

Acute Phenobarbital Poisoning in a Resource-Limited Setting: A Case Report of Successful Management through High Index of Suspicion and Immediate Care

Nanati Jemal^{1*}, Biruk Zenebe¹, Elezer Berhanu¹, Tesfaye Alemnew¹, Yafet Solomon¹, Bitania Debalke¹

ABSTRACT

A 33-year-old known epileptic female patient, who has been on phenobarbital 100 mg orally once daily for the past 6 years, presented to our emergency room after she was found unconscious. On presentation, she was unable to protect her airway and had significant oral secretions upon airway examination. Glasgow Coma Scale was 3/15 with severe respiratory compromise, necessitating immediate intubation and mechanical ventilation. Due to the high index of suspicion given the clinical presentation, serum phenobarbital level was determined and had shown to be markedly elevated. Hence, the diagnosis of phenobarbital poisoning was confirmed. Following this, the patient was promptly managed with two cycles of hemodialysis. After that, the patient regained consciousness. This case led us to conclude that clinicians need to have a high index of suspicion of medication overdose in epileptic patients and, therefore, should take a thorough medication history.

Keywords: Phenobarbital overdose, Phenobarbital poisoning, Epilepsy, Hemodialysis, case report

1. Addis Ababa University, Addis Ababa, Ethiopia.

Correspondence: Nanati Jemal

Email: nanatialiye@gmail.com

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1. Introduction

Phenobarbital, a first-generation antiepileptic, is commonly prescribed to treat generalized tonic-clonic seizures and focal seizures and as second-line management for status epilepticus.⁽¹⁾ Despite its efficacy in clinical practice, it is also associated with adverse side effects, some of which include depressed cardiorespiratory system, and loss of consciousness.^(2,3) This case report aims to showcase the clinical presentation of phenobarbital overdose and its management in resource-limited settings via the use of hemodialysis.

2. Case presentation

The patient was a 33-year-old female who has been a known epileptic for the past 6 years on phenobarbital 100 mg orally once daily for the past 2 years, with good adherence to the regimen. The patient had presented at our emergency with loss of consciousness of unknown duration (estimated around 4 hours) after she was found unconscious in her bedroom. There was no history of witnessed abnormal body movements, previous suicidal attempts, or significant medical history such as diabetes mellitus, hypertension, or cardiac issues. During the evaluation of the patient in the Emergency room, underlying psychological

stressors that could have prompted an intentional overdose were suspected but not explicitly confirmed.

On presentation at our hospital, the patient was unable to protect her airway with significant oral secretions and had desaturated to the level of 77% on room air. She was tachycardic to the level of 114. The respiratory drive was almost absent. With a Glasgow Coma Scale (GCS) score of 5/15 that had dropped to 3/15 within minutes, the patient was immediately intubated with an Endotracheal tube (6.5 mm). Secretions were suctioned, and the patient was put on a mechanical ventilator.

After a complete physical examination, a decreased air entry with crepitations was noted in the right lower one-third of the lung field. The rest of the physical examination remained normal.

Investigation

Upon the patient's arrival at the emergency room, a point of care ultrasound exam was performed, which revealed a collapsing IVC and bilateral b. lines. After the patient was stabilized, CBC, Serum electrolyte (K, Na, Cl, Ca), RBS, RFT, LFT, ECG, CXR, Brain CT scan, and Serum Phenobarbital were planned. The results are summarized in Table 1, Figure 1, and Figure 2.

Table 1: The investigation summary of the patient

Ordered Tests	Date (16/07/2024)	Date (17/07/2024)
Complete blood count	WBC= 5.4k with 86% Neutrophil and 11% lymphocyte Hgb= 14.9, HCT= 45.9, MCV= 93.8 PLT=179k	WBC= 7.54k with 82.6% Neutrophil and 10.1% lymphocyte Hgb= 10.2, HCT= 28, MCV= 90.3 PLT=139k
Renal Function Test	Ur= 15, Cr= 0.6	
Liver Function Test	AST= 16, ALT=10, ALP=49 TB=0.3, DB=0.085	AST= 16, ALT=8, ALP=43
Serum Electrolyte	Na+= 135, K+= 3.6, Cl-: 107	Na+= 142, K+= 3.3, Cl-: 107.6
Urine HCG	negative	
Urine Analysis	Non-revealing	
Infectious Panel	VDRL: Non-reactive, HepB Surface antigen: Negative, HCV antibody: Negative	
Serum Phenobarbital	88µg/ml	
Brain Computed Tomography (CT) Scan	Normal	

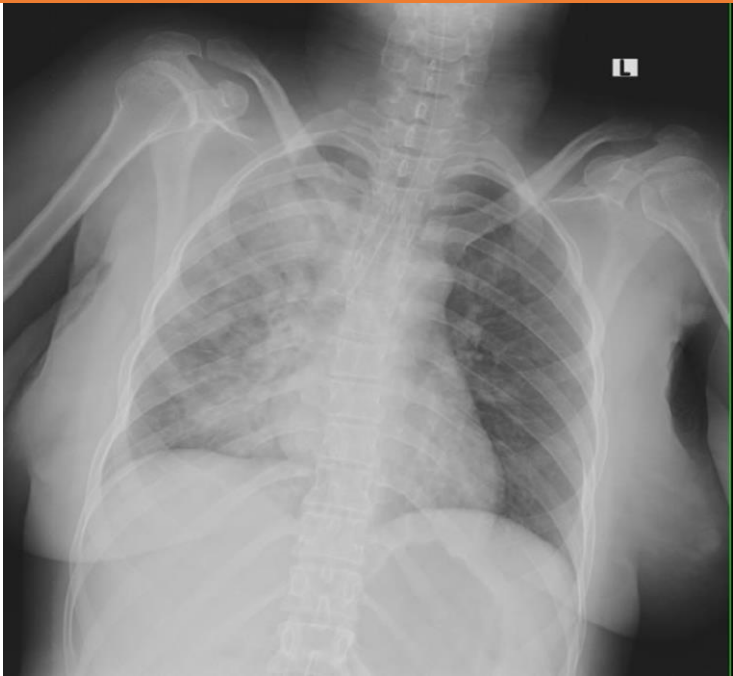


Figure 1: The chest x-ray imaging of the patient taken on 16/07/2024

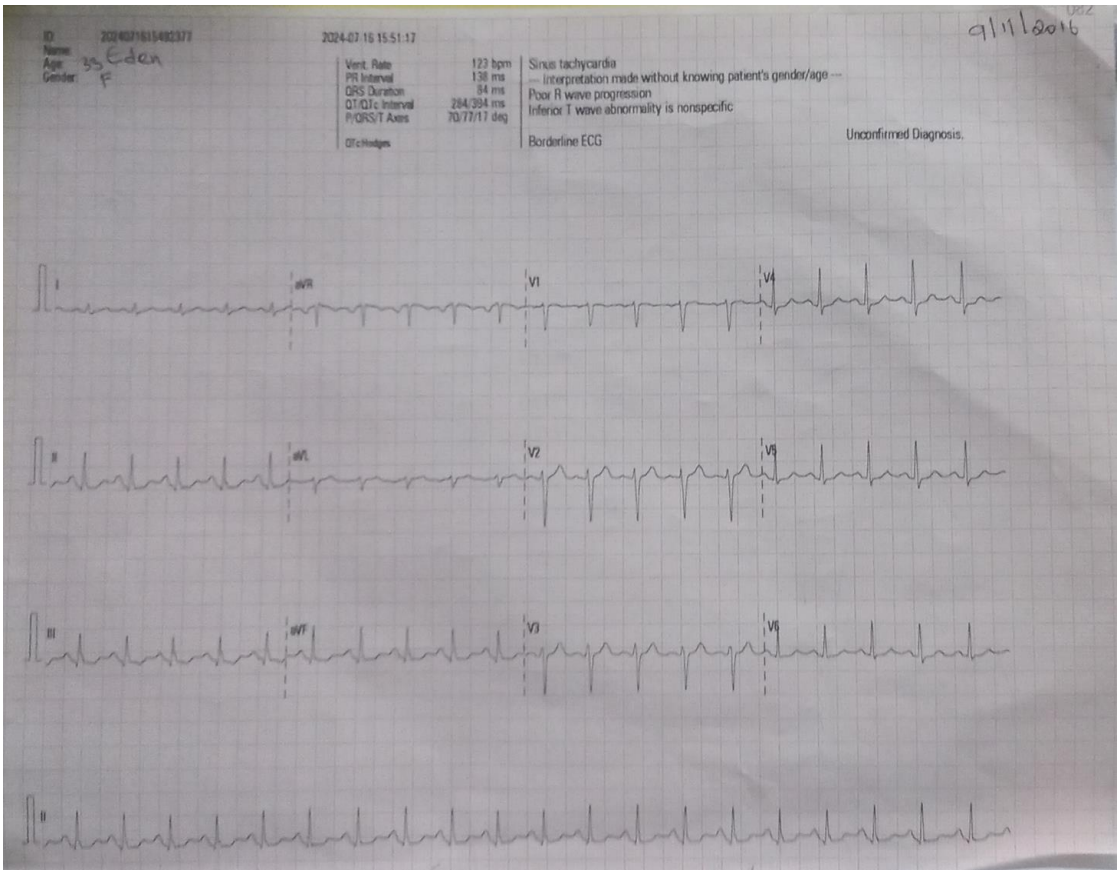


Figure 2: The ECG finding of the patient taken on 16/07/2024

Diagnosis

A diagnosis of coma secondary to acute phenobarbital overdose and aspiration pneumonia was made based on the clinical presentation and supportive investigation results.

Management

The patient was admitted to the red zone of the adult emergency room, put on mechanical ventilator support, and immediately resuscitated. She was on coma care and intravenously managed with maintenance fluid, morphine, omeprazole, diazepam, ceftriaxone, and metronidazole. She also underwent one session of hemodialysis in the emergency room and then was promptly transferred to the ICU and underwent a second hemodialysis for phenobarbital poisoning.

Follow up

After the two cycles of hemodialysis, the patient's clinical presentation and investigation panels improved, and she was extubated on the third day. After a few days of observation, she was discharged home.

3. Discussion

Phenobarbital is a commonly prescribed medication as a first-line management modality for generalized tonic-clonic and focal seizures, especially in resource-limited settings.⁽¹⁾ Its mechanism of action is activating the Gamma-Aminobutyric Acid type A receptors (GABA_A) either directly or by boosting Gamma-Aminobutyric Acid (GABA). This boosted neurotransmitter will then interact with the GABA_A and open the chloride channels for a longer period, increasing their influx into the brain cell membrane. This, in return, makes the inside of the cell more negative and stops the epileptic signals.⁽¹⁾

Phenobarbitals, with their potential to activate the receptors directly, their low clearance, and longer half-life, are commonly noted to have drowsiness as a side effect. Additional side effects include

restlessness, flat affect, ataxia, nystagmus, pulmonary edema, cardiorespiratory depression, particularly in rapid intravenous administration, and rarely symptoms of fever, rash, lymphadenopathy, and multiorgan affection as a result of the syndrome of hypersensitivity.⁽¹⁻⁶⁾

Acute Phenobarbital toxicity/overdose should be clinically diagnosed and promptly managed. While the concentration of serum phenobarbital may not match the degree of cardiorespiratory depression⁽⁷⁾, it is essential to determine the value while managing a patient with potential exposure to the drug or presenting with altered mentation. With a therapeutic range of 10-40 mcg/mL, serum phenobarbital concentration above 80 mcg/mL is potentially fatal, and levels exceeding 100 mcg/mL can result in death if not managed immediately^{8,9,10}. In addition to the toxicology screening, baseline investigations, ECG, and imaging are also needed to establish diagnosis in comatose patients and during their further management.

The best modality of treatment for phenobarbital poisoning is aggressive supportive care, including respiratory support and quick elimination of the drug from the body. The elimination methods include Multidose Activated charcoal (MDAC), hemoperfusion, hemodialysis, dialysis, and urine alkalization.⁽¹¹⁻¹⁶⁾ There is limited evidence to support the use of urine alkalization for phenobarbital overdose^(14,16), while MDAC and hemoperfusion are cited to be useful for severe and life-compromising toxicities.⁽¹²⁻¹⁶⁾ If hemoperfusion becomes challenging to implement, healthcare providers can alternatively include low-efficiency dialysis in their treatment plan.⁽¹⁾

In our patient's case, despite the lack of a clear clinical history that impaired the reliability of our secondary survey, a quick clinical diagnosis was made with the information provided. The patient, with a serum phenobarbital value of 88µg/ml, was promptly managed with two cycles of

hemodialysis, improving the patient's condition and ensuring a good recovery and discharge from the hospital.

This case, with a hypothesis of an intentional overdose and an unaddressed psychological stressor, also highlights a gap in comprehensive care. Healthcare providers are not only expected to monitor medication adherence in epileptic patients on long-term treatment, but they also need to include mental health checkups in their patient care, as undiagnosed and unaddressed stressors may lead to medication misuse. If clinicians incorporate routine psychological evaluation into epilepsy management, they are more likely to identify and treat such risks at an early stage and subsequently improve patient outcomes.

4. Conclusion

This case summarized that early intervention is crucial when managing patients with phenobarbital poisoning. Furthermore, healthcare providers need to have a high index of suspicion for overdose in patients who are taking chronic medications and acutely presenting with decreased mentation.

Abbreviation

ALP: Alkaline Phosphatase

ALT: Alanine Aminotransferase

AST: Aspartate Aminotransferase

Cr: Creatinine

Cl⁻: Chloride

CXR: Chest X-ray

DB: Direct Bilirubin

ECG: Electrocardiogram

GABA: Gamma-Aminobutyric Acid

GABA_A: Gamma-Aminobutyric Acid type A receptor

HBsAG: Hepatitis B Surface Antigen

HCT: Hematocrit

HCV: Hepatitis C Virus

Hgb: Hemoglobin

IVC: Inferior Vena Cava

K⁺: Potassium

LFT: Liver Function Test

MCV: Mean corpuscular volume

MDAC: Multidose Activated charcoal

Na⁺: Sodium

PLT: Platelet

RBS: Random Blood Sugar

RFT: Renal Function Test

TB: Total Bilirubin

Ur: Urea

WBC: White blood cells

VDRL: Venereal disease research laboratory test

Author Contributions

Nanati Jemal Aliye: Project administration and writing review

All authors: Data collection and Assembly

Biruk Zenebe Bekele: Reviewed and edited the first draft

Tesfaye Alemnew Haile: Reviewed and edited the second draft

Nanati Jemal Aliye: Reviewed and edited the third draft

Elezer Berhanu Zewde: Reviewed and edited the final draft

All authors: Manuscript writing

All authors: Final approval of manuscript

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Figure 1 was prepared by Yafet Solomon Shamebo

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