Can leukodystrophy be reversible?: A LTBL case report

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INTRODUCTION

Leukoencephalopathy with thalamus and brainstem involvement and high lactate (LTBL) is a hereditary disorder caused by homozygote mutations in the EARS2 gene. Patients exhibit developmental delay, hypotonia, and hyperreflexia. (1). We report a case of LTBL, showing significant improvement in neuroimaging and clinical findings.

CASE DESCRIPTION

A non-consanguineous three-year-old girl exhibited developmental delay from birth, with no family history of neurological diseases. Neurological examination showed prominent truncal hypotonia and hyperreflexia. Brain magnetic resonance imaging (MRI) at 17 months of age revealed extensive T2-hyperintensities on the cerebral white matter, cerebellum, thalamus, basal ganglia, pons, and medulla oblongata (Fig 1 A,B). The electroencephalogram (EEG) showed hypsarrhythmia, and levetiracetam was effective. Whole-exome sequencing yielded compound heterozygous EARS2 variants of c.C727T, p.H243Y and c.G164A, p.R55H. Carnithine, coenzyme Q10, multivitamin were started. After six months of treatment, she began to sit unassisted.

She was able to walk independent after the eight months of treatment and after one year, she could speak several words. The findings in brain MRI were significantly improved. At three years of age, lesions of subcortical white matter, talamus and dorsal mesencephalon were only persisted (Fig 1, E, F)

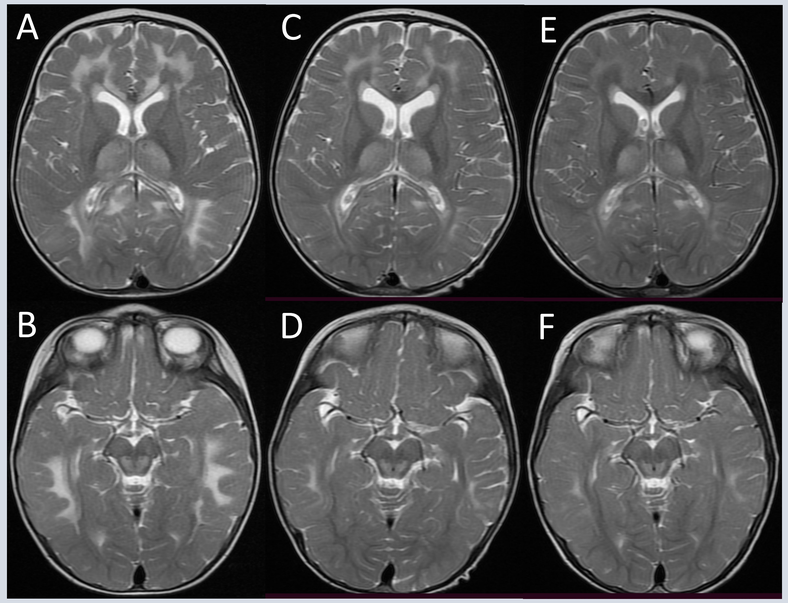

Figure 1. T2 axial images show hyperintense lesions in bilateral talamus, dorsal mesencephalon, and cerebral white matter (A, B) at 17 months, at 26 months (C,D),and at 3 years old (E,F).

CONCLUSION

Brain MRI in LTBL caused by EARS2 generally show bilateral symmetrical involvement of the cerebral white matter, thalami, midbrain, pons, medulla oblongata, and cerebellum. Findings include a spared periventricular rim while the posterior part of the corpus callosum is thin or absent. LTBL has a biphasic clinical course that the stabilization or improvement phase follows deterioration phase with clinical and neuroimaging findings (1). We present a case with recovery of brain lesions and healing of clinical symptoms in LTBL. The pathophysiological mechanism of clinical and radiological improvement in patients with EARS2 gene mutations is unclear. However, unique clinical and MRI findings of this disease may be an important clue for diagnosis.

REFERENCES

1. Sawada D, Naito S, Aoyama H, Shiohama T, Ichikawa T, Imagawa E, Miyake N, Matsumoto N, Fujii K. Remitting and exacerbating white matter lesions in leukoencephalopathy with thalamus and brainstem involvement and high lactate. Brain Dev. 2021 Aug;43(7):798-803.