■ Case vignette

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Epileptic Disorders

Reversible downbeat nystagmus induced by carbamazepine in a three-year-old child

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A boy aged three years at the time of consultation had a history of left frontal lobe epilepsy. Epilepsy appeared at the age of five months with infantile spasms (IS) that were controlled with vigabatrin, and he thereafter presented with focal seizures that became drug resistant. During focal seizures, he warned his parents, seemed to be afraid and had asymmetric tonic seizures, predominantly affecting the right hemibody, followed by asymmetric IS.

Clinical examination showed a left-handed boy with a slight language delay without any other neurological deficit. Interictal EEG disclosed spikes over the left frontal region and vertex and ictal video-EEG disclosed a beta discharge at electrodes F3-Fz. MRI showed white/grey matter blurring associated with hypersignal on FLAIR-weighted sequences in the left superior frontal gyrus, suggestive of focal cortical dysplasia. Stereo-electroencephalography (SEEG) was performed to circumscribe the seizure onset zone and to clarify its relationship with the motor cortex (*figure 1A*). Interictal spikes (*figure 1B*) as well as the onset of the discharge were located precisely within the electrodes close to the lesion, with rapid propagation to the mesial frontal cortex facing it. Consequently, tailored surgery was decided, and the patient has now been seizure-free for 10 years without antiepileptic drugs (AEDs).

One month before the SEEG, the patient who had had stereotyped focal seizures, presented with a new clinical manifestation that consisted of abnormal eye movements occurring several times a day without loss of consciousness (*see video sequence*). The neuro-ophthalmological examination revealed ocular movements consisting of a vertical nystagmus beating downwards, with very high amplitude, increasing in downgaze and decreasing in upgaze. The patient then tended to demonstrate a head posture with the chin positioned downwards in order to use upper visual gaze associated with dampened nystagmus, and probably because of his young age, he did not report ocillopsia. These ocular movements were consistent with a downbeat nystagmus (DBN) which is considered typical of cerebellar origin.

A new MRI eliminated a cerebellar lesion and the lack of concomitant SEEG change (*figure 1B*) excluded a new type of epileptic seizure. The role of the antiepileptic medication was then suspected. Two months before the SEEG, the medical treatment included vigabatrin, oxcarbazepine and lamotrigine. Carbamazepine (CBZ) was then introduced and one month later, the ocular manifestations occurred. Lamotrigine was stopped and stiripentol was added followed by an increase in the frequency of ocular movements and a decrease in usual seizures. At this time, the blood dosage of oxcarbazepine (10.2 mg/L) and CBZ (7.3 mg/L) were within therapeutic range (4-10 mg/L). Prior to SEEG, stiripentol was systematically stopped due to the potentiation of the anaesthetic drugs, without any ocular change. During SEEG, CBZ was

VIDEO ONLINE

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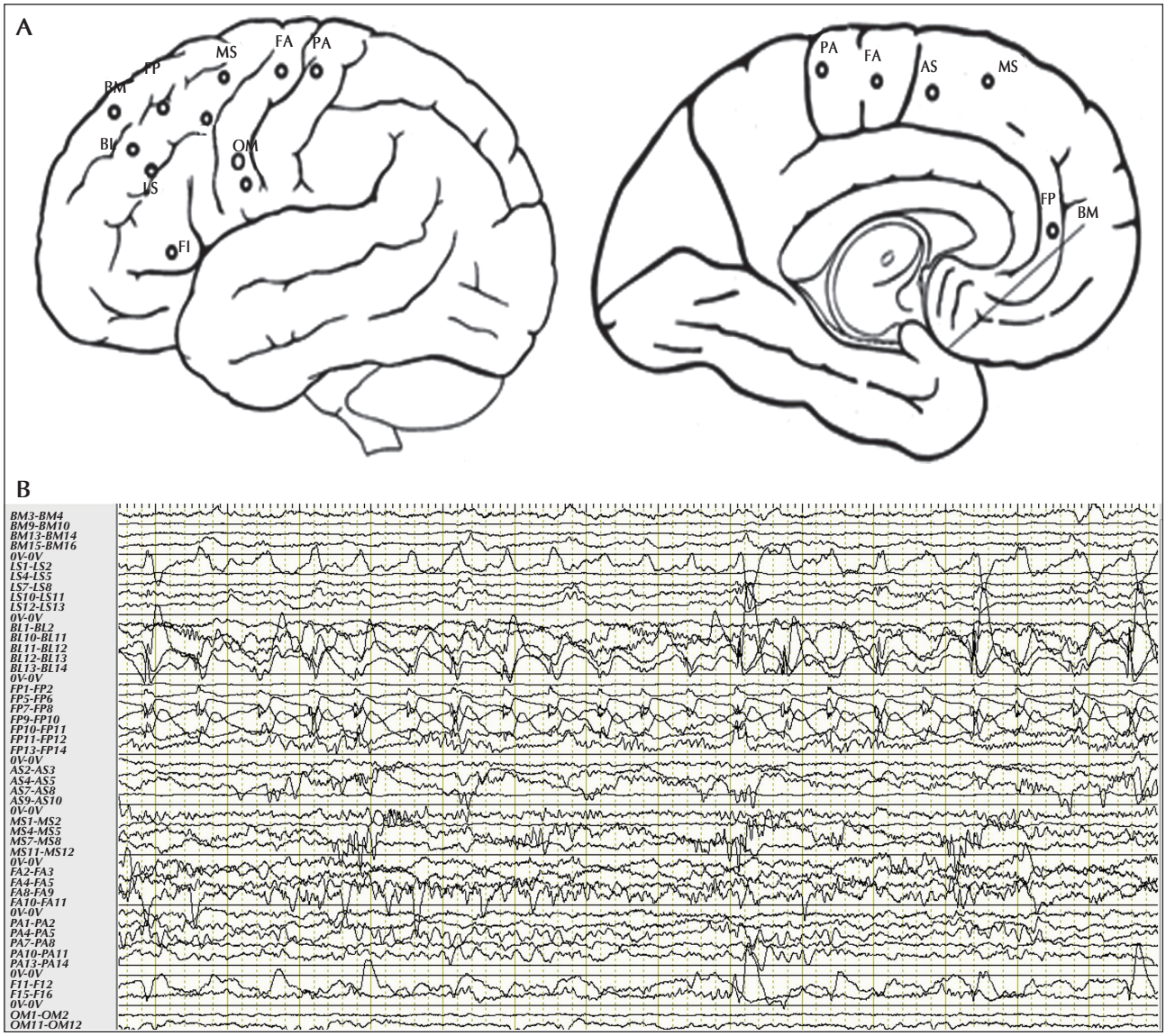

■ **Figure 1.** (A) Electrode implantation scheme. (B) SEEG recording during the ocular movements showing a continuous spike-and-wave activity at contacts FP 5-11 and BL 13-15 located within the focal cortical dysplasia. This activity is visible throughout the recording regardless of the presence or absence of abnormal eye movements.

stopped and immediately thereafter, the ocular movements completely ceased which confirmed, a posteriori, the effect of CBZ.

To the best of our knowledge, our patient is the first paediatric patient reported with DBN due to CBZ, as all other reports refer to adult patients [1-3]. CBZ is not the only anticonvulsant drug that may induce DBN, as phenytoin, valproate, lamotrigine, felbamate, lacosamide and gabapentin have also been reported [3]. DBN may be due to an idiosyncratic susceptibility to ocular motor side effects of anticonvulsants (AEDs) [2], an effect of over dosage [4-6] or may result from polytherapy with AEDs with sodium channel blocking properties [1, 3]. In our patient, the blood dosage of CBZ was within therapeutic range, but CBZ was associated with oxcarbazepine which also has sodium blocker properties as well as stiripentol which enhances the effect of both molecules. The pathophysiology of DBN in this case is attributed to the role of AED sodium channel blocking at Purkinje cells of the cerebellum. Other adverse ocular manifestations associated with CBZ toxicity include: diplopia and oscillopia, horizontal

gaze-evoked nystagmus, saccade abnormalities (slowing, inaccuracy, prolonged latency), smooth pursuit impairment, total ophthalmoplegia, oculogyric crisis and eyelid nystagmus [2, 4-8]. The peculiarity of our patient is that this is the first paediatric case to be reported, yet combination therapy is widely used in infants and children with drug-resistant epilepsies. ■

Disclosures.
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References

1. Chrousos GA, Cowdry R, Schuelein M, Abdul-Rahim AS, Matsuo V, Currie JN. Two cases of downbeat nystagmus and oscillopsia associated with carbamazepine. *Am J Ophthalmol* 1987; 103(2): 221-4.

2. Remler BF, Leigh RJ, Osorio I, Tomsak RL. The characteristics and mechanisms of visual disturbance associated with anticonvulsant therapy. *Neurology* 1990; 40(5): 791-6.

3. Wu D, Thijs RD. Anticonvulsant-induced downbeat nystagmus in epilepsy. *Epilepsy Behav Case Rep* 2015; 27 (4): 74-5.

4. Wirfs L, Whitworth K, Kellar J. Nystagmus associated with carbamazepine toxicity. *Clin Pract Cases Emerg Med* 2017; 1 (4): 441-2.

5. Seymour JF. Carbamazepine overdose. Features of 33 cases. *Drug Saf* 1993; 8(1): 81-8.

6. Schwartzman MJ, Leppik IE. Carbamazepine-induced dyskinesia and ophthalmoplegia. *Cleve Clin J Med* 1990; 57: 367-72.

7. Matarazzo M, Sánchez-Seco VG, Méndez-Guerrero AJ, Gata-Maya D, Domingo-Santos Á, Ruiz-Morales J, *et al*. Drug-related eyelid nystagmus: two cases of a rare clinical phenomenon related to carbamazepine and derivatives. *Clin Neuropharmacol* 2016; 39: 49-50.

8. Gorman M, Barkley GL. Oculogyric crisis induced by carbamazepine. *Epilepsia* 1995; 36(11): 1158-60.

Legend for video sequence

Three-year-old child presenting with downbeat nystagmus due to carbamazepine. One can observe ocular movements consisting of a vertical nystagmus beating downwards, with very high amplitude. During these movements, the patient does not complain of visual disturbance and speaks and behaves normally.

Key words for video research on www.epilepticdisorders.com

Phenomenology: adverse effect of antiepileptic drug: downbeat nystagmus
Localization: not applicable
Syndrome: not applicable
Aetiology: carbamazepine

TEST YOURSELF

(1) Which anticonvulsant drugs can induce downbeat nystagmus?

(2) What are the ophthalmologic side effects of carbamazepine?

Note: Reading the manuscript provides an answer to all questions. Correct answers may be accessed on the website, www.epilepticdisorders.com.