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A novel mutation in two siblings with sialidosis

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Background: Progressive myoclonus epilepsies (PMEs) are a group of heterogeneous genetic diseases [1], which include sialidosis. Sialidosis is an autosomal recessive lysosomal storage disorder caused by mutations in the neuroaminidase gene (NEU1) [2]. It is classified into type 1, a milder form with later onset, and type 2, a severe form with infantile onset and dysmorphic features. PMEs clinically present with epilepsy, cognitive impairment, ataxia and myoclonus. The macular cherry-red spot is a typical finding of sialidosis [3] however rare cases not presenting this sign have been reported[4]. Pharmacological treatment in PMEs is symptomatic, often requiring a polytherapy of antiepileptic drugs. Myoclonus is often the most disabling symptom, and tend to partially respond to treatments. Perampanel, a selective non-competitive AMPA receptor antagonist, has been recently described in small cases to ameliorate myoclonus in PMEs[5,6,7,8]

Aim: We describe two siblings with different clinical presentation, both diagnosed with sialodosis type 1 caused by the same novel mutation in NEU1 gene.

Case presentation: The female sibling reported gait disturbances since the age of 40, with progressive appearance of cerebellar ataxia and nystagmus. Years later, mild face and inferior limbs myoclonus appeared, with good response to Levetiracetam. The male sibling reported severe action myoclonus since the age of 45, with progressive loss of gait, and generalized epileptic seizures. Myoclonus caused marked disability in everyday life with partial response to a polytherapy of antiepileptic drugs. Add-on treatment with Perampanel was started, with amelioration of myoclonus and reduction of life disability. Both of them presented dysarthria, dysphagia and depression but no macular cherry-red spot. In both the cases, brain MRI did not revealed abnormalities and neurophysiological tests were consistent with cortical myoclonus. Genetical analysis revealed a novel mutation in NEU1 gene (c.134C>T p.Ser45Phe) in homozygosis in both the siblings.

Conclusions: We identified the novel c.134C>T p.Ser45Phe NEU1 mutation in two siblings presenting with clinically different PME. Besides, we report beneficial effect of Perampanel for myoclonus associated with PMEs.

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