The AarF domain containing kinase 3 (ADCK3) is a mitochondrial protein required for coenzyme Q (CoQ) biosynthesis. Loss of function mutations in the ADCK3 gene cause coenzyme Q10 (CoQ10) deficiency (#MIM 612016), resulting in mitochondrial dysfunction. Cerebella ataxia is its most common phenotype [1]. However, acute epileptic encephalopathy with stroke-like episodes has been reported in few cases [2]. Here, we report the case of a patient with novel ADCK3 mutations who presented with a homonymous hemianopsia, stroke like brain lesions in brain magnetic resonance imaging (MRI).

A 3-year-old girl presented with exercise intolerance, gait disturbance and occasional dysarthria following normal birth and development. Serum creatinine kinase and lactate dehydrogenase were elevated at 964 U/L (21-215 U/L) and 3,427 IU/L (255-455 IU/L). And serum lactate was high at 8.3 mmol/L (0.5-1.6 mmol/L). We observed ragged red fibers on muscle biopsy and identified mitochondrial respiratory chain complex 1 deficiency from biochemical tests. She was diagnosed with a mitochondrial disorder. The first generalized tonic seizure occurred at the age of 6 years and was administered anti-epileptic drugs. At 14 years of age, she presented with stroke-like episodes with severe headache, nausea, dysarthria, and left-sided hemianopsia. However, her brain MRI findings were normal.

Electroencephalogram (EEG) showed frequent epileptic discharges in the right occipital area. Those acute symptoms improved after 7 days of conservative management to reduce cerebral edema with hyperosmolar agent (mannitol) and high-dose corticosteroids. She reported another stroke-like episode with similar symptoms at the age of 18 years. In addition, she experienced sudden left-sided homonymous hemianopsia and dysarthria concomitant with ataxic gait and exercise intolerance. We detected generalized tonic seizure during her hospitalization. Repeated brain MRI showed focal areas of high-signal intensity in the right occipital lobe and dentate nucleus. Nonetheless, brain magnetic resonance angiography showed no abnormal vascular lesion. While there were frequent sharp wave discharges from both occipital areas in EEG, a visual field examination showed ipsilateral left hemianopsia.

Whole-exome sequencing was performed for accurate diagnosis because no significant variant was detected in the previous whole mitochondrial genome test. In this study, the compound heterozygous mutations were identified, namely c.655+1G > A and c.1015G > A (p.Ala339Thr) in the ADCK3 gene (NM_020247.4 and NP_064632.2). According to the American College of Medical Genetics and Genomics guidelines, c.655+1G > A is a novel pathogenic variant and c.1015G
>A is a likely pathogenic variant which has been reported in a patient with a homozygote mutation [3]. The variants were confirmed by Sanger sequencing in the proband and both parents and considering the autosomal recessive inheritance of the ADCK3 gene, it is likely that the asymptomatic parents were carriers. After genetic diagnosis, she has been taking CoQ10 supplements with 400 mg daily.

Hemianopia and stroke-like lesions are common symptoms of mitochondrial encephalopathy, lactic acidosis, and stroke-like episodes (MELAS). In a patient suspected of mitochondrial cytopathy with stroke-like lesions on brain MRI without pathogenic variants related to MELAS, it is recommended to consider testing for mitochondrial disorders caused by nuclear DNA mutations, including the ADCK3 gene.

ADCK3-related CoQ10 deficiency is a rare disease. Furthermore, the phenotype is neither classified systematically nor well known. Patients with ADCK3 mutations usually present with progressive cerebellar ataxia, exercise intolerance, and high-signal intensity of the dentate nucleus. However, they rarely report cardiomyopathy and nephrotic syndrome. In addition, her abdominal radiography revealed ovarian calcification and a mature ovarian teratoma was confirmed by ultrasound findings incidentally (Fig. 1). There are no reports of a definite association with the ADCK3 gene, which causes the deficiency of CoQ10, which plays an important role in antioxidant.

To our knowledge, this is the first report of a patient with novel compound heterozygous ADCK3 variants in Korea who showed signs of ataxia, exercise intolerance, homonymous hemianopsia, dysarthria, and teratoma. This report aims to expand the understanding of the genotype-phenotype spectrum associated with ADCK3-related CoQ10 deficiency.

This study was approved by the Institutional Review Board of Gangnam Severance Hospital (approval number: 3-2020-0393). Informed consent was waived by the board.
Conflicts of interest

No potential conflict of interest relevant to this article was reported.

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References