Metabolic or Ischemic Stroke in Succinic Semi-aldehyde Dehydrogenase Deficiency Due to the Homozygous Variant c. 1343 + 1_1343 + 3delGTAinsTT in *ALDH5A1*

With interest we read the article by Yoganathan *et al*. about a 15 months-old female with succinic semi-aldehyde dehydrogenase deficiency (SSAHD), manifesting with developmental delay and language deficits, who experienced an acute-onset right hemiparesis due to a "metabolic stroke" with MRI hyperintensity on diffusion-weighted imaging (DWI) and hypointensity on corresponding apparent diffusion coefficient (ADC) maps.[1] The lesion was interpreted as "stroke-mimic" as it had disappeared on follow-up MRI. We have the following comments and concerns.

It remains unclear what the authors mean with "metabolic stroke."[1] Do they mean an ischemic stroke in a patient with a metabolic disorder or do they mean a stroke-like episode (SLE)? as frequently seen in various mitochondrial disorders (MIDs).[2] Differentiation between these entities is crucial as treatment and outcome vary considerably between the two. According to the MRI images provided in Figure 1, the lesion looks as ischemic why it is curious that the authors classify the event as "stroke-mimic." Hyperintensity on DWI and corresponding hypointensity on ADC suggests cytotoxic edema and thus ischemic stroke. We should know after which interval the lesion completely disappeared and if any dynamic changes were observed until disappearance.

Treatment of ischemic stroke is well established, whereas the treatment of an SLE is under debate.[2-4] Depending on the pathophysiological hypothesis some experts recommend the application of antiepileptic drugs (AEDs) irrespective if patients present with clinical seizures or epileptiform discharges on electroencephalography (EEG),[3] whereas, propose the application of L-arginine, antioxidants, or steroids.[2,4] We should know which treatment the index patient received and if the treatment was effective or not.

Though the patient did not present with clinical seizures and though the EEG was normal, vigabatrin was given.[1] Since the effectivity of vigabatrin for seizures in SSAHD is questionable and since the patient never exhibited seizures, the authors should explain upon which rationale vigabatrin was applied. If the rationale was blocking off the GABA breakdown, as has been previously proposed,[5] this should explicitly be mentioned in the discussion. Missing in the report is a discussion of whether the mild clinical improvement was attributed to vigabatrin or was interpreted as spontaneous recovery from the metabolic defect.

It is reported that the patient had hyporeflexia but that nerve conduction studies were normal.[1] We should know if the patient also presented with muscle weakness, muscle wasting, elevated creatine-kinase (CK), and myogenic electromyography (EMG), and if the authors considered myopathy as the cause of hyporeflexia.

Missing in the report is a presentation of the vascular risk factors. We should know if the individual or family history was positive

for arterial hypertension, hyperlipidemia, diabetes, or atrial fibrillation. It should be reported if long-term ECG recording was carried out to exclude paroxysmal atrial fibrillation. We should know the results of the echocardiographic examination.

Imaging studies should be revised for cerebellar atrophy since it has been described as a cerebral manifestation of the disease.[6]

Overall, this interesting case report has a number of limitations and shortcomings which need to be solved before final conclusions can be drawn. Confirmation of the stroke as "metabolic" is required, treatment options for SLEs should be discussed, the rationale for the application of vigabatrin should be more extensively debated, and myopathy should be considered as the cause of hyporeflexia.

Author contribution

JF: design, literature search, discussion, first draft, FAS, CAS, RG: literature search, discussion, critical comments.

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Conflicts of interest

There are no conflicts of interest.

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