CASE SERIES

Treatment-emergent Affective Switch: A Case Series Study

Jesvin L Johnson[1], Shashwath Sathyanth M[2], Anil Kakunje[3]

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Abstract

Introduction: Bipolar disorder is a widespread psychiatric condition characterized by mood swings, impacting millions worldwide. It includes subtypes such as bipolar I and bipolar II, with differing manic and depressive episode patterns. Treatment encompasses medication, psychotherapy, and psychosocial interventions. Managing antidepressant use in bipolar disorder is crucial due to the risk of the treatment-emergent affective switch (TEAS), where antidepressants can induce shifts from depression to mania or hypomania, a complex phenomenon influenced by genetics, neurobiology, and environment. Atypical antipsychotics offer promise as mood stabilizers and TEAS risk reducers. Patient factors such as age, gender, and illness history also influence TEAS susceptibility. Recognizing and addressing TEAS is vital in clinical practice to prevent symptom exacerbation and functional impairment. In this case series, we delve into TEAS among bipolar patients receiving antidepressant treatment, aiming to deepen comprehension, enhance patient care, and inform future research.

Methods: This study includes nine cases obtained from a tertiary care center, with a focus on six selected cases diagnosed with bipolar affective disorder and TEAS as per the *International Classification of Diseases, Tenth Revision* (ICD-10) criteria. Case selection involved extensive interviews, data collection from hospital records, and discussions with treating psychiatrists. Consent was obtained and privacy was maintained. Demographic, social, and clinical information is presented, offering a comprehensive overview of the cases. These data provide insights into the occurrence and management of TEAS in bipolar affective disorder. Detailed case information can be found in the tables.

Keywords: Atypical antipsychotics, Bipolar disorder, Case report, Mood stabilizer, Treatment-emergent affective switch.

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Introduction

Bipolar disorder is an episodic psychiatric illness characterized by abnormal shifts in mood, energy levels, and activity.[1] Bipolar disorder is classified into several subtypes, with bipolar I disorder and bipolar II disorder being the most common. Bipolar I disorder is characterized by the presence of at least one manic episode, which is a distinct period of abnormally elevated, expansive, or irritable mood. These manic episodes may be accompanied by psychotic features. Bipolar II disorder, on the contrary, involves recurrent episodes of major depression and hypomania, a milder form of mania.

The treatment of bipolar disorder typically involves a combination of pharmacotherapy, psychotherapy, and psychosocial interventions. Mood stabilizers, such as lithium, valproate, and lamotrigine, are commonly used to manage both manic and depressive symptoms. However, antidepressant medications, are prescribed to treat depressive episodes in bipolar disorder. An essential aspect of bipolar disorder management is the treatment-emergent affective switch (TEAS), where certain medications, especially antidepressants, can trigger a shift from depression to hypomania, mania, or mixed states in individuals with bipolar disorder. The mechanisms behind this phenomenon involve complex interactions between genetics, neurobiology, and the environment. *International Classification of Diseases, Eleventh Revision* (ICD-11) recognizes genetic influence in bipolar disorder.[1] Genetic predisposition may significantly determine susceptibility to medication-induced mood instability.[2] McIntyre et al. discuss bipolar disorder's intricate neurobiology, suggesting neurotransmitter dysregulation (serotonin, dopamine, and norepinephrine) contributes to medication-triggered mood shifts.[3] Canadian Network for Mood and Anxiety Treatments (CANMAT) guidelines stress pharmacological management's importance, particularly in choosing mood stabilizers and antipsychotics to prevent mood switches.[4] The case report Mudigubba et al. case report indicates comorbidities impact on mood stability, potentially influencing treatment responses and TEAS risk.[5] Studies have shown that atypical antipsychotic acts as mood stabilizer along with reducing the risk of TEAS. In addition, certain patient characteristics have significance, including age, gender, and illness history, potentially impacting TEAS susceptibility.[6,7] The research by Mundo et al. explores antidepressant-induced mania variables, relevant to certain bipolar patients.[8,9] The study by Serretti et al. outlines clinical features of antidepressant-associated manic switches, aiding TEAS prediction and management.[10] Vieta et al. identify predictors of switching from mania to depression, revealing the intricate factors contributing to mood shifts.[11]

Treatment-emergent affective switch's consequences are notable, potentially worsening symptoms, functional impairment,

[1–3]Department of Psychiatry, Yenepoya Medical College, Mangaluru, Karnataka, India

Corresponding Author: Jesvin L Johnson, Department of Psychiatry, Yenepoya Medical College, Mangaluru, Karnataka, India, Phone: +91 8921595793, e-mail: jesvin96@gmail.com

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Table 1: The sociodemographic details and family history of all the cases

Case no.	*Age*	*Sex*	*Religion*	*Education*	*Occupation*	*Marital status*	*Family history*	*Comorbidities*
1.	40	Male	Muslim	SSLC	Not working	Unmarried	Absent	Nil
2.	60	Female	Muslim	Primary	Homemaker	Married	Absent	Type-2 diabetes mellitus
3.	25	Male Female	Muslim	Postgraduate	Not working	Married	Present	Nil
4.	20	Female	Muslim	Degree	Not working	Unmarried	Present	Nil
5.	22	Male	Muslim	10th grade	Daily wage laborer	Unmarried	Present	Nicotine dependence
6.	42	Male	Muslim	B.Tech	Engineer	Married	Absent	Alcohol harmful use
7.	26	Female	Christian	B.Tech	Engineer	Unmarried	Present	Nil
8.	35	Male	Hindu	12th grade	Auto driver	Married	Present	Nicotine dependence
9.	19	Female	Hindu	12th grade	Not working	Unmarried	Absent	Nil

B.Tech, bachelor of technology; SSLC, secondary school leaving certificate

and hospitalization.[11] Recognizing and managing it is pivotal in clinical practice, ensuring optimal outcomes for bipolar patients.

In this case series, we present cases that highlight the occurrence of TEAS in individuals with bipolar disorder undergoing antidepressant treatment. We aim to explore clinical features, risk factors, management strategies, and outcomes, contributing to our understanding of this phenomenon and promoting evidence-based practices for bipolar disorder management.

Methods

The cases presented in this study were obtained from a tertiary care center. A total of nine cases are included in the study, with a detailed description of two selected cases. The cases were chosen after diagnosing the patients with the bipolar affective disorder as per ICD-10 and establishing the diagnosis of TEAS. This was achieved through thorough interviews with the patients and their family members, the collection of data from previous hospital records, and discussions with the treating psychiatrist. Before publication, consent was obtained from the patients and their family members, and all personal details were kept confidential. Demographic data, social data, and clinical information were collected and are presented in Tables 1 and 2.

Case 1

A 40-year-old unmarried male, diagnosed with bipolar I disorder and obsessive–compulsive disorder (OCD) for over 15 years, presented to the emergency department with a two-week history of irritability, increased talkativeness, decreased sleep, heightened activity levels, grandiose ideas, excessive demands, and increased familiarity. The patient's family reported a sudden change in his behavior, with excessive and difficult-to-interrupt speech, irritability upon interruption, and an increased interest in topics such as religion, movies, and politics. Additionally, the patient displayed increased motor activity, spent money recklessly, disrupted sleep patterns, and exhibited irritability over trivial matters. Due to the severity of the symptoms and the patient's agitation, he was sedated with intramuscular haloperidol.

There was no history of psychiatric disorders in the family. Twenty days before the presentation, the patient experienced intrusive thoughts and tingling sensations on his penis, causing significant distress. Seeking relief, the patient self-administered fluoxetine (60 mg twice daily) obtained from a nearby pharmacy. Unfortunately, this led to a rapid escalation of symptoms, culminating in the current acute manic episode.

Due to the severity of symptoms and poor treatment adherence, the patient was admitted to the Department of Psychiatry. Fluoxetine was discontinued, and the patient was initiated on lithium (800 mg), quetiapine (100 mg), lorazepam (2 mg), chlorpromazine (CPZ 200 mg), and intramuscular haloperidol (5 mg as needed). To improve treatment adherence, a depot injection of flupenthixol (150 mg) was administered deep intramuscularly in the gluteal region.

Over 14 days, the patient showed significant improvement, with a reduction in manic symptoms and stabilization of mood. The patient was discharged after 21 days with continued maintenance treatment.

Case 2

A 60-year-old homemaker was brought to the outpatient department (OPD) of the Department of Psychiatry by her family due to a 10-day history of low mood, decreased interaction, frequent crying spells, death wishes, decreased sleep, and poor appetite. The family reported that she had been functioning well in her daily activities, taking care of herself and the household, and maintaining positive social interactions. However, a sudden behavior change was observed, characterized by decreased energy, sadness, frequent crying, insomnia, loss of appetite, and irritability towards her husband, leading to physical assaults. Due to the severity of the symptoms, the family sought psychiatric evaluation.

The patient had a known diagnosis of bipolar affective disorder I for the past 34 years. She had previously been prescribed lithium (800 mg), sertraline (50 mg), and clonazepam (0.5 mg), with a reported 60–70% improvement in her symptoms. However, she was non-compliant with medication, often claiming to be fine without it. Due to her symptoms, she was brought to the OPD of the Department of Psychiatry.

Considering the severity of the symptoms, the patient was admitted, and initiated on sertraline (50 mg), which was later optimized to 100 mg, lithium (800 mg), and lorazepam (2 mg). With this treatment regimen, the patient's low mood and decreased interaction improved, leading to her discharge. However, within a week of discharge, the patient's symptoms rapidly escalated.

She became talkative, hyperactive, and exhibited over-familiarity. Her sleep patterns were disrupted, and she accused her husband of having an extramarital affair and attempting to

Table 2: The clinical data of all the patients

Case no.	*1*	*2*	*3*	*4*	*5*	*6*	*7*	*8*	*9*
Diagnosis	OCD	Bipolar affective disorder-I	Post partum depression	Adjustment disorder-depressive reaction	Adjustment disorder-depressive reaction	Adjustment disorder- brief depressive reaction	Adjustment disorder-depressive reaction	Recurrent depressive disorder	Severe depression Catatonia
Duration of illness	20 years	34 years	3 months	2 months	2 weeks	2 months	3 months	10 years	8 months
Duration of treatment	20 years	33 years	2 weeks	1 month	5 days	2 weeks	1 month	3 weeks	6 months
Number of depressive episodes in the past	2	14	1	1	1	1	1	12	1
Number of manic episodes in the past	>10	4	0	0	0	0	0	0	0
Psychotic symptoms	Present	Present	Present	Absent	Absent	Present	Absent	Absent	Present
Mood stabilizer	Poor treatment adherence	Yes	No	No	No	No	No	No	Yes
TEAS antidepressant causing TEAS duration treatment	Fluoxetine 60 mg 20 days	Sertraline 50 mg 14 days	Sertraline 50 mg 2 weeks	Escitalopram 10 mg 1 month	Fluoxetine 30 mg 5 days	Fluvoxamine 150 mg 2 weeks	Sertraline 50 mg 4 weeks	Escitalopram 10 mg 3 weeks	Escitalopram 10 mg 12 days
TEAS management	Lithium 800 mg Quetiapine 200 mg CPZ 300 mg	Lithium 600 mg Quetiapine 100 mg	Lithium 600 mg Olanzapine 7.5 mg	Lithium 600 mg Olanzapine 2.5 mg	Valproate 1000 mg Olanzapine 7.5 mg	Lithium 800 mg Quetiapine 200 mg	Lamotrigine 100 mg Olanzapine 7.5 mg	Lithium 800 mg Quetiapine 200 mg	Valproate 500 mg Risperidone 4 mg

CPZ, chlorpromazine; OCD, obsessive–compulsive disorder

poison her. Due to the emergence of manic symptoms, sertraline was discontinued, and quetiapine (100 mg) was initiated.

Following the medication adjustment, the patient showed improvement, with a reduction in manic symptoms, stabilization of mood, and resolution of paranoid ideation. The patient was discharged after 14 days with instructions for continued treatment and close monitoring.

Discussion

The case series includes nine patients with various psychiatric diagnoses, such as bipolar disorder, postpartum depression, adjustment disorder, and recurrent depressive episodes with occasional hypomanic episodes. They all experienced mood shifts from depression to mania or hypomania due to changes in psychotropic medication, particularly antidepressants, underscoring the need for careful monitoring, especially in those with a bipolar disorder history or family background.

Our observations align with existing literature, including the World Health Organization's ICD-11 system and CANMAT/International Society for Bipolar Disorders (ISBD) bipolar disorder guidelines.[1,12] Various studies contribute insights into bipolar disorder, its comorbidities, late-onset, and treatment strategies.[2,6,7] Controlled studies by Tamada, Mundo, and Vieta highlight the need for vigilant monitoring when administering antidepressants to bipolar patients.[8,9,11]

In our study, a significant observation was that the majority of patients had a positive family history of bipolar affective disorder, which aligns with Isheeta Zalpuri's findings.[13] We also noted that two patients had severe depression, consistent with the research work of Josep Maria Haro, which reported increased severity in patients switching antidepressants.[14] Our study indicates a notably higher risk of manic switches, especially within the first month of antidepressant use, corroborated by the work of Tonguc D Berkol et al.[14,15]

Conclusion

The case series provides valuable insights into medication-induced mood shifts in bipolar disorder, from depression to mania or hypomania. Examining multiple cases reveals diverse patient demographics, including age, sex, and comorbidities, contributing to varied treatment responses. Illness duration, prior episodes, and treatment lengths also vary.

Treatment-emergent affective switch underscores the importance of comprehensive patient history assessment, considering family history and risk factors. Identifying high-risk individuals informs treatment decisions, guiding medication selection to minimize mood switch risk.

Managing this switch demands tailored approaches, involving dose adjustments, discontinuation of triggers, and introducing mood stabilizers. Success in stabilizing mood emphasizes personalized treatment and vigilant patient monitoring.

Orcid

Jesvin L Johnson https://orcid.org/0009-0008-3303-684X

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