducted during most recent admission. Our Occupational Therapist completed an Assessment of Motor and Process Skills (AMPS) assessment in which she presented with motor deficits arising from her MS which appeared to impact upon her activities of daily living, and a referral to Primary Care OT was completed.

Inpatient Treatment

During the most recent admission Sodium Valproate (Epilim Chrono) was increased to 200 mg mane and 400 mg nocte, and Quetiapine XL was increased to 150 mg nocte after a week. However, while on this combination regime she continued to present with hypomanic features. Therefore, Mirtazapine was decreased to 15 mg nocte. Sodium Valproate nocte dose was increased to 600 mg and dose of Quetiapine XR was increased to 250 mg nocte. The above changes assisted in reducing the frequency and severity of her mood changes and gradually she achieved remission and was discharged subsequently.

Her medications on discharge included: Quetiapine XR 250 mg nocte, Mirtazapine 15 mg nocte, Sodium Valproate 200 mg mane and 600 mg nocte. She was followed up in the community following discharge during which time she was noted to maintain remission. She continues to link in with the Neurology services and the local Day Hospital.

RCB Management

Step	Suggested treatment
1	**Withdraw antidepressants** in all patients[12–17] (some controversial evidence supports continuation of SSRIs[18,19])
2	**Evaluate possible precipitants** (e.g. alcohol, thyroid dysfunction, external stressors)[2]
3	**Optimise mood stabiliser treatment**[20–23] (using plasma levels), and **Consider combining mood stabilisers**, e.g. lithium + valproate; lithium + lamotrigine, or go to Step 4
4	**Consider other (usually adjunct) treatment options**: (alphabetical order; preferred treatment options in bold) **Aripiprazole**[24,25] (15–30 mg/day); Clozapine[26] (usual doses); Lamotrigine[27–29] (up to 225 mg/day); Levetiracetam[30] (up to 2000 mg/day); Nimodipine[31,32] (180 mg/day); **Olanzapine**[20] (usual doses); **Quetiapine**[33–36] (300–600 mg/day); Risperidone[37–39] (up to 6 mg/day); Thyroxine[40,41] (150–400 µg/day); Topiramate[42] (up to 300 mg/day)

Choice of drug is determined by patient factors – there are few comparative efficacy data to guide choice at the time of writing. **Quetiapine** probably has best supporting data[33–35] but there is no evidence of superiority over aripiprazole or olanzapine. Supporting data for levetiracetam, nimodipine, thyroxine and topiramate are rather limited.
SSRI, selective serotonin reuptake inhibitor.

Table modified from Maudsley Guidelines (13th Edition May 2018)

Discussion

The mental health of the patient stabilised over the admission despite the challenges resulting from the rapid cycling nature of her illness and the limited therapeutic options; particularly in view of past lithium toxicity and predisposition to recurrent urinary tract infections.

Neurology opinion recommended following guidelines on RCB management independently as it was felt that her MS was stable from a neurological standpoint and didn't warrant Immunomodulative therapy. Nor was there a suggestion of long-term steroid use as indicated by the demyelination load observed from repeated neuroimaging.

However due to risk of precipitating further mood disturbance, any medication changes must be carefully considered for its potential adverse effects on the mood, particularly steroid therapy. Also, it should be noted that the patient sustained transient cognitive deficits from Lithium toxicity which resolved with withdrawal of Lithium and treatment of co-morbid infection. This may reflect the low threshold of MS patients for developing such events.

References

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