

In Response To:

Giron C, Roze E, Degos, B, Méneret A, Jardel C, Lannuzel A, et al. Adult-onset generalized dystonia as the main manifestation of MEGDEL syndrome. *Tremor Other Hyperkinet Mov.* 2018; 8. doi: 10.7916/D8VM5VBQ

Letters

Dystonia is a Common Phenotypic Feature of MEGDEL Syndrome

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Dear Editor,

We read with interest the article by Giron et al.¹ about a 31-year-old male with 3-methylglutaconic aciduria with deafness, encephalopathy, and Leigh-like (MEGDEL) syndrome due to a compound heterozygote variant in the *SERAC1* gene. The article raises a number of comments and concerns.

In the case description, the authors mention that the patient had “a few episodes of subacute encephalopathy” triggered by fever.¹ What do the authors mean by “encephalopathy”? This is a non-specific term and only means that there was a cerebral abnormality. Which type of central nervous system (CNS) abnormality did the patient present with? Was there a psychiatric abnormality or was the neurological examination abnormal? Was there an abnormal finding on cerebral imaging previously carried out? Is the magnetic resonance imaging (MRI) scan presented in Figure 1 related to this episode? Was the electroencephalogram (EEG) normal? CNS abnormalities described in MEGDEL syndrome include psychiatric abnormalities (cognitive

decline, agitation, temper tantrum, insomnia) and neurological disease (psychomotor retardation, hypotonia, failure to thrive, spasticity, seizures, dystonia, dysphagia, ataxia, optic atrophy, spinal cord lesions, tremor, chorea, oral dyskinesias, dysarthria, Parkinsonism, and various structural abnormalities on imaging). Which of these CNS manifestations were found in the presented patient in addition to the cardinal features of MEGDEL syndrome and spasticity? Did the MRI show the typical “putaminal eye” sign (putaminal volume loss of the mid-dorsal putamen)?^{2,3}

Though the CNS is predominantly affected, MEGDEL syndrome is a multisystem disorder.⁴ In addition to the CNS, the ears, eyes, the heart, the gastrointestinal tract, the endocrine organs, the skeletal muscle, the peripheral nerves, and the bones may be involved.⁴ Otologic manifestations include hypoacusis. In the eyes, MEGDEL syndrome may manifest as strabismus or pigmentary retinopathy. Compared to other mitochondrial syndromes, cardiac involvement only includes arrhythmias and diastolic dysfunction. Gastrointestinal manifestations include drooling, vomiting, feeding difficulties,

ascites, bloating, and reflux. Hypoglycemia and short stature are the most frequent endocrine disturbances. The orthopedic problems that patients with MEGDEL syndrome develop include scoliosis, hip dislocation, strephenopodia, or abnormal posture of feet or head. Additionally, these patients may present with dysmorphism. Were any of these complementary features found in the presented patient?

Though dystonia has been reported in at least 13 patients with MEGDEL syndrome, it cannot be excluded that the patient described by Giron et al. had two different diseases. Was the patient genetically screened for mutations in genes associated with generalized dystonia?

MEGDEL syndrome is usually an early onset disease, manifesting at infancy or childhood. How do the authors explain the late onset in their patient? Recently, it has been shown that MEGDEL syndrome may not only have an infantile onset but also a juvenile, oligosymptomatic onset.⁵ However, a patient with an onset at age 24, as in the case described by Giron et al., has not been previously reported.

In summary, the interesting case described by Giron et al. requires more extensive and prospective clinical investigations, and investigation of first-degree relatives.

References

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