Ethylmalonic encephalopathy at age 33

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Abstract

Ethylmalonic encephalopathy is a genetic disease diagnosed usually in the first months of life with the following symptoms: hypotonia, chronic diarrhea, orthostatic purpura, lactic acidosis. It can lead to death in the early years of life without treatments. It is related to a mutation on the ETHE1 gene. We report here a case of a 33 years old patient.

The patient presented digestif symptoms like chronic diarrhea since his first years. Then he had minor praxis troubles noted at 6th years old, which didn't prevent him from a normal schooling. It was not until his 14th that he progressively presented a spasticity of the 2 inferior limbs.

A brain MRI is done then, which find hypersignals of putamen and caudate nucleus. A urinary organic acid chromatography finds rise ethylmalonate, isobutylglycine and isovalerylglycine. Acylcarnitine's dosage is in favor of a succinyl CoA dehydrogenase deficiency. Finally, a genetic analysis by exome finds a rare heterozygote composite mutation on ETHE1 (c.442 C>T and c.79 C>T), confirmed after segregation of the 2 parents at heterozygote state.

Then, from 2020 the patient is treated by Metronidazole and N-acetyl cysteine. He will unfortunately present a decompensation by losing abruptly walking capacity after a urinary infection, which destabilized his disease. The treatment was briefly interrupt and then resumed, but in 2021 he contracted an optic neuropathy caused by the metronidazole. Both treatments were then stopped and replaced by a bitherapy of riboflavin and coenzyme Q.

Moderate forms of ethylmalonic encephalopathy manifest in adulthood by a clinical presentation including spastic paraparesis and chronic diarrhea. The diagnostic must be evocated in front of this clinic without other diagnosis because it can benefit from a specific regimen. The hepatic transplantation can be discussed since we lack information in adulthood for now.

Image

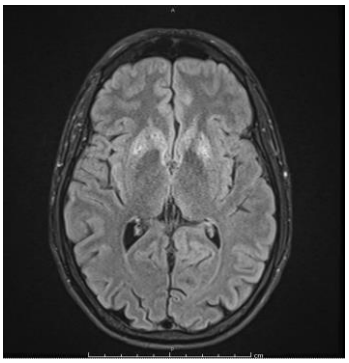


Figure 1 : hypersignal T2 on caudate nucleus and putamens (2021)

Recent Publications (minimum 5)

1 : Tiranti V, Viscomi C, Hildebrandt T et al. Loss of ETHE1, a mitochondrial dioxygenase, causes fatal sulfide toxicity in ethylmalonic encephalopathy. Nat Med 2009;15(2):200–5. https:/oi.org/10.1038/nm.1907

2 : Mancardi D, Penna C, Merlino A et al. Physiological and pharmacological features of the novel gasotransmitter: Hydrogen sulfide. Biochimica et Biophysica Acta 1787 (2009) 864–872. https://doi.org/10.1016/j.bbabio.2009.03.005

3: Viscomi C, Burlina AB, Dweikat I et al. Combined treatment with oral metronidazole and N-acetylcysteine is effective in ethylmalonic encephalopathy. Nature Medicine, 16(8), 869–871. https://doi.org/10.1038/nm.2188

4: Yoon H-R. , Hahn S. H, Ahn Y. M et al. Therapeutic trial in the first three Asian cases of ethylmalonic encephalopathy : Response to riboflavin. J. Inherit. Metab. Dis. 24 (2001) 870-873. https://doi.org/10.1023/a:1013948409790

5: Boyer M, Sowa M, Di Meo I. Response to medical and a novel dietary treatment in newborn screen identified patients with ethylmalonic encephalopathy. . https://doi.org/10.1016/j.ymgme.2018.02.008

6: Olivieri G, Martinelli D, Longo D, et al.Ethylmalonic encephalopathy and liver transplantation: long-term outcome of the first treated patient, Orphanet J Rare Dis (2021) 16:229. https://doi.org/10.1186/s13023-021-01867-5

7: Tam A, AlDhaheri NS, Mysore K, et al. Improved clinical outcome following liver transplant in patients with ethylmalonic encephalopathy. Am J Med Genet Part A. 2019;1–5. https://doi.org/10.1002/ajmg.a.61104



Biography

I'm a medical student currently in 3th year of neurological residency, beginning a complementary formation in neurometabolic.

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