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증 례

진행성 양측 백내장이 동반된 미토콘드리아 질환 1례

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A Case of Mitochondrial Respiratory Chain Defect with Progressive Bilateral Cararacts

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A striking feature of mitochondrial disorders is the vast heterogeneity in their clinical symptoms that ranges from a single organ to severe multisystem involvement. Though a variety of ocular symptoms such as ptosis, pigmentary retinal degeneration, external ophthalmoplegia, and optic nerve atrophy can occur in association with mitochondrial cytopathies, progressive bilateral cataracts are rare among their ocular findings. A 5-year-old girl with no previous medical history came to our hospital presenting symptoms of seizure. She started showing progressive developmental regression, increased seizure frequency, hypotonia, general weakness, dysphagia and decreased vision. Lactic acidosis was noted in metabolic screening test and we confirmed mitochondrial respiratory chain complex I defect in spectrophotometric enzyme assay using the muscle tissue. Progressive bilateral cataracts then developed and were fully evident at the age of 7. She underwent cataract extraction with posterior chamber lens implantation. We are reporting a case of mitochondrial respiratory chain defect with multiorgan involvements including bilateral progressive cataract, an uncommon ocular manifestation. Ophthalmologic evaluation is highly recommended not to overlook the possible ocular manifestations in mitochondrial disorders.

Key words: Mitochondria, Respiratory chain complex, Lactic acidosis, Cataract

Introduction

Mitochondrial cytopathy is a complex and heterogeneous multisystem disorder that is caused by mitochondrial dysfunction, particularly defects in the mitochondrial respiratory chain (MRC) complex and related aberrant oxidative phosphorylation[1,2]. It preferentially affects the muscle and nervous system while involving the cardiovascular, ophthalmic, skeletal, or gastrointestinal systems depending on each patient[3]. A variety of ocular symptoms and signs such as pigmentary retinal degeneration, external ophthalmoplegia and optic atrophy occur in association with mitochondrial cytopathies[4]. However, progressive bilateral cataracts are quite rare[5]. This report describes a 7-year-old female with mitochondrial respiratory chain complex I deficiency suffering bilateral cataracts.

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Case Report

The patient was a full term baby born after an uncomplicated pregnancy. She was the first child of healthy, nonconsanguneous parents. She developed symptoms of seizure the age of 5 years old and came to our hospital for evaluation. She then started showing other symptoms including progressive developmental regression, increased seizure frequency, hypotonia, general weakness, and dysphagia. She was full time wheelchair-bound and partially dependent for daily activities, able to do brief communication and had mild mental retardation. There were no definite abnormal findings in auditory function test and cardiac evaluation. Her brain magnetic resonance imaging (MRI) showed progressive diffuse cerebral and cerebellar atrophy while the magnetic resonance spectroscopy showed no significantly abnormal finding (Fig 1). Serum lactate was markedly elevated to 5.4 mmol/L with an elevated lactate to pyruvate ratio of 20:1. Urine organic acid showed severe lactic aciduria and ketonuria. Muscle biopsy was performed when she was 7 years of age. The residual enzyme activity of mitochondrial respiratory chain complex I was checked as less than 10% residual enzyme activity compared to that of the age-matched controls in spectrophotometric enzyme assay, therefore we confirmed mitochondrial respiratory chain complex I deficiency. However, she was not diagnosed with a specific syndrome of mitochondrial disease or mitochondrial myopathy in routine histology, immunohistochemistry, and electron microscopy examinations. She was consecutively referred to an ophthalmologist for evaluation of decreased vision. Fundus examination result was unremarkable but progressive bilateral cataract was noted (Fig. 2). The cataract progressed in a rapid rate for the following 5 months. She underwent right-side cataract extraction and posterior chamber lens implantation. After the operation, the right-side visual acuity improved. She started having regular ophthalmologic checkups to determine the need for the left-side cataract extraction. The cataract progressed rapidly, but she was unable to receive neither the extraction nor the lens implantation due to her poor general condition. She expired at the age of 8 because of sepsis.

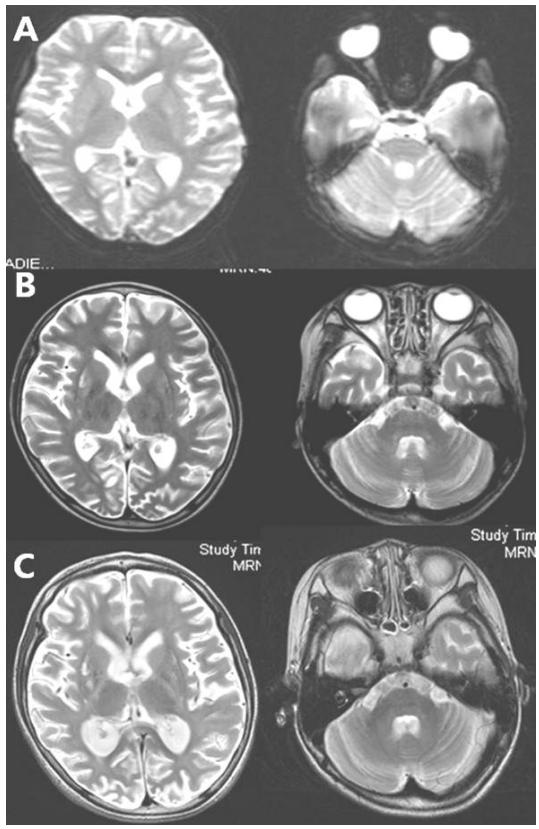

Fig. 1. Magnetic resonance image of the brain (T2 weighted image). (A) Axial T2-weighted magnetic resonance imaging when she was 5 years old demonstrated mild cortical atrophy and increased T2 signal in basal ganglia. (B) Axial T2-weighted magnetic resonance imaging when she was 6 years old revealed that cortical atrophy was progressed and T2 signal increased more in basal ganglia. Cerebellar atrophy was also noted. (C) Axial T2-weighted magnetic resonance imaging when she was 7 years old revealed progression of cortical atrophy and cerebellar atrophy as well as ventriculomegaly.

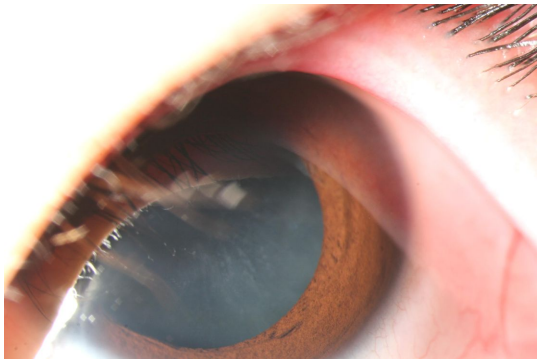

Fig. 2. Ophtalmologic evaluation. Fundus examination result was unremarkable but progressive bilateral cataract was noted.

Discussion

Mitochondrial cytopaties are known to show a diverse spectrum of clinical manifestations[6]. They involve the central and peripheral nervous system and as well as the muscular system resulting in patients suffering altered levels of consciousness, developmental delays, seizures, involuntary movements, peripheral neuropathies, hypotonia and muscle weakness[3]. They are also known to involve non-muscular systems such as cardiovascular, ophthalmic, auditory, gastointestinal, urologic, endocrinologic, and hematologic system[7].

Mitochondrial diseases that involve ocular symptoms as a major manifestation include chronic progressive external ophthalmoplegia (CPEO) and Kearns-Sayre syndrome (KSS), among others[8]. There are several studies describing the ophthalmological manifestations in patients with mitochondrial diseases[9,10]. However, a comprehensive literature search demonstrated that either information about ophthalmologic phenotypes were small case series, not discussed in detail. In this report we described a relatively rare ophthalmic manifestation of mitochondrial respiratory chain complex I deficiency. To our knowledge, the association of cataracts in childhood and complex I deficiency has been rarely reported in other countries and has not yet been reported in Korea.

Our patient had progressive developmental regression, increased seizure frequency, hypotonia, general weakness, dysphagia and cataract. Several classic mitochondrial disorders of ophthalmic importance include Leber Hereditary optic neuropathy, chronic progressive external opthalmoplegia (CPEO) or Kearns-Sayre syndrome, MERRF syndrome and MELAS syndrome. But none of these syndromes has been found to include progressive bilateral cataract[5].

We report a case of mitochondrial respiratory chain defect with multiorgan involvements including an uncommon ocular manifestation that is bilateral progressive cataract. Early ophthalmic evaluation of children with mitochondrial disorders or respiratory chain enzyme defects is very important to detect the various manifestations in mitochondrial disorders including the uncommon ones.

요 약

미토콘드리아 질환은 단일 장기에서부터 여러 장기에 걸쳐 침범할 수 있다는 임상 증상의 광범위한 이질성이 특징이다. 안검하수, 색소 망막 퇴화, 외안근 마미, 시신경 위축 등과 같은 다양한 안구 증상이 미토콘드리아 질환에서 함께 나타날 수 있지만, 진행성 양안 백내장은 미토콘드리아 질환의 안과적 증상에서 매우 드물다. 저자들은 미토콘드리아 호흡 연쇄 복합체 결핍 환자에서 흔치 않은 안구 발현 현상인 진행성 양안 백내장 침범 사례를 경험하였기에 보고하는 바이다.

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