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Letter to the Editor.

We read with interest the article by Uittenbogaard et al. about a 2yo male with maternally-inherited Leigh syndrome (MILS) due to the *ATP6* variant m.8993T > G at a heteroplasmy rate of 83% [1]. We have the following comments and concerns.

Normal development of the infant was interrupted by a vaccination with various vaccines at age 4 m [1]. Did the patient undergo CSF investigations after having developed floppy infant syndrome and was meningitis excluded? Why did the patient receive a second set of vaccines at age 6 m resulting in the inability of breastfeeding after the previous adverse reaction [1]?

Fig. 1 shows a significant increase of the size of the ventricles between age 4 m and age 9 m, suggesting hydrocephalus [1]. Cortical atrophy does not explain the dramatic dynamics, why it should be mentioned if the CSF pressure was increased and if the patient received a ventriculo-peritoneal shunt.

Infantile spasms (West syndrome) were treated with a combination of three antiepileptic drugs (AEDs) [1]. This unusual combination was obviously ineffective [1]. In a recent systemic review it has been shown that ketogenic diet may be beneficial in infantile spasms. Was ketogenic diet tried in the index case as well and was it beneficial? In addition to ketogenic diet and topiramate, West syndrome may respond to ACTH, steroids, and vigabatrin [2]. Were any of these alternative AEDs applied? In a study of 40 patients with infantile spasms, topiramate and levetiracetam were ineffective [3].

The variant m.8993T > G may not only manifest in the brain but also in the muscles [4], peripheral nerves (neuropathy), kidneys, or the eyes (retinitis pigmentosa, macular degeneration) [5]. Another feature

may be hypocitrullinemia. Were any of these phenotypic features detected in the index case?

In summary, additional data about the cause of hydrocephalus, the treatment of epilepsy, and the phenotypic spectrum are eligible.

Conflict of interest

There are no conflicts of interest.

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Author contribution

JF: design, literature search, discussion, first draft, SZ-M: literature search, discussion, critical comments.

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