

A CASE STUDY OF ULTRA RAPID CYCLING BIPOLAR DISORDER

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INTRODUCTION

Bipolar disorder (BD) has a multifactorial aetiology and has a prevalence rate of 15-20 percent in first-degree relatives of patients with BD indicating a genetic link. Twin studies have led to a concordance rate in monozygotic twins of 79 percent and in dizygotic twins of 19 percent. DNA markers have been identified through linkage studies and have been replicated in more than one study, particularly on chromosomes 18 and 22 (Badner & Gershon 2002). BD has a heritability of 60-80% (Johansson et al. 2019), but its aetiology is highly polygenic (Craddock et al. 2013, Haggarty et al. 2020). The gene Ankyrin-3 (ANK3) has been consistently associated with BD in several genome-wide association studies (Holmgren et al.2022). An autoimmune aetiology of BD has been popularized by Immunopsychiatrists (Berk et al. 2021, Khandaker et al. 2021, Teixeira et al. 2019, Pandarakalam 2022). The coexistence of BD with OCD is less talked about in the academic circles. Autoimmune aetiology of OCD is also gaining acceptance and needs further research (Pérez-Vigil 2016, Pearlman 2014, Hoekstra & Minderaa 2005, Mataix et al.2018). Weakening of OCD as a heralding symptom of the onset of hypomanic episode has been reported and such an observation warrants further substantiation. The case presented in this paper is illustrative of all these features.

More than four episodes per year are considered as rapid cycling cases of bipolar disorder. Cases with far frequent episodes are designated as ultra-rapid cycling and instances where mood swings occur within 24-hour period is recognized as ultra-ultra-rapid cycling or ultradian rapid cycling. Rapid cycling BD is reported to be much commoner among female patients whose illness started at an earlier age (Tavormina 2014). While some authors argue it as a distinct subtype of BD, a few still argue that it is a transient complication of the long-term course of BD (Montgomery et al. 2000). The constructs of ultra-rapid and ultradian rapid cycling have not been accurately corroborated. DSM-5 makes no reference to ultra-rapid or ultradian cycling. Rapid cycling is the only such term that

appears in the DSM, but sometimes the terms ultrarapid and ultra-ultra-rapid (ultradian) cycling are used to illustrate more frequent mood episodes.

CASE REPORT

Patient Annamma (not her real name) disclosed to her mother that she intended to kill herself. Annamma stated that there were signs telling her to join her father (deceased by suicide). He was 34 when he killed himself. She was turning 34 years old four days prior to admission. When he committed suicide, she saw a bright light when researching the Bible's view on suicide. She felt that this was a sign stating that suicide was a good thing for her. Her mood changed rapidly, and she began cleaning, wanting to bake cake after cake, and wanted to put music on and dance during the assessment. She was highly agitated and was restless. She appeared incongruent, with ideas of importance. She stated that she was excited about killing herself and she felt it was an adventure.

Annamma reported that she had developed mental health problems at the age of 17 to 18 years. She was initially treated with Sertraline by her general practitioner. When she was very depressed, she took an overdose of Sertraline, and she became extremely high. She began to put herself in risky situations. She thought she was famous and began to accumulate a lot of debts. She had repeated hospital admissions due to violent mood swings. She came to have a diagnosis of rapid cycling bipolar disorder and had a pattern of progressive deterioration. All her routine clinical investigations were within normal range. The MRI scan of the brain done during her previous hospital admission was unremarkable.

Violent Mood Swings

When Annamma was acutely unwell, her moods used to swing between elation to depression within 24 hours. For example, she had frequent short lived periods

of hypomanic episodes when she insisted that she was going to Thailand in the morning, but only to feel down in the dumps towards the end of the day characterised by psychomotor retardation and social isolation. There was distinct shift of mood and activity within a period of 24-48hrs. Multiple mood episodes of opposite polarity continued to occur during the early part of her hospital stay until an effective therapeutic regime was identified. The elated mood was always accompanied by grandiose thoughts that she could fly and on several occasions, she has experimented with the thought by trying to jump off from the fence or tables.

Obsessive Compulsive Disorder

As understood, obsessive compulsive disorder (OCD) may manifest with varying symptoms in different sufferers. In general, OCD causes a particular pattern of thoughts and behaviours. Annamma has her own specific OCD symptoms; she has a particular routine, structure, and organisation of her everyday activities. Annamma finds her OCD routine tiring and prefers to use electric ovens instead of gas because of her OCD. While dressing, she has to look at the mirror at a set number of times. She remembers having OCD traits right from childhood. For example, after a bath, she could not touch the ground or any objects. Her room was filled with unused objects and she was reluctant to throw them away resulting in the accumulation of unmanageable clutter.

The obsession caused a feeling of intense anxiety and distress in Annamma. Consequently, she was given to repetitive behaviours and mental acts. The compulsive behaviour appeared to temporarily relieve the anxiety, only to return with renewed force causing the cycle to commence again. Most patients with OCD experience both obsessive thoughts and compulsions, but one may be less obvious than the other and in the case of the patient in question, her obsessions dominate over the compulsions.

The comorbidity of OCD and BD is increasingly recognized in recent times. They share common symptoms but there are also symptoms differentiating the two conditions. Annamma stated with more insight that she is experiencing *Deja vu* feelings prior to the onset of high periods. She also claimed weakening of OCD symptom which heralds her hypomanic periods. Such an observation has been recently confirmed in clinical practice. Annamma described short lived elated periods as mini-high periods. She admitted that she gets such microscopic hypomania and depression frequently and that carries high morbidity

Risk Factors and Behaviours

During one of the high periods, Annamma stated that she could see her father behind the ceiling light, and she actually climbed a table and tried to open the light box to touch her father. She sometimes crawls on the floor like a cat and can be sexually disinhibited. When acutely unwell, she was heard to shout her slogan, "Death is an adventure". Annamma presented risky behaviours when she is feeling elated in mood. She has gone into details of how she would do this. She has sometimes become fixated with a plan to end her life and related this to previous bible-reading and having received signs. She can often overspend on unnecessary items, often relating to fixed beliefs around a specific topic. More recently when this patient had a manic episode, she reported that she could jump in front of a car because she had superpowers.

Annamma has reported that she will always harm herself as she would not harm anyone else. On several occasions, she has expressed her thoughts that she intends to end her life and, in the past, she had gone into detail of how she would do this. She has distinct warning signs of her elated and depressive periods.

Treatments

Eventually, Annamma became settled in the hospital with short periods of elation and short periods of depression. On a few occasions, she said that she could fly, and she is indestructible. Annamma responded to Haloperidol P.R.N, Semi-sodium valproate 1500mg in divided doses and lamotrigine 300mg were added. She was also given amisulpiride 300mg twice daily. Olanzapine had to be stopped because of metabolic syndrome and dyskinesic movements of lips. Quetiapine caused deglutition problems, she is allergic to risperidone, Haloperidol caused severe EPS, lithium caused embarrassing tremor which continued to persist even after stopping it. Lithium had to be replaced with Depakote.

During elated periods, she is at high risk of accidents. Annamma is highly embarrassed about the high periods. She once expressed her helplessness, "I can hide my depression, but I cannot hide my high periods and the indignity that goes with it." After trials with different mood stabilisers and psychotropics, Annamma responded favourably to the following combination of medications: Atypical antipsychotic namely amisulpiride 300mg b.d, Lamotrigine 100mg mane and 200mg nocte and Semi-sodium valproate 500mg mane and 1000mg nocte. Psychological therapies were introduced when her moods became stable with drug therapies. Cognitive behavioural therapy had beneficial effect and Annamma became more insightful about the

psychodynamics of her hypomania and depression. CBT helped her to identify triggers that may cause a mood episode and enabled her to develop healthy thinking and behavioural patterns to better manage her mood swings.

One of the features of this case is the sensitivity to different psychotropics.

- A. Quetiapine-deglutition problems
- B. Olanzapine-weight gain, dyskinesia
- C. Risperidone-allergic reactions
- D. Aripiprazole- heightened anxiety level
- E. Haloperidol-EPSE
- F. Antidepressants-hypomania
- G. Lithium produces tremor
- H. Clozapine is well known for inducing deglutition and therefore, may not be a future option because she had experienced deglutition problems while she was taking quetiapine.
- I. There is only scanty literature about the usefulness of antipsychotic agents like lurasidone, asenapine, cariprazine, ziprasidone etc.in the management of rapid cycling BD.

OCD symptoms stopped us from giving her ECT because of the potential risks of ECT precipitating OCD in isolated cases. Lamotrigine has been found to have some anti-obsessional effect (Badner & Gershon 2002). She was given 300mg of lamotrigine in divided doses with favourable effect as a mood stabiliser to control her depression and as an anti-obsessional drug. We were limited with drug choices for treating her OCD as they would destabilise her moods. Therefore, she was offered psychological therapies. The psychological treatment of choice for OCD, backed by numerous clinical trials, is cognitive-behavioural therapy (CBT) and exposure with response prevention (ERP).

We had to be patient until her mood became stable for the initiation of CBT and ERP. Annamma was offered sixteen sessions of CBT and ERP and she was willing to have them periodically in times of flare up of her OCD. Annamma was extremely concerned about her lithium tremor which was lingering on even after stopping it. She was tried on high dose of B_6 to control the lithium tremor as there are research studies indicating its favourable effect. In rapid cycling BD, polypharmacy could become inevitable and justifiable because of the high-risk factors.

DISCUSSION

Cases with far frequent episodes are designated as ultra-rapid cycling and instances where mood swings occur within 24-hour period is recognized as ultradian rapid cy-

cling. Annamma's presentation was that of ultradian rapid cycling. Suicidal risks, risks of accident and accidental death is high during the elated periods and the risks of impulsive and planned suicide becomes extremely high during low periods. Rapid cycling bipolar disorder is reported to be more common among female patients whose illness started at an earlier age (Marneros & and Angst 2000). While some authors argue it as a distinct subtype of bipolar disorder, a few still argue that it is a transient complication of the long-term course of BD (Marneros & and Angst 2000). Studies indicate that 20% of bipolar patients suffer from OCD.

Autoimmune aetiology has been recently brought to the etiological discussion of BD. This is mainly based on the observation of coexistence of other autoimmune disorders in the patient and close family relatives. Annamma's father suffered from Type 1 Diabetes Mellitus. The case I have presented is an example supporting the autoimmune aetiology of BD. One wonders whether this patient's idiosyncratic reactions to several of the psychotropic itself could be an autoimmune reaction. This case report of Ultra-rapid cycling bipolar disorder has most of the complexities of BD. Early recognition and vigilant therapeutic approach have been emphasized. Some of the unknown areas of bipolar disorder including association with autoimmunity and OCD are unveiled in this case and they pose several academic questions.

Limitations

As mentioned in one of the preceding paragraphs, we were limited with the choice of her medications. Annamma has been reminded of the fact that Valproate has a high teratogenicity potential and children exposed in utero to valproate have a high risk for congenital malformations and neurodevelopmental disorders. Moreover, she has been informed that she is on two anticonvulsants which could potentially cancel the effect of contraceptive pills. Standardised treatment measure is limited for rapid cycling BD. There are no psychometric measures to quantify response to treatment and prognosis and has to rely on the past experience of the clinician and clinical intuitions. The proposal for an autoimmune aetiology for OCD is based on the consensus of emerging clinical evidence and expert experiences but not on systematic randomized studies.

CONCLUSION

This presentation adds to the existing literature suggesting an association between bipolar and autoimmune disorders. Another interesting feature of this case is the coexistence of OCD with BD and OCD symptoms

becoming less before the onset of hypomanic phase. This supports the belief that OCD itself could be a defence mechanism against psychosis. OCD has also been argued as an autoimmune disorder. Coexistence of other autoimmune disorders in the immediate family circle is considered as a supporting observation to the autoimmune hypothesis of psychotic disorders and in the case of the presented case, her biological father suffered from Type I Diabetes Mellitus which is recognised as an autoimmune disorder, Identifying the autoimmune causes of OCD could inform better therapeutic options for the affected patients. Cases of this nature are a valuable contribution to the fledgling subspecialty of immunopsychiatry.

Formation of a tsunami analogy is useful in understanding the subtle autoimmune process leading to the psychopathology. The cause of tsunami is not in the sea water, but it is the shifting of the tectonic plates causing tsunami. Likewise, the autoimmune process leads to

the psychopathology of BD, but that will not explain the varied symptomatology which may be disorders of consciousness.

Ethical Considerations

Does this study include human subjects? YES

Authors confirmed the compliance with all relevant ethical regulations.

Conflict of interest

Relevant conflicts of interest/financial disclosures: The author declares that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest. No conflicts of interests and no funding Information on this case has been de-identified to protect anonymity.

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