Long Term Efficacy of Valproic Acid in a Case of PRRT2 Persistent Hemiplegic Migraine Aura

Luca Bartole, A. Granato, G. Garascia, P. Manganotti

Clinical Unit of Neurology, Headache Centre, Department of Medicine, Surgery and Health Sciences, University of Trieste, Trieste, Italy

Background and aims

Valproic acid (VA) is a broad-spectrum antiepileptic drug that enhances GABAergic inhibition, modulates voltage-gated sodium channels, and reduces cortical excitability, mechanisms relevant not only to epilepsy but also to migraine pathophysiology. Mutations in the CACNA1A, ATP1A2, SCN1A, and more recently PRRT2 genes are known to cause Familial Hemiplegic Migraine (FHM), with the first three accounting for the majority of cases and PRRT2 emerging as a newer contributor. Here, we report a case of FHM due to a PRRT2 gene deletion, showing complete and sustained remission of persistent aura under VA treatment, suggesting a potential therapeutic role of VA in genetically defined hemiplegic migraine.

Materials and methods

We retrospectively analyzed the clinical course of a 31-year-old male with a history of migraine since early childhood and progressive development of hemiplegic features.

Results

The patient initially presented with migraine without aura. At age 15, he began experiencing right-sided hemiparesis during attacks, later accompanied by hemihypoesthesia. At age 27, he developed exceptionally persistent right-sided sensorimotor symptoms lasting several months, confirmed on neurological examination. Neuroimaging and EEG were unremarkable. Multiplex ligation-dependent probe amplification revealed a heterozygous deletion of the entire PRRT2 gene, also present in his sister and mother, both with similar clinical phenotypes. Treatment with lamotrigine was initiated but discontinued after a few months due to emergent suicidal ideation. VA was then introduced at 300 mg daily for one week, followed by 300 mg twice daily. Within a few weeks, the aura symptoms resolved completely. The patient has remained attack-free and neurologically asymptomatic for over 36 months, with no reported side effects or significant laboratory abnormalities, apart from a negligible, near-normal increase in hepatic enzymes.

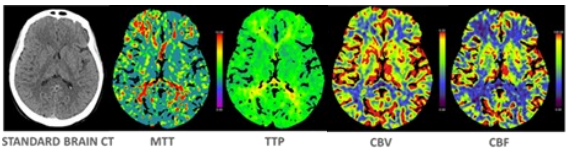

Figure 1 *Basal CT (the first one from the left) and qualitatively-assessed brain pCT images (the last four) acquired during acute FHM aura symptoms. CT: Computed Tomography; MTT: Mean Transit Time; TTP: Time To Peak; CBV: Cerebral Blood Volume; CBF: Cerebral Blood Flow*

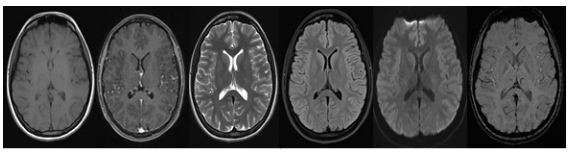

Figure 2 *Non-perfusion brain MRI sequences acquired during persistent FHM aura symptoms.*
c: contrast; FLAIR: FLuid-Attenuated Inversion Recovery; DWI: Diffusion-Weighted Imaging; SWI: Susceptibility-Weighted Imaging

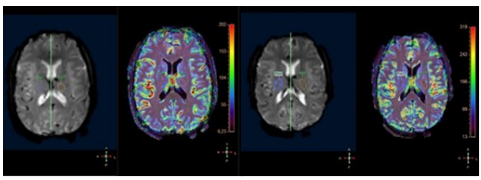

Figure 3 *Qualitatively-assessed pMRI images, relative to T_0 (on the left) and T_1 (on the right).*

Conclusions

The multimodal mechanisms of VA, reducing neuronal hyperexcitability, enhancing inhibitory transmission and potentially counteracting PRRT2-related synaptic dysfunction, may provide targeted benefit in this patient subset.

24-28 Ottobre 2025
Padova Congress
55° CONGRESSO SOCIETÀ ITALIANA DI NEUROLOGIA