Perirolandic Sign and Crossed Cerebellar Diaschisis in POLG-Related Disorder

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A 20-year-old female presented with recurrent episodes of partial motor seizures involving right-sided extremities without impaired awareness of 2 days duration. There were no systemic symptoms, and an initial workup including MRI Brain and EEG was unrevealing. She was diagnosed with focal epilepsy of probable cryptogenic etiology and was initiated on levetiracetam. Seizures recurred after 8 weeks, and semiology continued to be right focal motor seizures in the emergency room. However, episodes were prolonged and frequently culminated into loss of awareness and secondary generalization. She had amenorrhea for 6 weeks, and pregnancy test was positive. She was loaded with antiepileptics per protocol for status epilepticus and required mechanical ventilation. Repeat MRI [Figure 1a] revealed a focal hyperintensity in left precentral gyrus. CSF analysis was unremarkable. She remained seizure-free for 24 hours, after which she developed epilepsia partialis continua involving her right upper extremity. A detailed workup for infection, autoimmune, and metabolic causes was noncontributory.

Epilepsia partialis continua progressively evolved into generalized seizures, and ultimately super refractory status epilepticus. Repeat imaging [Figure 1b-f] revealed an increase in the extent of signal changes with restricted diffusion in left cerebral cortex, now involving anterior frontal regions, parietal and occipital lobes, and a new left thalamic involvement, without contrast enhancement. Right cerebellar hemisphere also revealed signal changes with restricted diffusion suggestive of crossed cerebellar diaschisis. Additional imaging was unrevealing for arterial or venous thrombosis. Over the following days, she gradually developed jaundice and progressive liver failure. Blood lactate, which was initially normal, was notably elevated after the onset of jaundice, despite normal perfusion. Comprehensive genetic workup revealed a pathogenic variant in POLG1 (c.2243G>C, pW745S) confirming POLG-related disorder. She eventually succumbed to the illness, despite optimal supportive management and mitochondrial cocktail.

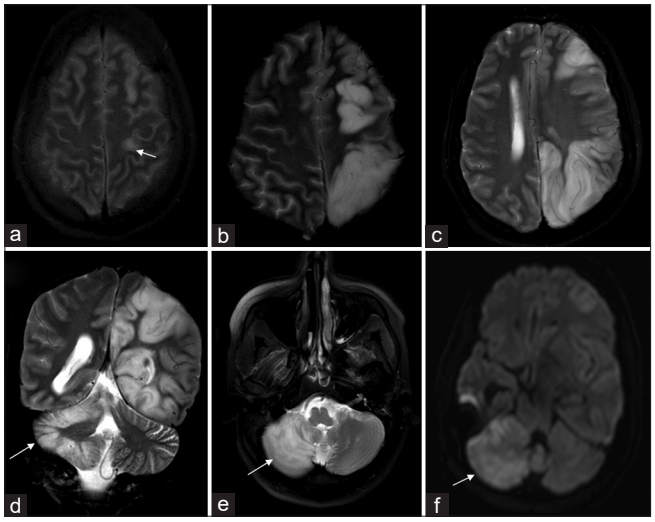

Figure 1: MRI shows focal hyperintensity in left precentral gyrus (a). Repeat imaging after a week later showed the increased extent of signal changes in left cerebral cortex, now involving anterior frontal regions, parietal, and occipital lobes (b-d) with restricted diffusion. Signal changes involving right cerebellar hemisphere (d and e) with restricted diffusion (f) indicate crossed cerebellar diaschisis

Clinical manifestations of POLG-related disorders are heterogeneous, ranging from well-defined clinical syndromes to overlapping neurological and multisystem manifestations including neuro regression, seizures, stroke-like episodes, myopathy, neuropathy, ataxia, external ophthalmoplegia, and liver failure. Epilepsia partialis continua is a common presenting symptom.[1] Neuroimaging findings of unilateral or bilateral perirolandic, and thalamic signal changes are one of the pathognomic neuroimaging findings.[1] Majority of the affected individuals have eventual disease progression and fatality.

Reduced perfusion and hypometabolism in the contralateral cerebellar hemisphere have been demonstrated in crossed cerebellar diaschisis (CCD) and has classically been in association with supratentorial strokes, tumors, and status epilepticus.[2,3] CCD has only rarely been described with POLG and other mitochondrial disorders.[4] Available evidence suggests the location of cortical lesion rather than severity, as the indicator for the development of CCD.[2] However, pathophysiology and clinical implications are not completely understood at this time. Finding of CCD in mitochondrial disorders might indicate prolonged seizure activity. Repeat imaging might reveal atrophy of the involved regions including the contralateral cerebellum. This might implicate the involvement of cortico-ponto-cerebellar pathways in seizure propagation. Knowledge of these imaging findings might suggest a diagnostic clue on the underlying etiology, dictate management in the appropriate clinical scenario, and might predict prognosis.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have

given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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