A case with mutation of VPS13D: Leigh syndrome or spinocerebellar ataxia?

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OBJECTIVE

Leigh syndrome (LS), the most common childhood mitochondrial disorder, has characteristic clinical and neuroradiologic features. The mutations directly or indirectly affect the activity of the mitochondrial respiratory chain or pyruvate dehydrogenase complex. The clinical course is characterized by a rapid deterioration of cognitive and motor functions, in most cases resulting in death due to respiratory failure. The patients present with identical, symmetrical lesions in the basal ganglia or brainstem on MRI (1). Here we report a rare case of LS with mutation of VPS13D (vacuolar protein sorting 13, yeast, homolog of D) which is mostly known as cause of spinocerebellar ataxia type 4.

CASE

A six-month-old male patient, born to a nonconsanguineous family, was presented with epileptic spasm. Neurological examination showed developmental delay, lack of eye contact and truncal hypotonia, feeding difficulties with loss of appatite. Head control was not acquired yet, distonia was seen. The electroencephalogram was showed hypsarrhythmia and antiepileptic treatment was started. Brain MRI showed symmetric lesions of corpus striatum and diffusion limitation (Fig 1). Mitochondrial disorders were considered and whole exome sequencing (WES), and CGH array analysis was performed. Mitochondrial cocktail was started.

Although genetic tests resulted normal; clinical, MRI findings and improvement of symptoms with mitochondrial cocktail directed us to reanalyze WES for mitochondrial disorders. VPS13D mutation is detected which causes Spinocerebellar ataxia, newly identified gene for Leigh syndrome.

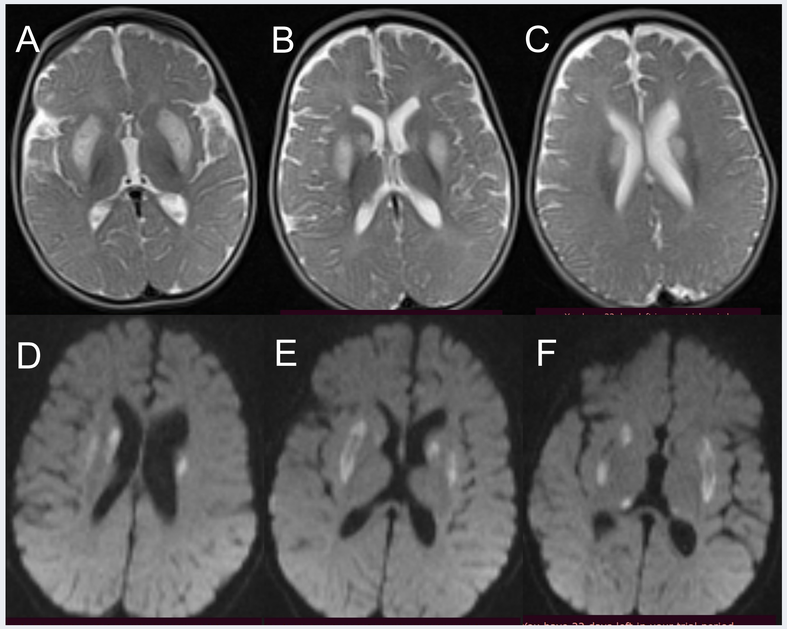

Figure 1. T2 axial images, show hyperintense lesions in bilateral symmetrical nucleus caudatus and putamen (A,B,C). Diffusion weighted imagines (DWI) show diffusion restriction in nucleus caudatus, putamen and medial thalamus (D,E,F).

CONCLUSION

Spinocerebellar ataxia is a group of diseases characterized by progressive gait ataxia, dysarthria, and oculomotor disorders was reported to be caused by many mutations, and VPS13D gene mutations represent the essential component. The specific function of VPS13D was unknown in humans before 2018. Recently, it was reported to encode a ubiquitously expressed protein with an important role in mitochondrial size, autophagy, and clearance. Therefore, mutations in this gene can lead to abnormal mitochondrial morphology and dysfunction (2). The genetic causes of Leigh syndrome are heterogeneous, with a poor genotype-phenotype correlation, mutations in over 60 genes, both nuclear and mitochondrial DNA encoded, have been shown. In most patients, exome sequencing has accelerated the discovery of new genes involved in Leigh syndrome, providing novel insights into the pathophysiological mechanisms. The VPS13D mutations were reported as a cause of atypical Leigh syndrome (1). This report highlights typical clinical presentation and MR findings with newly reported genetic mutation.

REFERENCES

1. Lee JS, Yoo T, Lee M, et all. Genetic heterogeneity in Leigh syndrome: Highlighting treatable and novel genetic causes. Clin Genet. 2020 Apr;97(4):586-594.

2. Huang X, Fan DS. Autosomal recessive spinocerebellar ataxia type 4 with a VPS13D mutation: A case report. World J Clin Cases 2022; 10(2): 703-708