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Case Report



Simultaneous Onset of Bipolar Disorder and Epilepsy: Unraveling the Neurobiological Links in a Case Report

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Abstract

Introduction: Bipolar disorder often presents with alternating episodes of depression and mania or hypomania. It shares similarities with epilepsy, including its episodic nature and response to similar medications. The common underlying neurobiological mechanisms of these conditions and the temporal association in this case raise the question of a possible link between the two conditions.

Case Presentation: A 51-year-old woman presented with manic symptoms following an exacerbation of seizure attacks after discontinuing her antiepileptic medications. She experienced generalized tonic-clonic seizures without aura, each lasting 2 - 3 minutes, followed by postictal confusion. During episodic clusters of seizures, lasting 10 - 20 days, she had 1 - 4 seizures daily. Her first seizure and manic episode occurred simultaneously at the age of 20. Manic symptoms, including elevated mood, grandiosity, reduced need for sleep, talkativeness, irritability, and auditory and tactile hallucinations, consistently emerged during seizure exacerbations. Neurological examination was normal, and mood symptoms improved with seizure control.

Discussion: The patient's case highlights the close link between epilepsy and bipolar disorder. The overlap in pharmacological treatments, particularly antiepileptic drugs like valproate and carbamazepine, suggests a shared pathophysiology. Potential mechanisms include dysfunction in neurotransmitter systems, such as GABA and purinergic signaling, and structural brain changes. Recent studies suggest that abnormalities in Ankyrin-G isoforms may contribute to the comorbidity.

Conclusions: This case demonstrates a temporal association between seizure activity and bipolar symptoms, suggesting that epilepsy may be a contributing factor in the development of bipolar disorder. This could indicate a possible association between the two conditions. Further studies are required to explore the underlying mechanisms and improve therapeutic approaches for comorbid epilepsy and bipolar disorder to help clinicians achieve an exact diagnosis and effective management.

Keywords: Bipolar Disorder, Bipolar I Disorder, Epilepsy

1. Introduction

Bipolar disorder is marked by alternating episodes of depression and either mania (bipolar I) or hypomania (bipolar II). Manic and hypomanic episodes involve distinct periods of elevated or irritable mood, increased energy, and heightened activity, representing a noticeable change from previous behavior. Bipolar I is characterized by manic symptoms lasting for one week or severe enough to require inpatient treatment, whereas bipolar II involves milder hypomanic episodes lasting for at least 4 days and does not necessitate hospitalization but can still cause impairment in important areas of functioning. Patients with bipolar disorder may experience various psychotic symptoms, including delusions and hallucinations. The presence of atypical psychotic symptoms may suggest an underlying medical cause (1, 2). Some medical conditions can develop mood symptoms; one such condition is epilepsy, where symptoms of depression and mania can be observed, and there is a high rate of seizure and bipolar disorder comorbidity (3).

Epilepsy is a chronic neurological disorder marked by a persistent tendency to produce seizures that occur without any immediate trigger from the central

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nervous system. It is also characterized by the neurobiological, cognitive, psychological, and social impacts resulting from recurrent seizures (4). There are similarities between epilepsy and bipolar disorder, including their episodic nature, the potential role of kindling mechanisms, and the effectiveness of certain antiepileptic drugs in treatment. Studies suggest possible common underlying neurobiological and neuroanatomical factors to both bipolar disorder and epilepsy (5). A systematic review highlights the significant prevalence of psychiatric disorders among individuals with epilepsy, with mood disorders being the most commonly reported comorbidity. Specifically, bipolar disorder was found in 6.2% of the epilepsy population studied, which is notably higher compared to the general population. This association could be attributed to shared pathophysiological mechanisms between epilepsy and mood disorders, including alterations in brain structures and neurotransmitter systems (6). This case report highlights a rare and clear temporal association between seizure exacerbations and the onset of manic episodes without prior depressive symptoms. The immediate emergence of manic features following seizures, along with the stabilization of mood after seizure control, provides valuable insight into the potential shared neurobiological pathways between epilepsy and bipolar disorder.

2. Case Presentation

A 51-year-old unmarried woman presented to the psychiatric emergency department with symptoms of a manic episode following an exacerbation of seizure attacks. The patient's seizure exacerbation began approximately two months ago, following the discontinuation of her medications, which included levetiracetam (2000 mg/day), sodium valproate (1000 mg/day), and clobazam (10 mg at night). The patient's seizure episodes were characterized by generalized tonic-clonic seizures without any aura. Each seizure lasted approximately 2 - 3 minutes, occasionally accompanied by urinary incontinence, and was followed by a postictal period of reduced consciousness lasting about 10 - 15 minutes. Additionally, she had focal seizures during the day, presenting as consistent jerking of the left upper limb. Neurological examinations, including cranial nerve assessments and tendon reflex evaluations, were normal. There was no evidence of papilledema. Sensory, motor, and limb strength evaluations were within normal limits.

Concurrently with these symptoms, the patient gradually developed signs of elevated mood, increased

energy, reduced need for sleep, irritability, talkativeness, and formal thought disturbance. These symptoms were accompanied by grandiose delusions and auditory and tactile hallucinations, leading to significant impairment her occupational, social, and interpersonal in functioning. The patient's psychiatric symptoms first appeared at the age of 20, following her first seizure, presenting as a mixed episode of bipolar disorder. After controlling the seizures with antiepileptic drugs (sodium valproate 1500 mg/day and lamotrigine 100 mg/day) and a second-generation antipsychotic (olanzapine 10 mg/day), her psychiatric symptoms were also controlled, and she maintained normal functioning. Over the years, whenever she discontinued her medications, she experienced the onset of her illness, including one mixed episode and two manic episodes, all of which occurred immediately following seizure exacerbations. Based on DSM-5TR criteria, she was diagnosed with bipolar and related disorder due to epilepsy. Over the course of her illness, the patient experienced three episodic clusters of seizures, each lasting about 10 - 20 days. During these periods, she had between 1 to 4 seizures per day, all following the same tonic-clonic pattern. Importantly, the onset of these seizure clusters coincided with the emergence of mood episodes.

Further examination revealed that the patient's father had a history of epilepsy, though no psychiatric disorders were found among her relatives. The patient had no history of trauma, and no other medical conditions were diagnosed. Her MRI showed no pathological findings, and her EEG indicated slow background waves. Thyroid function and electrolyte tests were also within the normal range. The patient's mood symptoms resolved after the seizures were controlled by the administration of levetiracetam 1000 mg, sodium valproate 1000 mg, and clobazam 10 mg. The remaining psychotic symptoms were resolved with the prescription of 5 mg olanzapine.

3. Discussion

Bipolar disorder and epilepsy are known to have similarities in their course, progression, and response to treatment. The GABAergic mechanisms targeted by some antiepileptic drugs have been suggested to affect both conditions. Additionally, studies have highlighted the potential role of dopamine and glutamate in bipolar disorder and their modulation of epileptic activity. In voltage-gated ion channels, sodium, calcium, and potassium channels could play a role in the etiology of both disorders (7, 8). Kudo et al. in 2001 showed in a study that manic symptoms in patients with epilepsy differ from those in patients with bipolar disorder, such as rapid cycling and fluctuating mood disturbances (9). However, in our case, this difference was not observed, which could indicate that a type I bipolar disorder developed following epilepsy, rather than a manic episode occurring during a seizure.

In the context of comorbid bipolar disorder and epilepsy, the overlap in pharmacological treatments, particularly those targeting purinergic signaling, provides a compelling area for further investigation. Lithium, valproate, and carbamazepine, widely recognized for their efficacy in bipolar disorder, also demonstrate significant anticonvulsant properties. These medications appear to exert their effects by modulating ATP and adenosine levels, suggesting a shared pathophysiological mechanism between the two conditions. The identified adenosine deficit, a critical factor in both disorders, suggests that purine metabolism may be an essential therapeutic target. This overlap not only highlights the potential for treatment synergy but also underscores the importance of considering the biochemical underpinnings when selecting therapeutic strategies for patients with comorbid bipolar disorder and epilepsy. Purines have been linked to various neurological and psychiatric disorders. The adenosine-increasing effects of several antiepileptic and antimanic therapies suggest that an adenosine deficit may play a fundamental pathogenic role in bipolar mania, similar to its established role in epilepsy (10).

Recent studies have underscored the importance of Ankyrin-G isoforms in regulating neuronal function, particularly concerning bipolar disorder and epilepsy. The imbalance in Ankyrin-G isoforms, especially in parvalbumin-positive interneurons and excitatory principal cells, has been implicated in the disruption of sodium channel function and neuronal excitability. This molecular phenotype could potentially underlie the comorbidity observed between epilepsy and bipolar disorder, suggesting that abnormalities in Ankyrin-G may sensitize neural circuits, contributing to the development of both conditions (11). Neuro-endocrine disturbances, such as a hyperactive hypothalamicpituitary-adrenal axis resulting in increased cortisol secretion and anatomical changes identified with MRI and volumetric measurements, such as temporal and frontal lobes atrophy, were also seen in patients with bipolar disorders and epilepsy (12).

The novelty of this case lies in the clear temporal association between seizure onset and the emergence of manic symptoms, with no preceding history of depressive episodes. Unlike previous reports where mood disturbances in epilepsy often include depression or are difficult to distinguish from ictal phenomena, our patient demonstrated distinct manic episodes directly following seizure exacerbations. Moreover, the patient's consistent pattern of seizure control correlating with stabilization emphasizes mood the potential neurobiological link between epilepsy and bipolar disorder. This clear temporal and symptomatic relationship, observed in the absence of major neurological deficits and structural brain abnormalities, offers a unique contribution to understanding the comorbidity of these two conditions.

4. Conclusions

As previously mentioned, bipolar disorder and epilepsy have a high comorbidity, and numerous studies have identified significant overlaps in neurotransmitter pathways and ion channels between the two conditions. From a neuroanatomical perspective, there are multiple common regions involved in both disorders. These findings suggest a strong association between the symptoms of these two conditions. However, in our case, the clear temporal association between the onset of bipolar disorder and epilepsy may indicate that epilepsy could be the underlying cause of bipolar disorder rather than manic symptoms occurring during a seizure. In other words, the onset of epilepsy might disrupt shared neurobiological mechanisms. leading to the development of bipolar disorder. Despite the absence of a positive family history and other neuropsychiatric and neurobiological factors, the common etiologies of bipolar disorder remain the most plausible in this case. A closer examination and broader studies are needed to investigate this hypothesis further to help clinicians achieve an exact diagnosis and effective management of cases with this possible causal comorbid condition.

Footnotes

Authors' Contribution: F. Sh. contributed in the design and conception of the work, participate in clinical management of the patient as psychiatrist, reviewed, and edited the final version. B. A. contributed in the conception of the work, did the literature search, and contributed to drafting the manuscript and editing the manuscript.

Conflict of Interests Statement: The authors declare no conflict of interest.

Data Availability: In order to preserve the privacy of the patients, the datasets used in this work are not

accessible to the general public. However, the corresponding author can provide them to anyone who makes a valid request.

Ethical Approval: This study was approved by the Ethics Committee of Mazandaran University of Medical Sciences under the license number: IR.MAZUMS.REC.1403.289.

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References

- Chakrabarti S, Singh N. Psychotic symptoms in bipolar disorder and their impact on the illness: A systematic review. World J Psychiatry. 2022;12(9):1204-32. [PubMed ID: 36186500]. [PubMed Central ID: PMC9521535]. https://doi.org/10.5498/wjp.v12.i9.1204.
- Nierenberg AA, Agustini B, Kohler-Forsberg O, Cusin C, Katz D, Sylvia LG, et al. Diagnosis and Treatment of Bipolar Disorder: A Review. *JAMA*. 2023;**330**(14):1370-80. [PubMed ID: 37815563]. https://doi.org/10.1001/jama.2023.18588.
- 3. Li J, Ledoux-Hutchinson L, Toffa DH. Prevalence of Bipolar Symptoms or Disorder in Epilepsy. *Neurology*. 2022;**98**(19). https://doi.org/10.1212/wnl.000000000200186.
- 4. Beghi E. The Epidemiology of Epilepsy. *Neuroepidemiology*. 2020;**54**(2):185-91. [PubMed ID: 31852003]. https://doi.org/10.1159/000503831.

- Mazza M, Di Nicola M, Della Marca G, Janiri L, Bria P, Mazza S. Bipolar disorder and epilepsy: a bidirectional relation? Neurobiological underpinnings, current hypotheses, and future research directions. *Neuroscientist.* 2007;13(4):392-404. [PubMed ID: 17644769]. https://doi.org/10.1177/10738584070130041101.
- Lu E, Pyatka N, Burant CJ, Sajatovic M. Systematic Literature Review of Psychiatric Comorbidities in Adults with Epilepsy. *J Clin Neurol.* 2021;**17**(2):176-86. [PubMed ID: 33835737]. [PubMed Central ID: PMC8053555]. https://doi.org/10.3988/jcn.2021.17.2.176.
- Amann B, Grunze H. Neurochemical underpinnings in bipolar disorder and epilepsy. *Epilepsia*. 2005;46 Suppl 4:26-30. [PubMed ID: 15938708]. https://doi.org/10.1111/j.1528-1167.2005.463006.x.
- Simmonite M, Steeby CJ, Taylor SF. Medial Frontal Cortex GABA Concentrations in Psychosis Spectrum and Mood Disorders: A Metaanalysis of Proton Magnetic Resonance Spectroscopy Studies. *Biol Psychiatry*. 2023;93(2):125-36. [PubMed ID: 36335069]. [PubMed Central ID: PMC10184477]. https://doi.org/10.1016/j.biopsych.2022.08.004.
- Kudo T, Ishida S, Kubota H, Yagi K. Manic episode in epilepsy and bipolar I disorder: a comparative analysis of 13 patients. *Epilepsia*. 2001;**42**(8):1036-42. [PubMed ID: 11554891]. https://doi.org/10.1046/j.1528-1157.2001.0420081036.x.
- Daniels SD, Boison D. Bipolar mania and epilepsy pathophysiology and treatment may converge in purine metabolism: A new perspective on available evidence. *Neuropharmacology*. 2023;241:109756. [PubMed ID: 37820933]. [PubMed Central ID: PMC10841508]. https://doi.org/10.1016/j.neuropharm.2023.109756.
- Lopez AY, Wang X, Xu M, Maheshwari A, Curry D, Lam S, et al. Ankyrin-G isoform imbalance and interneuronopathy link epilepsy and bipolar disorder. *Mol Psychiatry*. 2017;22(10):1464-72. [PubMed ID: 27956739]. [PubMed Central ID: PMC5798616]. https://doi.org/10.1038/mp.2016.233.
- Kanner AM, Shankar R, Margraf NG, Schmitz B, Ben-Menachem E, Sander JW. Mood disorders in adults with epilepsy: a review of unrecognized facts and common misconceptions. *Ann Gen Psychiatry*. 2024;23(1):11. [PubMed ID: 38433207]. [PubMed Central ID: PMC10910742]. https://doi.org/10.1186/s12991-024-00493-2.