



Case Report

Anticonvulsant-induced downbeat nystagmus in epilepsy

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ABSTRACT

We report data from two patients who developed reversible downbeat nystagmus (DBN) while using AEDs within the therapeutic range. All previous reported cases of epilepsy with drug-induced DBN related to toxic levels of AEDs were summarized, and DBN was found mostly occurring in those using a sodium channel blocking AED. We propose that in our cases, the DBN with therapeutic AED levels may be explained by additive effects of sodium channel blockers. Adverse drug effects should be considered as a cause of DBN in people with epilepsy treated with multiple AEDs.

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1. Introduction

Iatrogenic down beat nystagmus (DBN) in people with epilepsy is rare and has been reported in the context of intoxication with anti-epileptic drugs (AEDs) [1]. We describe two patients who developed reversible DBN while using AEDs within the therapeutic range.

2. Case reports

2.1. Case 1

A 30-year-old man with refractory epilepsy following perinatal occipital lobe infarction was referred to our center with episodes of oscillopsia 1 h after taking his AEDs (lamotrigine 150 mg bid, valproic acid 600 mg bid, gabapentin 400 mg tid, and carbamazepine 400 mg bid). He noted that oscillopsia while reading could be prevented by keeping his book upward. He had DBN on examination. All AED levels were within the therapeutic range (Table 1). Downbeat nystagmus disappeared immediately after reduction of lamotrigine; subsequently, gabapentin was withdrawn without seizure increase.

2.2. Case 2

A 38-year-old woman with refractory epilepsy due to tuberous sclerosis complex and a hypothalamic giant cell astrocytoma presented with oscillopsia. She had weekly clusters of predominantly complex

partial seizures despite taking multiple AEDs. The complaints started following a change of medication: introduction of lacosamide 100 mg bid and tapering of topiramate. At the time of referral, she used valproic acid, levetiracetam, lamotrigine, and topiramate (Table 1). The oscillopsia was continuous without clear fluctuations following drug intake. Downbeat nystagmus and ataxia were noted at examination. There was no evidence of AED intoxication (Table 1). Lacosamide was discontinued, and the DBN and ataxia disappeared.

3. Discussion

In these cases, the drug levels were within the therapeutic range, but the temporal relationship between oscillopsia and drug ingestion (Case 1), the response to change to the drug treatment (Case 1 and Case 2), and also the impressive amount of AEDs suggested a drug-related cause. An ultimate proof would require a drug challenge, but this was not feasible in these cases.

Downbeat nystagmus is thought to result from impairment of the vestibulocerebellum, flocculus, or paraflocculus, that serves as the output pathway for information on movement, coordination, and balance from the cerebellar cortex [1–3]. In our two cases, the relevant drugs lamotrigine and lacosamide are both sodium channel blockers. In addition, both subjects were on combination therapy with other AEDs with sodium channel blocking properties (carbamazepine and valproic acid in Case 1, lamotrigine and valproic acid in Case 2). We reviewed the PubMed database (search terms: DBN and epilepsy) and identified nine previously reported cases with epilepsy and drug-induced DBN (Table 1). Most cases were related to toxic AED levels (lamotrigine, phenytoin, and felbamate). In one case, lamotrigine toxicity was likely, but not established; in another case, DBN was associated with therapeutic

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Table 1

Summary of previous reported and presented cases with epilepsy and anticonvulsant-induced downbeat nystagmus (DBN).

Age	Sex	Etiology	Specific cause	Medication: total daily dosage (mg)	AED serum levels with, <i>without</i> DBN (µg/ml)	Absence of DBN following AED reduction (R) or withdrawal (W)	Reference	
23	F	Unknown		Lorazepam 2 Lamotrigine 400	Gabapentin 1200 Lamotrigine 19.9 [#]	Lamotrigine (R)	[4]	
34	F	Structural	Meningitis	Lamotrigine 500	Valproic acid 1250 Lamotrigine 27.0 [#] , 18.8	Valproic acid (R)	[4]	
31	F	Unknown		Carbamazepine 1200 Topiramate 200	Lamotrigine 600 Carbamazepine 9.4	Lamotrigine not assessed	[5]	
51	M	Structural	Gunshot	Phenytoin 400	Phenytoin 38 [#] , 18	Phenytoin (W)	[6]	
54	F	Unknown		Phenytoin 400 Phenobarbital 120 Primidone 250	Perphenazine 12 Thioridazine 200 Phenobarbital 24	Phenytoin (W)	[6]	
19	F	Unknown		Phenytoin 150 Carbamazepine 800	Primidone 750 Phenytoin 14, 14	Phenytoin (R)	[7]	
23	F	Structural	Adhesions found in posterior fossa (Meningitis?)	Primidone 750 Phenytoin 300 Carbamazepine 800	Acetazolamide 1000 Methosuximide 600 Phenytoin 20 [#] , 9.8 Primidone 6	Phenytoin (W)	[7]	
18	F	Unknown		Carbamazepine 1800	Carbamazepine 9.6, 6.9	Carbamazepine (R)	[8]	
44	M	Structural	Concussion	Felbamate (dosage not reported)	Haloperidol 3 Benztropine 2 Felbamate 110 [#]	Felbamate (W)	[9]	
30	M	Structural	Perinatal occipital lobe infarction	Valproic acid 1200 Carbamazepine 1200	Lamotrigine 300 Gabapentin 3600 Valproic acid 74, 53	Lamotrigine 9.08, 6.8 Gabapentin 11.5, 3.8	Lamotrigine (R) Gabapentin (W)	This paper
38	F	Structural	Tuberous sclerosis complex; hypothalamic giant cell astrocytoma	Valproic acid 2000 Levetiracetam 2000	Lamotrigine 200 Lacosamide 200 Levetiracetam 19.1, 23.2	Lamotrigine 7.6, 7.1 Lacosamide 5.0	Lacosamide (W)	This paper

DBN = downbeat nystagmus, AED = antiepileptic drug, F = female, M = male.

[#] Toxic level.

levels of carbamazepine. As in our cases, all subjects suffered from refractory epilepsy, and most (7 out of 9) were using multiple AEDs. All AEDs that have been associated with DBN (carbamazepine, phenytoin, lacosamide, and lamotrigine) have sodium channel blocking properties except for felbamate.

Voltage-gated sodium channel (Nav) 1.1 and Nav1.6 channels are the primary voltage-activated sodium channel isoforms expressed in cerebellar Purkinje neurons and might explain the association between DBN and sodium channel blocking AEDs [10]. We suggest that the occurrence of DBN within the therapeutic range may be explained by additive effects of sodium channel blockers as in our two cases or by an increased propensity for DBN due to epilepsy etiology (e.g., encephalopathy with cerebellar dysfunction).

4. Conclusion

Adverse drug effects should be considered as a cause of DBN in people with epilepsy treated with multiple AEDs, particularly those with sodium channel blocking properties even in the absence of toxic levels. Prompt recognition of this adverse effect is important to avoid an incorrect diagnosis.

Ethical standard

We confirm that we have read the Journal's position on issues involved in ethical publication and confirm that this report is consistent with the guidelines.

Conflicts of interest

On behalf of all authors, the corresponding author states that there is no conflict of interest.

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