Retracted: Bipolar Affective Disorder: A Case of Antidepressant-Induced Hypomania

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This article has been retracted.

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This article was erroneously approved due to a technical error on the editorial side. The Cureus Journal of Medical Science greatly regrets this errors and any inconvenience caused to the authors or readers as a result. Following careful consideration by the journal's editorial board, we have determined that this article must be retracted as we have several critical concerns that cannot be addressed via erratum. These issues are listed below.

1. The dosage information for valproate, citalopram, quetiapine and valproate is not included nor is there sufficient explanation regarding the frequency and duration of treatment.
2. Information regarding sedation such as dose, frequency, protocol is not included.
3. The hypomania timeline and symptoms are not included nor is it explained why or how the hypomanic patient was admitted.
4. Details regarding the cessation of sedatives are not included.

Abstract

Bipolar affective disorder (BAD) is found among 1-3% of the world's population and leads to a significant burden due to its chronicity. This report describes a case of antidepressant-induced BAD, presenting in the hypomanic phase. Diagnostic criteria in the American Psychiatric Association's Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5) were used for the diagnosis, after having performed investigations and excluding organic causes. The patient presented with typical features of altered mood, pressured speech, hyperactivity, and irritability. He was diagnosed according to the criteria available and managed promptly.

Categories: Family/General Practice, Psychiatry, Psychology

Keywords: bipolar affective disorder, bad, antidepressant, hypomania, bipolar disorders, common mental disorders

Introduction

Bipolar affective disorder (BAD) is a mood disorder characterized by episodes of mania, hypomania, and depression [1]. It can be subdivided into two types, 1 and 2; type 1 presents with mania alongside major depressive and hypomanic episodes, whereas type 2 presents with at least one hypomanic and depressive episode in the absence of mania [1].

According to the World Health Organization (WHO), BAD is the 46th most common cause of disability in the world, especially as most patients never receive treatment [2,3]. On average, it has a lifetime worldwide prevalence of 1-3% among adults, translating to approximately 75-225 million people [4]. Usually, it presents between the age of 18-20 years, with no gender predominance [5]. BAD is initially evaluated in a presenting patient by conducting a psychiatric history, and mental state examination; this includes an interview to assess for any depression, mania, hypomania, suicidal thoughts, or psychotic features [1]. Specialized diagnostic criteria provided in the American Psychiatric Association's Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5) are used when a disorder is suspected; organic causes must also be excluded before it can be cemented as a diagnosis [1]. Furthermore, family history is another important indicator of suspicion for the disorder [6].

The fundamental difference between mania and hypomania lies in the intensity of symptoms. Mania presents with more intensity than hypomania, and results in significant dysfunction, often necessitating hospitalization [7]. If psychotic symptoms are present, the episode is defined as mania [1]. The major symptoms characterizing these episodes are elevated and labile mood, the pursuit of stimulation, increased energy, and exaggerated self-confidence [1,8]. The depressive state mainly features dysphoria, slowed mental and physical activity, and loss of interest in pleasurable activities, among other symptoms [7]. Symptoms of both these states may manifest simultaneously in some patients.

BAD-suspected individuals present with features of altered mood, which can be depressive or manic, depending on the episode that is dominating at the time of presentation, or a combination of both [1]. These features typically manifest by way of disruption of mood, sleep, energy, activity, and behavior [1]. During the episodes, some patients may remit to become euthymic, whereas others can change from one spectrum of the syndrome to the other without any period of euthymia in between [9]. Usually, the first lifetime episode of BAD is depressive in 54%, mixed in 24%, and manic in 22% of patients [10].

Pharmacotherapy is the mainstay of the treatment of BAD, alongside psychotherapy. Typically, the drug used to treat the acute episode is continued as maintenance therapy, and these drugs include lithium, valproate, quetiapine, and lamotrigine, to name a few [11]. The side effects of drugs must be considered while prescribing them to the patient. Each drug has its benefits; lithium has been shown to reduce suicide risk, whereas valproate reduces the chance of relapse by 30% [12,13].

In this report, we illustrate the disease course and treatment of a man diagnosed as a case of BAD, with an acute hypomanic episode, who presented to our clinic. Investigations showed no organic cause for the presenting complaints of hyperactivity, irritability, and aggressive physical behavior; his psychiatric history and interview, alongside his score on the Young Mania Rating Scale (YMRS), were indicative of his condition.

Case Presentation

A 52-year-old male, a known case of BAD for five years with concomitant history of uncontrolled hypertension and type 2 diabetes mellitus (T2DM) for two years, presented to the psychiatry department with complaints of hyperactivity, pressured speech, irritability, and aggressive behavior escalating to physical violence for the past few months. His premorbid personality was described as friendly, diligent, and sensitive; he had worked at his previous job for 15 years. However, during the past three months, he had become excessively conversational with dialogues showing increased religiosity, and volatile, which had resulted in numerous arguments with family, and he had sometimes resorted to physical violence; additionally, he admitted to having a death wish. Furthermore, his appetite had increased, and he experienced decreased sleep. He spoke in a hurried manner, in English, which was not the norm for him, and continuously overexpressed his achievements. Lastly, there were no delusions of control, hallucinations, thought broadcasting, withdrawal, or persecution upon presentation.

He had been diagnosed with BAD five years ago when he had developed complaints of intermittent depression, alongside ongoing elevated mood, reduced sleep, increased appetite, and hyperactivity. He had been started on valproate but had demonstrated poor compliance and follow-up. After two years, he had begun experiencing episodes of social withdrawal, anhedonia, and increased somnolence. At this point, citalopram had been added as an adjunct to his ongoing medication for his depressive symptomatology. His symptoms had been adequately controlled for the next one year, following which he had presented to another psychiatry clinic with symptoms of elevated mood, volatility, and after having gambled a large sum of money on a cricket match. This had led to his voluntary hospital admission. He had been managed with an increased dose of valproate; sedation had been given depending on the patient's behavior. He had been discharged after two weeks, with a prescription of valproate and citalopram. Two years later, he presented to our facility with symptoms of hypomania for three months. His family history was significant for hypertension; however, there were no psychiatric illnesses in the family.

Physical examination revealed an agitated man with a body temperature of 98.6 °F, pulse rate of 84/minute, blood pressure of 140/80 mmHg, and respiratory rate of 19 breaths/minute. On inspection, the patient was irritable, dressed appropriately, and was conversing in English, which was not the norm for him. Furthermore, there was no scleral icterus, sub-conjunctival pallor, or pedal edema. There was an old scar present on his left forearm, which was 3 cm in length vertically. Systemic examination was unremarkable.

Based on clinical symptoms, a working diagnosis of hypomania was made, which was further reaffirmed using YMRS, an 11-item scale accepted by the Royal College of Psychiatrists and frequently used to evaluate manic symptoms. Our patient scored 19/60, which signifies hypomania. Moreover, his recent acts of physical aggression towards his family and colleagues led to his hospitalization on psychiatric grounds, due to his being potentially harmful to others. Furthermore, metabolic workup was done to exclude organic causes.

Investigations revealed normal hemoglobin (13.5 g/dL), white blood cell count (6,800/mm³), and electrolytes. His HbA1C was mildly raised (7.1%); his fasting lipid profile showed significantly raised

triglycerides (219 mg/dL) and very light density lipoproteins (43 mg/dL). Liver function tests (LFTs) revealed a mildly increased serum glutamic pyruvic transaminase (43 U/L), whereas other metabolic workup results were normal.

Upon admission, he was started on quetiapine and valproate for symptomatic relief. Clonazepam was added as a central nervous system depressant. His regular medications for hypertension and T2DM were continued after necessary adjustments following re-evaluation by an internal medicine specialist. Haloperidol with promethazine was set aside for chemical restraint if needed.

Late into day three of admission, the patient became agitated, insisting on offering his evening prayers at the local mosque. Multiple attempts were made to counsel the patient but to no avail. He became increasingly confrontational, ultimately attacking one of the nurses. This led to him being physically restrained; however, he still could not be calmed down. Owing to the risk he posed to the ward staff and himself, it was decided to chemically restrain the patient using haloperidol with promethazine.

His condition remained relatively unchanged the following day; however, there were no violent outbursts. By day five, the patient was less combative, though his speech remained pressured. The following day saw further improvement in his symptoms, yet some self-important ideation persisted with the patient claiming to have “discovered multiple cures by merely sitting in the communal lounge, while the medical team had failed to cure him over several days”. His YMRS score had dropped to 15.

By day nine, the patient’s psychiatric manifestations continued to improve, especially his mood, sleep, and irritability; his YMRS score further dropped to 9. Based on this progressive clinical improvement, it was decided to begin tapering off sedation. Cessation of sedatives was completed on day 11; at this point, he had remained episode-free for two days and had a YMRS score of 4. The patient was allowed a half-day leave on day 13 to assess his psychiatric fitness for a safe discharge in the near future.

By day 15, the patient had experienced no significant episodes for seven days, and his YMRS score was 2 due to slight mood and motor elevation. Based on his evident response to treatment, significantly improved YMRS score, and no further episodes of physical aggression, it was decided to discharge him after detailed counseling regarding warning signs of worsening disease, and maintenance of regular follow-ups. His discharge medications consisted of valproate only; his antidepressant was discontinued until further notice due to the potential risk of re-exacerbation of hypomania. The rest of his regular medications were to be continued as advised by the physician. He was scheduled to follow up in a week for psychiatric re-evaluation.

Discussion

BAD is a condition that affects 1-3% of the world’s population and results in a significant burden due to its chronicity. It is often further aggravated as most patients do not seek treatment until the disorder is at a full-blown stage, resulting in hospitalization or cases of homicide or suicide [2,6]. Therefore, communal recognition of mental health, timely diagnosis, and prompt intervention are paramount to help mitigate the burden caused by the disorder.

Patients with BAD may demonstrate one of two phases, manic or depressive. The manic phase involves core symptoms of elevated or irritable mood, increased energy, inflated self-esteem, decreased sleep, pressured speech, and flight of ideas; the differentiation of mania from hypomania is mainly based on the presence of psychotic symptoms [2,8]. On the other hand, the depressive phase is characterized by depressed mood, anhedonia, hypersomnia, fatigue, and suicidal ideation [7]. As our patient presented with an acute episode of hypomania, his symptoms were closely related to the manic phase discussed. He complained of hyperactivity, pressured speech, irritability, and aggressive behavior including physical violence; however, the absence of psychotic symptoms, and a low YMRS score, ruled out the diagnosis of mania.

The blood tests performed for the patient comprised complete blood count, thyroid function tests, renal function tests, and LFTs, among others. As there are no blood tests or imaging available that can be used to help diagnose BAD, these tests were performed to exclude any other possible explanation of the symptoms that were present.

Currently, guidelines suggest using pharmacotherapy with one of the four first-line drugs: lithium, valproate, quetiapine, or lamotrigine [11,14]. Valproate was preferred in our patient as it had adequately controlled his symptoms prior to the current episode. Furthermore, valproate has been shown to reduce the chance of relapse of episodes by 30%, which was a concern in this case [13]. The main reason that valproate is not utilized before lithium in literature is due to its teratogenicity; however, this was not a concern in our case as our patient was not a female [15].

The most important aspect of our patient’s medical history was the fact that he had been prescribed an antidepressant alongside his valproate. It has been established that antidepressants in BAD can precipitate a hypomanic episode, especially in the absence of concurrent lithium as a mood stabilizer [16]. Initial studies have found that antidepressant usage in BAD may precipitate hypomania in 30-70% of patients; however,

newer studies estimate that number to be around 27-40% and advise against their usage unless lithium is given alongside [7,16]. The adverse effect of concurrent use of antidepressants with valproate was thought to be the main cause of the current hypomanic episode in our patient. Furthermore, it was hypothesized that his previous history of a similar hypomanic event had stemmed from the same process as he had always been prescribed an antidepressant with valproate. Antidepressants were discontinued upon admission in this case.

Conclusions

BAD has affected the lives of more than 200 million people around the world, with many of them receiving no treatment due to delayed diagnosis. This mismanagement leads to an increased disease burden as it causes patients to be hospitalized due to the progression and severity of symptoms. Even though our patient had been diagnosed in the past, his management had been inappropriate due to the addition of antidepressants to his valproate regime, which had led to hypomanic episodes presently and in the past as well. The use of antidepressants has been controversial in BAD due to a lack of research and definitive guidelines; such resources may help clinicians make evidence-based treatment decisions regarding combination drug regimes. This study highlights the importance of understanding the triggering factors that may cause hypomanic episodes in patients of BAD receiving multidrug therapy.

Additional Information

Disclosures

Human subjects: Consent was obtained or waived by all participants in this study. **Conflicts of interest:** In compliance with the ICMJE uniform disclosure form, all authors declare the following: **Payment/services info:** All authors have declared that no financial support was received from any organization for the submitted work. **Financial relationships:** All authors have declared that they have no financial relationships at present or within the previous three years with any organizations that might have an interest in the submitted work. **Other relationships:** All authors have declared that there are no other relationships or activities that could appear to have influenced the submitted work.

References

1. American Psychiatric Association: Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5). American Psychiatric Association, Arlington, VA; 2013. <https://books.google.com.pk/books?id=-JivBAAAQBAJ&printsec=frontcover&dq=Diagnostic+and+Statistical+Manual+of+Mental+...>
2. Morselli PL, Elgie R: GAMIAN-Europe/BEAM survey I--global analysis of a patient questionnaire circulated to 3450 members of 12 European advocacy groups operating in the field of mood disorders. *Bipolar Disord*. 2003, 5:265-278. [10.1034/j.1399-5618.2003.00037.x](https://doi.org/10.1034/j.1399-5618.2003.00037.x)
3. Murray CJ, Vos T, Lozano R, et al.: Disability-adjusted life years (DALYs) for 291 diseases and injuries in 21 regions, 1990-2010: a systematic analysis for the Global Burden of Disease Study 2010. *Lancet*. 2012, 380:2197-2223. [10.1016/S0140-6736\(12\)61689-4](https://doi.org/10.1016/S0140-6736(12)61689-4)
4. Pedersen CB, Mors O, Bertelsen A, et al.: A comprehensive nationwide study of the incidence rate and lifetime risk for treated mental disorders. *JAMA Psychiatry*. 2014, 71:573-581. [10.1001/jamapsychiatry.2014.16](https://doi.org/10.1001/jamapsychiatry.2014.16)
5. Seedat S, Scott KM, Angermeyer MC, et al.: Cross-national associations between gender and mental disorders in the World Health Organization World Mental Health Surveys. *Arch Gen Psychiatry*. 2009, 66:785-795. [10.1001/archgenpsychiatry.2009.36](https://doi.org/10.1001/archgenpsychiatry.2009.36)
6. Craddock N, Sklar P: Genetics of bipolar disorder. *Lancet*. 2013, 381:1654-1662. [10.1016/S0140-6736\(13\)60855-7](https://doi.org/10.1016/S0140-6736(13)60855-7)
7. Goodwin FK, Jamison KR: Manic-Depressive Illness: Bipolar Disorders and Recurrent Depression, 2nd Edition. Oxford University Press, New York, NY; 2007.
8. Mitchell PB, Loo CK, Gould BM: Diagnosis and monitoring of bipolar disorder in general practice. *Med J Aust*. 2010, 193:S10-13. [10.5694/j.1326-5377.2010.tb03890.x](https://doi.org/10.5694/j.1326-5377.2010.tb03890.x)
9. Judd LL, Akiskal HS, Schettler PJ, et al.: The long-term natural history of the weekly symptomatic status of bipolar I disorder. *Arch Gen Psychiatry*. 2002, 59:530-537. [10.1001/archpsyc.59.6.530](https://doi.org/10.1001/archpsyc.59.6.530)
10. Kupfer DJ, Frank E, Grochocinski VJ, Cluss PA, Houck PR, Stapf DA: Demographic and clinical characteristics of individuals in a bipolar disorder case registry. *J Clin Psychiatry*. 2002, 63:120-125. [10.4088/jcp.v63n0206](https://doi.org/10.4088/jcp.v63n0206)
11. Yatham LN, Kennedy SH, Parikh SV, et al.: Canadian Network for Mood and Anxiety Treatments (CANMAT) and International Society for Bipolar Disorders (ISBD) 2018 guidelines for the management of patients with bipolar disorder. *Bipolar Disord*. 2018, 20:97-170. [10.1111/bdi.12609](https://doi.org/10.1111/bdi.12609)
12. Hayes JF, Pitman A, Marston L, Walters K, Geddes JR, King M, Osborn DP: Self-harm, unintentional injury, and suicide in bipolar disorder during maintenance mood stabilizer treatment: a UK population-based electronic health records study. *JAMA Psychiatry*. 2016, 73:630-637. [10.1001/jamapsychiatry.2016.0432](https://doi.org/10.1001/jamapsychiatry.2016.0432)
13. Cipriani A, Reid K, Young AH, Macritchie K, Geddes J: Valproic acid, valproate and divalproex in the maintenance treatment of bipolar disorder. *Cochrane Database Syst Rev*. 2013, 2013:CD003196. [10.1002/14651858.CD003196.pub2](https://doi.org/10.1002/14651858.CD003196.pub2)
14. Goodwin GM, Haddad PM, Ferrier IN, et al.: Evidence-based guidelines for treating bipolar disorder: Revised third edition recommendations from the British Association for Psychopharmacology. *J Psychopharmacol*. 2016, 30:495-553. [10.1177/0269881116636545](https://doi.org/10.1177/0269881116636545)
15. Briggs GG, Freeman RK, Yaffe SJ: Valproic acid. *Drugs in Pregnancy and Lactation: A Reference Guide to Fetal and Neonatal Risk*. Wolters Kluwer, 2015. 1:1449.

16. Henry C, Sorbara F, Lacoste J, Gindre C, Leboyer M: Antidepressant-induced mania in bipolar patients: identification of risk factors. *J Clin Psychiatry*. 2001, 62:249-255. [10.4088/jcp.v62n0406](https://doi.org/10.4088/jcp.v62n0406)