

Case Report

Are we Overdiagnosing Bipolar Disorder?

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ABSTRACT

Bipolar disorder (BD) is an established diagnostic entity used by clinicians for over a century. It is distinguished by the distinct manic and depressive episodes with interepisode euthymia. It has an illness course where both recovery and recurrences are a rule and has a good long-term prognosis, as reported earlier by Emil Kraepelin. There is an opinion in the current literature that BD is often underdiagnosed as unipolar depression, and based on that opinion, spectrum concept was introduced. Here, we present 5 cases to highlight that overdiagnosis of BD is also not infrequent and we discuss its reasons and therapeutic implications.


Key words: *Bipolar disorder, implications, overdiagnosis*

INTRODUCTION

A 32-year-old male, software professional, consulted at our Asha Bipolar Clinic (ABC) a few months ago for treatment of his psychiatric disorder for which he was taking treatment since 2012. He came along with his wife. At present, he is asymptomatic. He was diagnosed as having bipolar disorder (BD) and was advised to take medications regularly for extended period of time without break. The patient was on lithium/valproate/quetiapine/bupropion for varying periods of time but not on regular basis. He had three depressive episodes of significant severity with suicidal risk, each episode lasting for more than 4–5 months due to which he suffered absenteeism and so was not eligible for promotions. He is most distressed about his professional work and growth. He had a brilliant academic career and graduated from an IIT (top technology schools in India), and his concern was regarding his work

performance. Treatment was not of much help and also was giving side effects, according to the patient. When we reviewed his course of illness, it seemed that he had recurrent episodes of depression with a personality showing obsessive traits and proneness to irritability. No clear episode of mania was found. His wife's description of "Hyper" was found to be his bouts of irritability secondary to "situational related" frustration. Treatment directed at depression with suitable antidepressant could have helped him better! This is not being judgmental but trying to apply the lessons learnt at ABC, from our mistakes, over a decade!

Patients like these are not uncommon and often lead us to examine our clinical knowledge and skills about a particular psychiatric condition. There are multiple issues at stake in such a scenario, which have to be sorted out with care to benefit the patient. We, at ABC,

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consider BD as complex with regard to its presentation, medical management, and clinical application of the newer changes in its concept.

BD is a well-recognized condition not only in the medical circles but also, of late, in the popular media and lay public. Normal mood swings “refined by Google” are being presented as mood disorders!

India has a long way before substantial mental health goals are achieved, which is because of the poor and skewed distribution of the resource personnel. In this scenario, there is a definite chance that illnesses are being underdiagnosed and undertreated. Underdiagnosis might also happen with BD, as with any other mental illness, and there are many scientific reports claiming just that. However, contrary to those reports, we, through this case series, intend to show that there can also be a significant possibility of overdiagnosis of BD. We discuss some of the reasons behind such occurrences.

CASE REPORTS

These cases were selected from the database of ABC, a clinic for mood disorders, which has about

16,000 patients; out of which, 1800 people are diagnosed as BD and about 7000 as major depressive disorder (MDD). We have selected five cases due to their similarity in presentation and course during the follow-up [Table 1]. All of the presented cases have good compliance and were followed up at ABC with a frequency of at least once in 3 months. Patients’ names are changed to prevent their identification.

Case 1

Case 1 is a 60-year-old man with a family history of “BD” in his elder brother who was treated with lithium and who died due to chronic kidney disease. Case 1 presented at our clinic ABC 25 years ago with a history of two “manic” episodes and 2 depressive episodes being treated with lithium. He was euthymic at the time of this first consultation at our clinic. His previous consultant referred him as patient shifted his residence to the present city. The patient had significant lithium-induced tremors for which he was put on propranolol which did not give him a satisfactory relief. During follow-up, over a period of years, he never had recurrence of manic episodes but a few milder depressive episodes for which he was treated with escitalopram 10–20 mg for brief periods of 3–4 months. The patient was happy over

Table 1: Relevant clinical characteristics of cases described in the case series

	Case 1	Case 2	Case 3	Case 4	Case 5
Age of onset (years)	30	40	26	20	18
Duration of illness (years)	30	29	22	9	8
ABC follow-up (years)	25	10	10	6	3
Diagnosis at presentation	Bipolar disorder - euthymia	Bipolar disorder - euthymia	Bipolar disorder - depression	Bipolar disorder - mania	Bipolar disorder - ? Mania
Family history	1° - BD	1° - ?BD probable RDD	1° - ?BD - probable RDD	1° - OCPD, 2° - psychosis, 1° - OCD	1° - Postpartum Depression
Number of reported mood episodes before ABC	2 “Mania,” 2 depression	Unclear	Unclear	1 Mania (includes 1 aggressive episode)	5 depression 2 “Mania”
Informants	Self	Son - Case 3	Mother - Case 2	Parents	Parents
Comorbidity	-	-	?OCD	OC symptoms	-
Manic episodes noted during follow-up	None	None	None	None	None
Depressive episodes noted during follow-up	Many	1	1	None	2 - including one episode with irritability
MS during follow-up	Lithium 800 mg - initial 10 years Lamotrigine 200 mg - 8 years	Quetiapine 50 mg + topiramate 50 mg + escitalopram 20 mg	Valproate 1000 mg - 10 years + fluoxetine 20 mg	Nil	Lithium 900 mg - initial 7 months; valproate 1000 mg - 3 months
Clinical challenge	“Mania” only in the past history	“Mania” only in the past history	“Mania” only in the past history	Classifying aggressive episodes	Classifying aggressive episodes
Current diagnosis	?RDD	?RDD	?RDD	OCD	RDD
Current treatment	Escitalopram 20 mg	Imipramine 150 mg + escitalopram 20 mg + clonazepam 1 mg	Under care of different psychiatrist	Escitalopram 60 mg and clomipramine 150 mg	Escitalopram 20 mg

1° – First degree relative; 2° – Second degree relative; BD – Bipolar disorder; OCD – Obsessive-compulsive disorder; OC symptoms – Obsessive and compulsive symptoms; RDD – Recurrent depressive disorder; ABC – Asha bipolar clinic; OCPD: Obsessive-compulsive personality disorder; MS – Mood stabilizers

the control of his mood symptoms but had constant worry about his hand tremors as his job, a banker, involved lot of writing work. After about 10 years of follow-up, a decision was taken to challenge the course of illness with gradual withdrawal of lithium (reasons being – no manic episodes in 10 years and significant tremors) and maintain him on lamotrigine. Patient never had any manic episode. He had milder depressive episodes only, whose frequency did not change, and he was treated with brief antidepressant medication. After a period of another 8 years, lamotrigine was withdrawn gradually and he is maintained on about 10 mg of escitalopram. Patient's disease course did not worsen in the last 7 years while he is on escitalopram alone. Over past 25 years, he went through multiple personal stressors including marital separation for few years, intellectual disability in his son who later died at the age of 11 years. Currently, he works as an assistant manager in the banking sector. **The clinical questions are – (1) Was the original diagnosis of BD correct? (2) Is he one of those rare patients who had only 1–2 manic episodes without any further episodes of mania in the follow-up period of 25 years! (3) Was there requirement of long-term maintenance of lithium and lamotrigine in this patient? The only reason the clinician continued “Mood Stabilizers” for almost two decades was because of the belief that these medicines were helping him immensely in preventing the manic episodes, which might not be true.^[1] During the entire period of about 25-year follow-up, we have observed only occasional mild depressive episodes and never any manic or hypomanic episodes.** Lithium was tapered and stopped due to intolerable hand tremors, which were causing disability at workplace. For the last 7 years, he is being treated with escitalopram 20 mg and is doing well.

Case 2

Case 2 is a 69-year-old widow from a rural background who presented to ABC 10 years ago, with her son (Case 3 in this series) who also was diagnosed elsewhere as BD. She has premorbid anankastic personality traits, and past history suggests episodic course of illness with alternating periods of irritability and depressive features lasting for few days each. She presented at our clinic in 2007 with diagnosis of BD and euthymia and was on a combination of topiramate 50 mg, quetiapine 50 mg, and escitalopram 20 mg. The patient had two more children, a daughter who settled in the USA and a son who lived in Australia. Her medication was not changed, as she was asymptomatic. Same medications at same doses were maintained for the last 10 years because of various factors such as patient and her children were unwilling for any change due to the remitted status and fearing a recurrence of illness and her only caregiver was a son (Case 3) who was also being treated as BD leading to a poor social support. poor social support

and also due to absence of medical comorbidities or any abnormality in periodic laboratory tests during follow-up. “Possibility of quetiapine at the smaller dose of 50 mg with augmentation from topiramate 50 mg giving her euthymic status” was a lingering thought in the clinician's mind. She developed major depressive episodes; first mood episode in our clinic in 2016 presenting with agitated depression, intense suicidal ideation, and suicidal attempt of high lethality. She was managed as an inpatient admission with selective serotonin reuptake inhibitors (SSRIs) initially but later with electroconvulsive therapy and tricyclic antidepressants. She is currently on 150 mg of imipramine and 20 mg of escitalopram and 1 mg of clonazepam. On this dosage for the last 6 months, she is asymptomatic now and is functional and active. **The clinical dilemmas – (1) Was the diagnosis of BD correct? (2) Was it a rare case of total euthymia till September 2016, after one episode of mania? (3) Was quetiapine effective as mood stabilizer at a dose of 50 mg? (4) Was she suffering from depressive disorder only with one episode in the past and another severe episode last year with an interepisodic euthymic period lasting for 10 years? (5) Was escitalopram effective as prophylactic drug for her depressive episodes for 10 years? (6) Should we revise her diagnosis to recurrent depressive disorder (RDD) now? (7) How long should we continue the current antidepressant medication? 8. Can I stop all the psychotropic medication after about 2 years from now?**

Case 3

Case 3 is a 48-year-old man with a family history of psychiatric illness in his mother (Case 2). He presented to ABC 10 years ago with a diagnosis of BD, currently depressed. Caregiver reported of significant improvement in the depressive symptoms with the current medication – valproate 100 mg and fluoxetine 20 mg. It was also reported that Nareshkumar had significant obsessive symptoms such as orderliness and excessive cleanliness with exaggerated irritable reactions on occasions. The depressive symptoms recovered completely in about a month and the patient was euthymic. The patient was on regular medication and follow-up with periodic visits along with his mother. Till 6 months ago, he remained asymptomatic without any manic or depressive episodes. He was maintained on the same dose of medications – valproate at 1000 mg as mood stabilizer and fluoxetine at 20 mg to help control of his obsessive features. **Medication was not changed as he was maintained in the state euthymia at every follow-up, and laboratory reports did not warrant any drug-induced adverse events.** Fluoxetine was continued, with cautious worry, to help contain his obsessive symptoms and he never had manic switch. Six months ago, he developed significant depressive

symptoms along with exacerbation of obsessive features associated with outbursts of irritability. Repeated evaluation did not show any features suggestive of mania. **Retrospective analysis – (1) Did he ever have manic episodes or episodes of irritability were mistaken as manic episodes? (2) Patients with obsessive-compulsive disorder (OCD)/obsessive-compulsive personality disorder (OCPD) are known to exhibit significant irritable temperament which could have mislead the clinician! (3) Was the euthymic state the mood stabilizing effect of valproate or the natural course of the disorder? (4) Prolonged maintenance on fluoxetine did not precipitate switch! (5) Does it warrant a revision of diagnosis to RDD with OC symptoms and if so do we stop valproate? (6) Can we maintain him on SSRI alone in the long-term?**

Case 4

Case 4 presented to ABC at 20 years of age with history of duration of illness for 9 years. Family history of OCD in mother, OCPD in elder brother, and psychotic disorder in 2nd degree relative is present. At the time of his first consultation, caregivers informed about his suffering from a brief manic episode, lasting for about 2–3 weeks, about a year ago, for which he was treated at a local hospital as inpatient. Medication was discontinued after a month as he became asymptomatic. Mother reported patient having frequent mood swings for the last 3 years lasting from a few hours to days. Reportedly, he is again aggressive for the last 2 days with extreme irritability, verbal abusiveness, breaking articles at home, and also with bursts of crying spells. The duration criterion was not satisfied in this patient, but the patient was given diagnosis of BD, keeping past history in mind – a patient with possible ultrarapid or ultradian cycles. Patient was admitted with a diagnosis of BD, currently mania and was started on lithium and olanzapine. On detailed evaluation during his inpatient stay, it was found that patient is having OCD with significant OCPD and temperamental trait of extreme anger on minor provocation. We have revised the diagnosis to OCD. **The clinical challenge in this case was that irritability and aggressive outbursts are misinterpreted as manifestation of mania leading to the mistaken diagnosis of BD.** We have been observing that this pattern of presentation with irritability, validity provided by DSM-5, has become a deep pit of mistakes even for seasoned clinicians sometimes leading to involuntary admissions. **Irritability being given an almost equal weightage, similar to elation, as an important diagnostic criterion in DSM-5 may need a revisit by the experts.** Therapeutic implications are huge as we are well aware – (1) Unwarranted “mood stabilization” for years. (2) Required and useful medications, antidepressants, are not prescribed for fear of switch. This patient of ours is now on a combination

of clomipramine 150 mg and escitalopram 60 mg for the last 6 years with significant relief in his clinical symptoms of OCD. Bouts of irritability have subsided significantly and he did not have any episode of mania in the last 6 years.

Case 5

Case 5 has an illness of 8 years’ duration with the onset at 18 years of age. There is family history of post-partum depression in her elder sister. She had “7 mood episodes” including 2 episodes, which consisted of significant irritability and dysfunction and were reported as manic episodes. The clinical challenge in this case was when in October 2016, relatives brought her for admission with the complaints of a month long irritability and aggression. She was treated with valproate 1000 mg considering the episode as a relapse of a manic episode. However, during the inpatient stay, first admission at our center, it was concluded that the clinical presentation of 8 years’ duration was not of BD. **Diagnosis is revised as RDD with OCPD with significant situation-related irritability as premorbid trait. Valproate was discontinued. She is currently on escitalopram 20 mg for about 2 years and remains euthymic.**

DISCUSSION

The case histories of five patients presented here have the following common features:

1. **The clinical risk of overdiagnosis of BD in these cases can probably be due to the informants presenting the symptoms of irritability and anger outbursts as “mood swings”**
2. **MDD with episodes of irritability getting diagnosed as BDs**
3. **Personality disorders especially OCPD/personality traits with rigidity and low frustration tolerance being misdiagnosed as BD**
4. **Continuation of medications for extended periods of years with the belief “Mood Stabilizers are helping the patients maintain the state of euthymia.”**

Retrospective history is only as good as the informant because various biases can creep into the informant’s version. “Hypomania”, push for redefining duration criterion,^[2] categories of subsyndromal symptoms, or ultradian, ultrarapid cycling^[1,3] make a clinician’s job more challenging in diagnosing BD.^[4] The clinician has to treat the whole person who is suffering which includes thinking through the relationship of psychiatric symptoms with personality and coping systems.

Follow up over years – the available safeguard

In such a scenario, we understand that the only way ahead for the clinician is to carefully follow the patient over years. Clinician has the obligation to observe

whether the initial diagnosis is holding up to the test of diagnostic stability overtime or whether there are other explanations for symptoms, which were initially mistaken as manic or hypomanic symptoms.

In the presented cases, that is what made us to question the initial diagnosis and in two of our patients to revise the diagnosis. The follow-up did not show any recurrence of mania or hypomania nor did it lead to switch even when high doses of antidepressants were used. Meanwhile, there was an alternative explanation for the irritability, which was anyway not fulfilling DSM-5 criteria for either mania or hypomania. **As Karl Leonhard once said, we believe that the diagnosis of a mental illness includes a prognosis.** Hence, when a disorder is not following its described usual prognostic course, there arises a need to reexamine our initial diagnosis!

Dilemmas in clinical decision-making

Cases 2 and 3 in this series present an interesting case to discuss how the clinical decision-making gets affected by the psychosocial factors in the patients' lives. Case 2 was continued on what normally is unacceptable and irrational, i.e., combination of topiramate, quetiapine, and escitalopram because of relatives' unwillingness to accept change in the medication, as patient is asymptomatic and "doing well" on these doses. The argument was in case of the unfortunate situation of relapse, no immediate relative is available to take care of her. From the treating clinician's point of view, her periodic laboratory investigations were normal, she had no other medical comorbidities and in "perfect state of euthymia". Case 3 was continued on valproate for the last 10 years despite the doubt about the authenticity of the initial diagnosis of BD. Here too, the consent of relatives was not available to make any changes in the medication, as any such change was perceived as adventurism on the part of treating clinician by the relatives living abroad. They could not understand the reason for such a change in view of his remitted status and absence of any recurrence till 2016. **Though such collaborative clinical practice supports garnering the healthcare consumer's trust and ensures compliance, it places its own limitations on the clinical decision-making as observed in the Cases 2 and 3.**

Alternative explanations

Elsewhere, we have pointed out the importance of personality traits in the presentation of symptoms,^[5] which means that a "check-list psychiatric classification" which does not consider all of a person's available data such as the personality and family history may need a revision for a more comprehensive classification. Of course, clinical data have its own limitations, but we have to make best use of what is available at least until powerful scientific measures such as biomarkers come

in to help us diagnose and treat better.

In the presented cases, though the patient presented with severe agitation, sometimes for inpatient care, it does not mean that it somehow counts for a manic episode. They had personality traits which predisposed them for irritability and even assault, in some cases, on caregivers. **Newer diagnoses such as disruptive mood dysregulation disorder may offer alternate ways of conceptualizing such instances of aggression, which can be misdiagnosed as mania!**

Is there a price we pay for overdiagnosis of bipolar disorder?

Above mentioned cases represent the few, albeit frequent, instances which can lead to overdiagnosis of BD.

There is price to pay for such mis (over)-diagnosis such as can be described:

1. **BD is conceptually and also popularly understood as one of the severe mental illnesses and this diagnosis has more impact on stigma than say a depressive disorder label might have**
2. **From a clinical point of view, mis (over)-diagnosis leads to unnecessary mood stabilizer and antipsychotic agent use which can have unacceptable and intolerable side effects**
3. **It also leads to hesitant and less than optimal use or often nonuse of anti-depressant agents with all the caution that guidelines want us to exercise, the result being "undertreatment" of depressive episodes**
4. **Compromised treatment plan is a price that clinician has to pay wherein she/he cannot provide best care possible to the suffering person.**

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