The Importance of Examination in Febrile Convulsions: Hypotonic Infant Case with Coenzyme Q10 Deficiency

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Introduction

Coenzyme Q10 (CoQ10) is found in the inner mitochondrial membrane, which is involved in many mitochondrial respiratory chains. [1] Although coenzyme Q10 can be obtained from the diet, the main source of poor bioavailability is endogenous synthesis.[2] It is a rare multisystem disorder with a variable clinical phenotype.[3] Among the genes that cause primary CoQ10 deficiency is the COQ4 gene. COQ4 is located on chromosome 9q34.11 and encodes a COQ4 protein of 265 amino acids. [4] Although the exact properties of COQ4 are unknown, it has been observed to play an important role in the stabilisation of the CoQ multienzyme complex.[5] Pathogenic crises in the COQ4 gene include severe, chronic clinics; it may present as neonatal-onset encephalopathy, infantile developmental delay, epilepsy with or without hypertrophic cardiomyopathy, and ataxia beginning in childhood with similar attacks.[6]

Case

A 2 years and 5 months old male patient, who first applied to us at the age of 4 months due to febrile convulsions, was followed up due to lack of head control and central hypotonicity. The patient had atrophy on magnetic resonance imaging (MRI) of the brain. MRI spectrography showed deep reverse lactate peaks at 1.3 ppm and basal ganglia involvement. Echocardiography was normal. COQ4/NM_016035/EXON5 c.437T>G p.(Phe146Cys) homozygous mutation was detected in the whole exome sequence analysis, which was sent due to the persistence of seizures during follow-up, failure to reach developmental milestones, consanguinity between the parents and the history of an ex-sibling diagnosed with Joubert syndrome. Family segregation analysis revealed a heterozygous mutation in both the mother and father. High dose CoQ10 treatment was started and he was followed up with a diagnosis of primary CoQ10 deficiency. After CoQ10 treatment, the patient's seizures decreased and the duration of his current seizures was shortened. At his most recent physical examination, he had head control and was able to sit with support.

Discussion

A total of 44 cases of COQ4 mutation from 36 families have been reported in the literature. In all cases, the central nervous system was the most frequently affected system, as in our patient. Global developmental delay was found in all cases. Seizures are the second most common clinical symptom in patients and the mean age of onset has been reported to be 2 months.[6] Our case presented after a febrile seizure at the age of 4 months. However, the clinical spectrum and progression vary from patient to patient. Mutations in COQ4 exons 1-4 have been associated with late onset, slower progression, responsiveness to CoQ10 therapy, and a relatively long life expectancy. On the other hand, pathogenic mutations in exons 5-7 have been reported to be associated with early onset and early mortality, and these patients are less likely to respond to CoQ10 treatment.[7]

Conclusion

COQ4 mutation is a rare cause of CoQ10 deficiency. Early detection of CoQ10 deficiency, which is a rare disease, and initiation of coenzyme treatment are important for disease progression. Whole exome analysis in patients with clinical findings and family history is necessary for diagnosis and early treatment.

References

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