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Severe adverse drug reactions to multiple antiepileptics in a frail elderly patient: Case report

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Abstract

Introduction: We report elderly, frail woman with difficult to control seizure who was trailed on multiple Enti-Epileptic medications (AEDs) who later needed a Permanent Pace Maker inserted to control life threatening bradycardia due to a rare Adverse Drug Reaction (ADR) of one of the anti-epileptic medications. **Case presentation:** A 79-year-old woman developed generalised seizures and experienced severe adverse reactions to five different AEDs, including haematologic, cardiac, and dermatological complications. Although previously suffering from a subdural hematoma earlier in the year an MRI head scan on admission showed no acute intracranial findings and slight improvement in the previously noted subdural haematoma and mild oedema in the left hemisphere compared to previous CT. She was trialled on Phenytoin but developed severe life-threatening bradycardia which is a rare adverse drug effect, and it is probable that due to her age and overall frailty this greatly increased the risk of a cardiovascular incident. **Conclusion:** Seizure management in frail elderly patients is a complex task, particularly when adverse drug effects limit the effectiveness of common AEDs. This case demonstrates the importance of choosing AEDs with a more favourable side-effect profile, closely monitoring for ADRs, and considering alternative therapies and highlights the importance of personalised treatment plans in this vulnerable population.

Keywords: Tonic-clonic seizures; Bradycardia; Thrombocytopenia; Frailty; Antiepileptics.

Introduction

Epilepsy in the elderly is a growing concern, with the prevalence increasing as the population ages. Management of seizures in frail elderly patients is complicated by comorbidities, poly pharmacy, and the increased risk of Adverse Drug Reactions (ADRs). Antiepileptic drugs, while effective in controlling seizures, carry significant risks in older patients, particularly those with frailty or pre-existing medical conditions. This report examines the case of a frail elderly patient with uncontrolled seizures who experienced multiple severe ADRs from AEDs.

Timeline

2024-10-01

Admission for recurrence of Tonic-clonic seizures

2024-10-04

Levetiracetam increased → Thrombocytopenia

Sodium Valproate could not be initiated → Due to concern of Pancytopenia

2024-10-10

Lacosamide initiated → Severe bradycardia (HR 42 bpm)

2024-10-15

Lamotrigine initiated → Bullous pemphigoid

2024-10-31

Phenytoin initiated and titrated per patient response → Bradycardia and 11.28s pause on ECG

2025-01-22

Permanent pacemaker inserted

2025-01-23

Topiramate started → seizure control and no ADRs

Case Presentation

The proband is a female born in 29/07/1941 with a past medical history of Hypertension, chronic kidney disease, pre-diabetes, and a traumatic Subdural Hematoma (SDH) one year prior. She was a frail lady who required assistance with activities of daily living. The patient had no family history of epilepsy or seizures but was already on an antiepileptic drug for her last Intracranial bleed. She presented with generalised tonic-clonic seizures with no focal neurologic deficits noted on initial assessment. Due to this levetiracetam was increased at a dose of 125 mg twice daily. Levetiracetam is known for its efficacy to control seizures with a relatively low side-effect profile. However, after increasing the therapy to 750 mg BD, blood tests revealed thrombocytopenia with a platelet count of 5×10^9/L and to manage this situation the patient received two platelet transfusions. The onset of thrombocytopenia was attributed to levetiracetam, which is known to cause rare but serious haematological adverse effects, including thrombocytopenia [3], particularly in elderly patients [7]. Sodium valproate was not an option due to the same concern.

Lacosamide which was advised by Neurology was trialled however the patient developed severe bradycardia with a heart rate of 42 bpm (normal range: 60–100 bpm). Lacosamide has been linked to car-

diovascular adverse effects, including bradycardia and arrhythmias, especially in older individuals or those with pre-existing heart conditions [8]. Given the severity of the bradycardia, lacosamide was stopped after neurology consult.

Lamotrigine was considered as the next option. However, after initiating the therapy the patient developed a severe flare of bullous pemphigoid, a rare but serious cutaneous condition. Lamotrigine has been associated with various dermatological adverse effects, including life-threatening rashes, and in this patient, it precipitated the onset of bullous pemphigoid [10]. As a result, lamotrigine was discontinued. Dermatological advice was sought, and they advised for steroid therapy doxycycline to manage this.

Phenytoin was prescribed at a dose of 100 mg twice daily. Unfortunately, the patient experienced another episode of bradycardia, with a heart rate of 40 bpm. Cardiologists at that point did not feel the bradycardia was due to the drug. So we arranged a 24-hour ECG tape which showed 26 pauses in her heart rate, the longest of which lasted 11.28 seconds. Phenytoin is known to cause cardiac side effects, particularly bradycardia, due to its effects on sodium channels (Zhu et al., 2020) and has been associated with cardiac conduction disturbances, including bradycardia and Atrioventricular (AV) block, particularly in older adults [1]. These pauses raised concern for potential life-threatening arrhythmias. Due to the severity of the bradycardia and pauses on the ECG the patient had further cardiac evaluation and assessment and it was determined that the patient required a permanent pacemaker to prevent further dangerous episodes of bradycardia and potential syncope or cardiac arrest.

After the failure of multiple AEDs, the patient's seizures remained uncontrolled. Given the extensive history of ADRs, topiramate 25 mg twice daily was initiated as advised by the neurologist as an alternative until the heart rate was corrected. Topiramate is generally well-tolerated in the elderly population and is less likely to cause the severe hematologic and cardiovascular effects observed with other drugs in this case [9]. The patient was closely monitored for any adverse effects, and fortunately, no significant side effects were noted after a month of therapy. Her seizures became more controlled, and she demonstrated improved quality of life with minimal adverse effects. She also experienced no further recurrence of bullous pemphigoid, and her cardiac status stabilized post-pacemaker.

The main concern associated with topiramate therapy is cognitive impairment. Cognitive dysfunction, such as memory problems, difficulty concentrating, and slower processing speed, has been observed in patients taking topiramate [12]. This side effect was particularly concerning in populations at high risk, such as the elderly so we arranged for an outpatient neurology appointment to see how the patient was managing and to evaluate if we could restart phenytoin after the permanent pacemaker insertion once the heart rate was corrected. We also booked an outpatient memory clinic appointment to assess her cognitive function and memory

Diagnostics

Labs	Platelet count dropped to $5x10^9$/L on levetiracetam.
ECG	Revealed pauses; longest = 11.28 seconds on phenytoin.
Dermatology consultation	Confirmed bullous pemphigoid from lamotrigine.
Imaging	CT brain (routine monitoring) showed no acute findings. MRI showed no acute intracranial findings and slight improvement in the previously noted subdural haematoma.

Patient perspective

Due to frailty and comorbid conditions, direct commentary from the patient was not obtained. However, family members noted improved alertness, function and no more seizures post-topiramate initiation.

Discussion

This case illustrates the vulnerability of frail elderly patients to severe ADRs from commonly used AEDs. It emphasizes:

- The need for cautious, step-wise AED selection.
- The importance of monitoring for hematologic, dermatologic, and cardiac side effects.
- The utility of topiramate as a relatively safer alternative in elderly populations, albeit with monitoring for cognitive impairment.

Conclusion

Managing seizures in frail elderly patients is particularly challenging due to their reduced physiological reserves and the potential for significant ADRs. The elderly are at an increased risk of side effects from AEDs due to altered pharmacokinetics, such as decreased renal and hepatic function, and the presence of multiple comorbidities [12]. This case underscores the importance of individualized care and careful monitoring when prescribing AEDs in this population. Several AEDs were trailed in this case, with each presenting significant adverse effects. Levetiracetam caused thrombocytopenia, lacosamide and phenytoin both caused bradycardia, and lamotrigine triggered a severe dermatologic reaction. These ADRs are well-documented in the literature and highlight the need for clinicians to carefully consider the risks and benefits of AED therapy in frail, elderly patients (Bauer et al., 2018) [8]. Topiramate, while not without potential side effects, offers a safer alternative for elderly patients. It has a lower risk of hematologic and cardiovascular adverse effects, and it is associated with a more favourable safety profile in the elderly population [9].

Informed consent: Informed consent was obtained from the patient's legal representative for publication of this case report.

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