Ahmad Dahlan Medical Journal
VOL 6, No. 2, 216-221
http:// http://journal2.uad.ac.id/index.php/admj

Case Report

Multidimensional Clinical Challenges in a Female with Chronic Epilepsy on Phenytoin: A Case Report

[1]Syafira Laila Nurulita*, [2]Rusdi Lamsudin
Email (Corresponding Author) : *syafiralailanurulita@gmail.com
[1]Department of Neurology, Faculty of Medicine, Universitas Islam Indonesia, Yogyakarta, Indonesia
[2]Department of Neurology, Faculty of Medicine, Universitas Ahmad Dahlan, Yogyakarta, Indonesia

ARTICLE INFO

Article history
Received 29 Aug 25
Revised 03 Okt 25
Accepted 07 Okt 25

Keywords
epilepsy,
phenytoin,
sexual dysfunction,
clobazam,
comprehensive management

ABSTRACT

Epilepsy is a long-standing neurological disorder defined by recurrent, unprovoked seizures, affecting more than 50 million individuals globally and influencing physical, mental, and social aspects of life. Continuous administration of antiepileptic drugs (AEDs) such as phenytoin is a common therapeutic strategy; however, prolonged use may result in adverse effects that complicate treatment. This case report describes a 40-year-old woman with epilepsy since the age of four, presenting with recurrent seizures, impaired memory, headaches, and sexual dysfunction. Her most recent event was an absence seizure accompanied by upward eye deviation and tongue biting. Electroencephalography (EEG) demonstrated generalized spike-and-wave patterns. The patient was treated with phenytoin and folic acid, with the recent addition of clobazam, leading to favorable outcomes, including reduced seizure frequency, improved sleep, and diminished anxiety and dizziness. A persistent reduction in libido, first noted during adolescence, was suspected to be associated with long-term phenytoin use. Additionally, dental problems such as caries and tooth impaction were believed to worsen headache intensity. This case emphasizes the need for a comprehensive approach to epilepsy care, considering psychological conditions, cognitive impairment, and oral health. Prompt recognition of AED-related side effects and individualized treatment planning are essential to optimize patient outcomes.

INTRODUCTION

Epilepsy is a persistent neurological disorder marked by repeated, unprovoked seizures, impacting more than 50 million people worldwide and potentially diminishing quality of life across physical, emotional, and social spheres. Its clinical presentation is highly diverse, encompassing various seizure types and comorbid conditions, which demand a comprehensive and multidisciplinary approach to management. Long-term use of antiepileptic drugs (AEDs) continues to be the mainstay of therapy; however, it frequently poses challenges due to potential adverse effects that can complicate treatment. This report describes the case of a 40-year-old

woman with long-standing epilepsy, discussing the strategies employed in her management and examining the possible association between prolonged phenytoin therapy and sexual dysfunction[1–3].

CASE PRESENTATION

A 40-year-old woman visited the neurology outpatient clinic for follow-up after experiencing a seizure episode five days earlier. She had been diagnosed with epilepsy since the age of four, with the initial event being a febrile seizure occurring when her body temperature exceeded 38°C. The latest episode was characterized as an absence seizure, accompanied by upward deviation of the eyes and tongue biting. No aura preceded the event, and it was followed by postictal disorientation and memory loss. Over the years, she had exhibited multiple seizure types, including generalized tonic–clonic and absence seizures.

In addition to her seizure history, the patient reported experiencing left-sided, pulsating headaches for the past six months. These headaches were linked to dental problems, including caries and tooth impaction, which significantly disrupted daily functioning. Six months earlier, she had suffered a severe bout of dizziness that required a month of bed rest and was accompanied by nausea and vomiting. She also complained of cognitive issues, such as impaired memory, confusion, and disorientation.

The patient described a long-standing history of affective disturbances, including marked anxiety, fearfulness, and emotional instability, particularly when discussing sensitive subjects such as family issues, separation, or death. These psychological symptoms had persisted for years and gradually worsened, at times accompanied by somatic signs such as tachycardia. She also noted a decline in sexual desire beginning in adolescence, which was suspected to be linked to prolonged phenytoin use. Her obstetric history included a full-term delivery via vacuum extraction, with the pregnancy marked by poor maternal nutrition and lack of antenatal care, potentially affecting her neurological development. Cardiovascular assessment, including ECG and echocardiography, yielded normal findings, suggesting her tachycardia was likely psychogenic.

The patient had been receiving continuous phenytoin therapy since the age of 15. Although effective for seizure control, long-term treatment had been associated with side effects, notably sexual dysfunction. She also took folic acid supplementation to prevent deficiency and support neurological health. Recently, clobazam was prescribed three times daily, leading to better seizure control, reduced anxiety, improved sleep quality, and diminished dizziness. She had previously used phenobarbital but discontinued it due to excessive sedation and cognitive impairment.

On examination, the patient was alert and oriented but appeared anxious. Vital signs showed normal blood pressure 103/68 mmHg, tachycardia with heart rate 121 beats per minute (bpm), respiratory rate 20 breath per minute, normal body temperature 36,5^{o}C and oxygen saturation 98% on room air. Neurological assessment revealed no focal deficits. Cardiovascular examination demonstrated normal heart sounds without murmurs. Oral evaluation identified dental caries and impacted teeth, which were believed to exacerbate her headaches. EEG results showed generalized spike-and-wave discharges consistent with absence seizures. Routine laboratory tests, including complete blood count and metabolic profile, were within normal limits.

DISCUSSION

Epilepsy treatment often requires prolonged administration of antiepileptic drugs (AEDs), which may result in a variety of side effects. Phenytoin, one of the frequently prescribed AEDs, has been linked in several reports to sexual dysfunction. While the precise pathophysiological mechanism remains unclear, it is thought that that phenytoin may disrupt hormonal regulation and alter neurotransmitter activity, accelerating sexual hormone metabolism, and stimulating the production of the hormone binding globulin resulting in decreased free testosterone (FT). Furthermore, its direct action on the central nervous system could impair sexual arousal and performance[4–7].

In this patient, the persistent decrease in libido is likely associated with long-term phenytoin exposure. Nevertheless, sexual dysfunction is a multifactorial condition; psychological distress, chronic illness, and the inherent impact of epilepsy on sexual health must also be considered. The onset of her symptoms during adolescence aligns with the initiation of phenytoin therapy, strengthening the suspected link.[8-9]

Her history of headaches and dental pathology suggests a potential relationship between oral health and neurological manifestations Studies show that people with epilepsy have significantly poorer dental outcomes than non-epileptic controls of similar age, characterized by more decayed and absent teeth, limited restorative or prosthetic treatment, and higher periodontal and abrasion scores. This condition is partly caused by the use of phenytoin, which is associated with gingival hyperplasia. Conditions such as dental caries and tooth impaction can aggravate headache intensity, underscoring the value of thorough dental assessment and management in individuals with chronic neurological disorders. Early dental intervention may alleviate pain and contribute to overall well-being. Furthermore, headaches are a common (>10%)

adverse effect of anti-seizure medication, and are most often associated with carbamazepine, phenytoin, lamotrigine and levetiracetam[10-12].

Cognitive impairment is another common concern in epilepsy, influenced by the underlying neurological disorder, medication effects, and the psychosocial burden of chronic disease. Prolonged phenytoin therapy has been specifically associated with deficits in memory and cognition, which can interfere with daily functioning and reduce quality of life. Prolonged use of phenytoin has been associated with folate and vitamin B12 deficiency, which subsequently leads to elevated homocysteine levels. Hyperhomocysteinemia has been implicated in neurotoxicity and vascular dysfunction, thereby contributing to cognitive impairment in affected patients. In this case, the management plan incorporated continued use of phenytoin and folic acid, with the addition of clobazam to address breakthrough seizures. Her prior intolerance to phenobarbital—manifesting as excessive sedation and cognitive slowing—illustrates the need for personalized treatment selection and close monitoring. Ongoing evaluation of therapeutic efficacy and side effects is vital to balance seizure control with quality of life[9–13].

Clobazam, a benzodiazepine derivative used as an adjunctive AED, acts by potentiating gamma-aminobutyric acid (GABA) activity, thereby stabilizing neuronal excitability. In this patient, its use was associated with reduced seizure frequency and duration, improved mood stability, decreased anxiety, and relief from dizziness. Its anxiolytic effects likely contributed to improved sleep quality, which in turn may further reduce seizure risk[14–16].

Restorative sleep plays a crucial role in epilepsy management, as sleep deprivation can trigger seizures in susceptible patients. By enhancing both seizure control and overall well-being, clobazam addresses multiple therapeutic goals. However, given the risks of tolerance and dependence, long-term administration should be carefully supervised, with periodic dose adjustments based on clinical response and side effect monitoring[17 – 20].

CONCLUSION

This case underscores the multifaceted nature of epilepsy management, particularly when complicated by multiple comorbidities. Long-term adverse effects of antiepileptic drugs (AEDs), such as sexual dysfunction, require careful consideration due to their profound influence on patients' quality of life. Optimal seizure control depends on regular follow-up, continuous monitoring, and individualized treatment strategies. A comprehensive care plan should also address psychological symptoms, cognitive deficits, headaches, and oral health problems. Further investigation is needed to clarify the mechanisms behind AED-induced sexual dysfunction and to establish effective therapeutic interventions.

REFERENCES

1. Weinstein S. Seizures and epilepsy: An overview. Epilepsy: The Intersection of Neurosciences, Biology, Mathematics, Engineering, and Physics. 2016;65–77.
2. Srivastav Y, Prajapati A, Agrahari P, Kumar M. Review of the Epilepsy, Including Its Causes, Symptoms, Biomarkers, and Management. Asian Journal of Research in Medical and Pharmaceutical Sciences. 2023;12(4):64–84.
3. Brodie MJ, Besag F, Ettinger AB, Mula M, Gobbi G, Comai S, Aldenkamp AP, Steinhoff BJ. Epilepsy, Antiepileptic Drugs, and Aggression: An Evidence-Based Review. Pharmacol Rev. 2016;68(3):563–602.
4. Kanner AM. Most antidepressant drugs are safe for patients with epilepsy at therapeutic doses: A review of the evidence. Epilepsy and Behavior. 2016;61:282–286.
5. Mulaf M. The pharmacological management of psychiatric comorbidities in patients with epilepsy. Pharmacological Research. 2016;107:147–153.
6. Potnis VV, Albhar KG, Nanaware PA, Pote VS. A Review on Epilepsy and its Management. Journal of Drug Delivery and Therapeutics. 2020;10(3):273–279.
7. Calabrò RS, Cerasa A. Drug-Induced Sexual Dysfunction in Individuals with Epilepsy: Beyond Antiepileptic Compounds. Medicines (Basel). 2022;9(3):23.
8. Brenk-Franz K, Häuser W, Brähler E, Schneider N, Hoy M, Strauß B. Sexual Dysfunctions and Health-Related Impairment in Patients With Chronic Disease. Deutsches Arzteblatt International. 2024;121(2):66-67.
9. Atif M, Sarwar MR, Scahill S. The relationship between epilepsy and sexual dysfunction: a review of the literature. Springerplus. 2016;5(1):2070.
10. Samami M, Najar-Karimi F, Eghbali BB, Sanati AH, Rad AH. Oral and dental health status in patients with chronic headache. BMC Oral Health. 2024;24(1).
11. Rastogi S, Rastogi R. Dental care associated with patients suffering from neurological disorders. Chapter. April 2022. doi:10.52305/MEHM5624.
12. Bauer, P.R., Tolner, E.A., Keezer, M.R. *et al.* Headache in people with epilepsy. *Nature Review Neurologyl* 2021;**17(9)**, 529–544.
13. Xu Y, Zhang N, Xu S, Xu H, Chen S, Xia Z. Effects of phenytoin on serum levels of homocysteine, vitamin B12, folate in patients with epilepsy: A systematic review and meta-analysis (PRISMA-compliant article). *Medicine (Baltimore)*. 2019;98(12):e14844.
14. Sarma AK, Khandker N, Kurczewski L, Brophy GM. Medical management of epileptic seizures: Challenges and solutions. Neuropsychiatric Disease and Treatment. 2016;12:467–485.
15. Ghosh S, Sinha JK, Ghosh S, Sharma H, Bhaskar R, Narayanan KB. A Comprehensive Review of Emerging Trends and Innovative Therapies in Epilepsy Management. Brain Sciences. 2023;13(9):1305.
16. Potnis VV, Albhar KG, Nanaware PA, Pote VS. A Review on Epilepsy and its Management. Journal of Drug Delivery and Therapeutics. 2020;10(3):273–9.
17. Satishchandra P, Rathore C, Apte A, Kumar A, Mandal A, Chauhan D, et al. Evaluation of one-year effectiveness of clobazam as an add-on therapy to anticonvulsant monotherapy in participants with epilepsy having uncontrolled seizure episodes: An Indian experience. Epilepsy & Behavior. 2022;130:108671
18. Sumadewi KT, Harkitasari S, Tjandra DC. Biomolecular mechanisms of epileptic seizures and epilepsy: a review. Acta Epileptologica. 2023;5(1):28.
19. Moore JL, Carvalho DZ, St Louis EK, Bazil C. Sleep and Epilepsy: a Focused Review of Pathophysiology, Clinical Syndromes, Co-morbidities, and Therapy. T*he Journal of The American Society for Experimental Neurotherapeutics*. 2021;18(1):170-180.
20. Manole AM, Sirbu CA, Mititelu MR, Vasiliu O, Lorusso L, Sirbu OM, et al. State of the Art and Challenges in Epilepsy—A Narrative Review. Journal of Personalized Medicine. 2023;13(4):623.
21. Michaelis R, Tang V, Wagner JL, Modi AC, Lafrance WC, Goldstein LH, et al. Psychological treatments for people with epilepsy. The Cochrane Database of Systematic Reviews. 2017;10 (10): CD012081.
22. Spanos S, Hutchinson K, Ryder T, Rapport F, Goodwin N, Zurynski Y. Integrated Care in Epilepsy Management: A Scoping Review of the Models and Components of Health and Social Care Delivery. International Journal Of Integrated Care. 2024;24(1):18.
23. Kathiravan M, Kavitha S, Shanthi R. To determine the effect of long-term antiepileptic drug on the serum folate and vitamin B12 among epileptic patients. Scientific Report. 2021;11(1):4393.
24. Gupta M, Tripp J. Phenytoin. [Updated 2023 Jul 10]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2025 Jan-. Available from: https://www.ncbi.nlm.nih.gov/books/NBK551520/