EXPERIENCE OF CENOBAMATE IN A PATIENT WITH DOUBLE CORTEX

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Introduction

Subcortical band heterotopia (SBH), also known as “double cortex,” is a neuronal migration disorder characterized by symmetric bands of ectopic gray matter located under the cortical mantle. SBH is frequently associated with drug-resistant epilepsy and variable degrees of intellectual disability. The overall incidence of type 1 lissencephaly is estimated at approximately 1 in 100,000 live births and the pathogenic variants in the PAFAH1B1 (LIS1) and DCX genes account for a significant proportion of cases [1]. Cenobamate, a new anti-seizure medication with a multimodal mechanism of action, has shown efficacy in adults with focal drug-resistant epilepsy [2].

Case Report

Remote pathological history

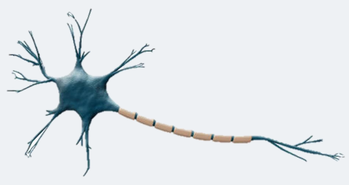
- Female
- 33 years old
- Right-handed
- Born after a full-term pregnancy without complications
- No family history of neurological diseases
- First epileptic seizure at the age of four.

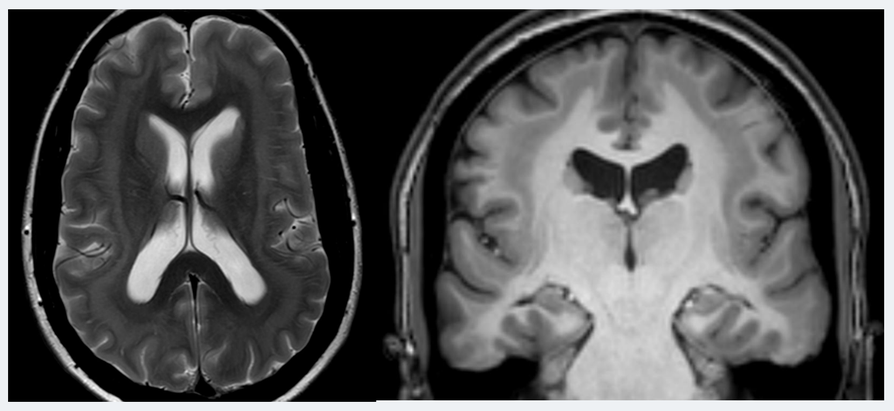
Diagnostic work-up

- Brain MRI, performed at the age of 10, revealed a subcortical band heterotopia (SBH)
- Neuropsychological assessment documented a moderate cognitive impairment (IQ 44 on the Leiter-R scale)
- Genetic testing identified a deletion involving exons 3, 4, and 5 of the DCX gene
- EEG showed multifocal epileptiform activity

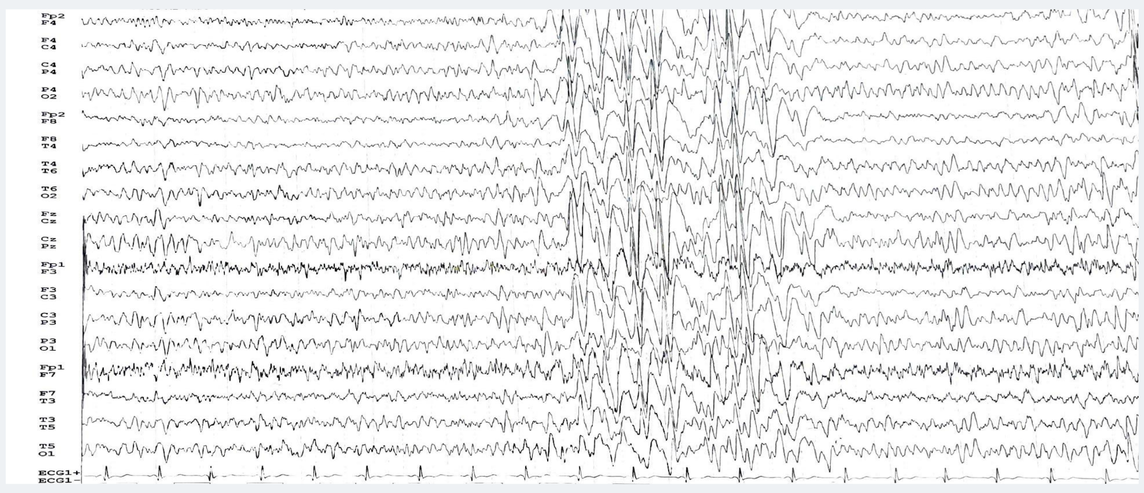
Clinical history

- Daytime and nighttime episodes characterized by swallowing automatisms, staring and subsequent clonic activity involving all four limbs, each lasting a few minutes
- Daily seizures, including drop attacks with head deviation, resulting in sudden falls and repeated traumatic injuries
- Drug-resistant epilepsy since disease onset, requiring multiple therapeutic attempts





Axial T2 weighted scan — Coronal T1 weighted scan



Intercritical EEG

History of antiseizure drugs

- Valproat
- Lamotrigine
- Levetiracetam
- Topiramate
- Clobazam
- Cannabidiol

Management decision

In February 2023, cenobamate (Ontozry®) was introduced and titrated up to 200 mg/day, in add-on to carbamazepine 1.1 g/day and clobazam 20 mg/day.

Follow up

After 9 months:
Seizure frequency decreased from 15/day to 2–3/week

However, the patient developed significant adverse effects:

- Somnolence
- Confusion
- Motor incoordination
- Intense headache
- Behavioral disturbances
- Increased gamma-glutamyl transferase (GGT)

NECESSARY SUSPENSION OF THE MEDICATION.

RECURRENCE WITH MULTIPLE DAILY SEIZURES

Decision making

Gradual reintroduction after 2 months→ 100 mg/day
↳ Good tolerability
↳ Favorable clinical response

After approximately one year, the dose was increased to 150 mg/day.

Current therapy:

- Cenobamate 150 mg/day
- Carbamazepine 1.2 g/day
- Clobazam 20 mg/day

Seizures: <10/month

No relevant adverse effects

Conclusions

Cenobamate demonstrated marked antiseizure efficacy in a patient with a DCX-related cortical malformation, even at intermediate doses and within a polytherapy regimen. This case highlights the importance of individualized approaches to tolerability management, avoiding premature discontinuation in responders. Furthermore, the potential synergistic or additive effects of adverse events arising from pharmacological combinations should be carefully considered [3].

References

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