Fatal Cerebellar Edema in Leigh Syndrome Due To the Variant m.9176T>C May Not Only Be Attributable to a Stroke-Like Lesion

Abstract:

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LETTER TO THE EDITOR

With interest we read the article by Edwards, L. S. et al., (2020) about a 19 years old female with Leigh syndrome due to the variant m.9176T>C in MT-ATP6 (Edwards, L. S. et al., 2020). The patient experienced sudden onset cerebellar edema leading to posterior fossa compression, tonsillar descent, and death despite immediate surgical decompression (Edwards, L. S. et al., 2020). We have the following comments and concerns.

The report has a number of shortcomings. First, it is not mentioned if cerebellar edema occurred bilaterally or unilaterally. Knowing this is crucial for identifying the cause of the edema.

Second, we do not agree with the classification of the disease as “adult” Leigh syndrome (Edwards, L. S. et al., 2020). The patient was 19 years old at presentation but is described with long-standing bilateral hypoacusis (Edwards, L. S. et al., 2020). Since hearing impairment is a frequent manifestation of a mitochondrial disorder (MID), the initial manifestation of the disease was the hearing problem before age 19 years. Furthermore, the patient was described with bilateral ptosis, which presumably was present also already before age 19 years. Thus, the patient cannot be classified with adult Leigh syndrome, at most as paediatric Leigh syndrome with survival into adulthood.

Third, we do not agree with the classification of the cerebellar edema as vasogenic. The authors only present a CT-scan which shows edema, tonsillar descent, and the emerging hydrocephalus but does not allow classification of the edema. Of interest would be an MRI, to see if there was hyperintensity on diffusion weighted imaging (DWI) and hyperintensity on oxygen-extraction fraction MRI (OEF-MRI) which presumably was present also already before age 19 years. Additionally, SLLs show up as hyperintensity on perfusion weighted imaging (PWI) and hypointensity on oxygen-extraction fraction MRI (Fins Terer, J., & Aliyev, R. 2020).

Fourth, the cause of the edema remains unclear. Though we agree that a SLL, as has been previously reported (Oyama, M. et al., 2020), cannot be excluded, various differential diagnoses of a cerebellar edema have not been considered. These include ischemic stroke, cerebellitis, posterior reversible or encephalopathy syndrome (PRES), bleeding, lymphoma, or metastasis. A strong argument against a SLL is that SLLs usually do not go along with edematous expansion of the lesion and do not exhibit a mass effect.

Missing is a prospective investigation for multisystem involvement (Danhelovska, T. et al., 2020). Though the patient was young, affection of organs other than the brain and the muscle is conceivable. Of particular interest is if there was any type of cardiac involvement, such as hypertrophic respectively dilated cardiomyopathy, or noncompaction. Assuming that cerebellar edema was due to an ischemic stroke, it is conceivable that there was spontaneous dissection of vertebral artery or that there was embolic occlusion of a vertebral artery secondarily leading to ischemic stroke. Missing in this respect is
a description of the intra- and extra-cerebral arteries. An acute ischemic stroke would show up on multimodal MRI as DWI hyperintensity and as ADC hypointensity.

It is unusual that blood gas analysis revealed alkalosis despite lactic acidosis. How do the authors explain this discrepancy? Was alkalosis due to compensatory hyperventilation?

Missing is the lactate level in the cerebrospinal fluid. If increased, it would be an argument in favour of a SLL. Was cerebral lactate elevation documented by MR-spectroscopy?

Overall, this interesting case report would profit from addressing the shortcomings above. More likely than a SLL was an ischemic lesion responsible for the cerebellar edema.

REFERENCES