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Letter to the Editor

Psychosis in Leigh syndrome

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With interest we read the article by Satogami et al. about a 15 years old male with Leigh-syndrome due to thiamine-responsive pyruvate-dehydrogenase (PDH) deficiency (Satogami et al., 2017). The diagnosis was genetically confirmed, revealing a mutation in the E1α gene (Satogami et al., 2017). The patient recovered under a dosage of 3000 mg/d respectively 4500 mg/d thiamine per day (Satogami et al., 2017). We have the following comments and concerns.

We do not agree that Leigh syndrome in this case was thiamine-responsive. If we regard psychosis as a manifestation of the underlying metabolic disease, thiamine was ineffective. Despite increase in the dosage of thiamine, the psychotic episode continued. The patient was discharged 2 months after onset of psychotic manifestations under thiamine 4500 mg/d without significant improvement.

Were causes of psychosis other than the PDH-deficiency in the proband excluded? An alternative possible cause could be primary thiamine deficiency (Sasaki et al., 2010). Were thiamine serum levels determined before starting the substituion and at onset of psychosis? Could the episode of psychosis be due to intoxication with thiamine? 3000 mg/d respectively 4500 mg/d is fairly high daily dosage. Psychotic episodes in patients with a mitochondrial disorder (MID) may be also associated with a SLE (Finsterer, 2009). Did the patient undergo DWI and ADC sequences on MRI? Was there any indication for a stroke-like lesion (SLL), manifesting as vasogenic edema with a non-vascular distribution? Was a non-convulsive status epilepticus as the cause of psychiatric alterations considered and were antiepileptic drugs (AEDs) provided? Did the patient receive contrast medium when undergoing cerebral MRI? Were there any indications for immune encephalitis on MRI or cerebrospinal fluid (CSF) investigations? Were immune encephalitis antibodies determined? Did the patient undergo lumbar puncture or magnetic resonance spectroscopy (MRS) to see if there was elevated cerebral lactate or not?

It is not conceivable why the patient was discharged despite ongoing psychosis without remittance. Did the patient receive any antipsychotic medication in addition to increasing the dosage of thiamin and paliperidone? Did the patient undergo further follow-up? For how long was paliperidone administered?

We should be informed if the mutation occurred in a homozygous or heterozygous state. Furthermore, the authors should mention the particular mutation to see if it has been previously described or not. Information should be also provided about the genetic status of the parents and siblings of the proband. Did he inherit the mutation from the mother or father or from both?

MIDs frequently present as mitochondrial multiorgan disorder syndromes (MIMODSs) (Finsterer and Bastovansky, 2015). Were organs other than the brain affected in the proband? Did the authors prospectively investigate the proband for MIMODS? Were there any muscular, nerve, ophthalmologic, otololgic, endocrine, cardiac, pulmonary, gastrointestinal, renal, bone, hematological, or dermal abnormalities?

Antispychotic drugs have been reported to inhibit the PDH complex (Sacks et al., 1991). Did the authors observe deterioration of psychosis under palpiperidone? The strongest inhibition was reported with chlorpromazine and thioridazine and the lowest with fluphenazine and thiothixene (Sacks et al., 1991).

Overall, this interesting case could profit from clarification of some inconsistencies and provision of additional clinical data. Serum thiamine levels before and after the psychotic episode should be provided. In case the patient continuous to be psychotic an AED treatment should be tried.

Author contribution

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

Conflict of interest

There are no conflicts of interest.

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