Phenotypic variability of HIBCH deficiency

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Letter to the Editor

In a recent article, Yamada et al. reported about a family in which 4 members carried a mutation in the HIBCH gene. Mutation carriers manifested clinically with Leigh-like features and ketoacidosis. We have the following comments and concerns.

Patient II/2 was reported to have experienced subarachnoid bleeding. Which was the cause of subarachnoid bleeding? Was it due to trauma or sporadic? Which were the results of the CT-, MR-investigations or conventional angiography? Was an aneurysm detected? Which was the Hunt-Hess score at onset of the SAB? Which treatment was applied? Aneurysm formation has been reported as a rare manifestation of mitochondrial disorders. Were other family members investigated for familial aneurysm formation? The discussion about the cause of ketoacidosis should be broadened.

Patient II/2 died from heart failure. What was the cause of heart failure? Was there cardiac involvement in form of hypertrophic, dilative, histiocytoid, or restrictive cardiomyopathy, noncompaction, or Takotsubo syndrome? So far, cardiac disease has not been reported in patients with HIBCH deficiency. Was terminal heart failure attributable to acidosis?

In a previously described patient, optic nerve atrophy has been reported as a phenotypic manifestation of HIBCH deficiency. Which was the visual acuity in the two presented patients? Were the pupillary light reflexes normal? It would be interesting to be informed about the results of the fundus investigations, OCT investigations, and the visually evoked potentials.

The authors stress that only 4 cases with HIBCH deficiency have been reported thus far. Meanwhile, however, a number of additional patients has been reported. Additional phenotypic features according to these recent reports include syndactyly, paroxysmal dystonia, diarrhoea, permanent dystonia, ataxia, cerebral atrophy, or muscle hypotonia. Determination of CSF lactate was normal in patient II/2 and not carried out in patient II/4. We should be informed about the findings on MR-spectroscopy, in particular if a lactate peak was detectable.

Overall, this interesting study would profit from a more extensive discussion about the cause of subarachnoid bleeding in patient II/2, about the ocular manifestations in the cohort, and about the cause of heart failure in patient II/2. Prospective investigations for phenotypic features described above should be initiated.

References


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