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*Abbreviations:* AT, Adipose tissue · CT, computed tomography · FPG, fasting plasma glucose · 2-h PG, 2-h plasma glucose

# Acute metabolic cataract as a first manifestation of diabetes mellitus in a 12-year-old girl

**Keywords** Juvenile cataract · Mitochondrial diabetes · 3243 mitochondrial tRNA mutation · Oxidative stress · MELAS

*To the Editor:* We report a case of juvenile cataract and Type 2 diabetes in a 26-year-old female (154 cm, 51 kg). A sibling of her mother had impaired glucose tolerance. Polydipsia and leg paresthesia were apparent in this patient with cataract since the age of 10, and she was diagnosed with diabetes at the age of 12. On her first visit, her intelligence and physical examination results were normal, except for bilateral cataracts (an unusual manifestation in a 12-year-old girl). Ptosis, ophthalmoplegia and hearing loss were not observed. Her fasting plasma glucose concentration was 25.3 mmol/l, and her $HbA_{1c}$ was 20.1%. Other laboratory examination data were normal. She began intensive insulin treatment and 4 months later her $HbA_{1c}$ rapidly decreased to 5.9%, and the leg paresthesia disappeared. She underwent successful bilateral cataract extraction with intraocular lens implantation. Four years later, she stopped insulin therapy and has been under excellent control ($HbA_{1c}$ 6.0%) with oral hypoglycaemic agents, and she has been free of symptoms.

Neuroimaging findings at the globus pallidus are a sign of MELAS (mitochondrial myopathy, encephalopathy, lactic acidosis and stroke-like episodes) or mitochondrial diabetes. In this patient, high intensity areas in the bilateral globus pallidus were noted on T1-weighted magnetic resonance imaging at the age of 18 (Fig. 1). However, she was not recognised as showing signs of mitochondrial disease, because the results of detecting mitochondrial DNA (*mtDNA*) mutation at position ***3243*** were negative in the laboratories, where the cut-off degree of heteroplasmy ranged from 0.2 to 1%. Informed consent was obtained and the study was approved by the local ethics committee of Saiseikai Central Hospital. Other important data, as to whether other family members had considerable mitochondrial *DNA* mutation, were not available.

A new technology using real-time PCR with a TaqMan Probe was introduced in *Diabetologia* [1], which can quantify as little as 0.001% of the *3243 mtDNA* mutation in blood cells.

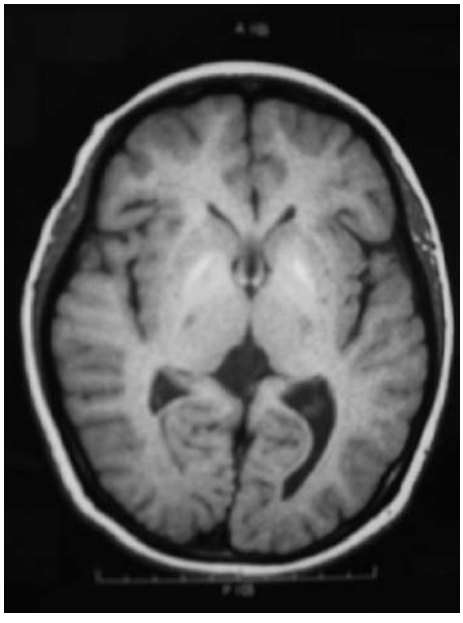

**Fig. 1.** High intensity areas in the bilateral globus pallidus were noted on T1-weighted magnetic resonance imaging

DOI 10.1007/s00125-004-1333-7
Received: 5 September 2003 / Revised: 24 November 2003
Published online: 11 February 2004

That study [1] reported that the *3243* mutation rates are 0.0115±0.0001% in young patients with diabetes. This patient at age 20 was shown to have a mutation rate of 0.09%, which is >3SD above the average of diabetic subjects in the study population of [1]. These results, together with abnormal finding on MRI, support that this patient has a mild type or atypical type of mitochondrial diabetes due to *3243 mtDNA* mutation. Nevertheless, whether the *3243* mutation is maternally inherited or is a somatic accumulation due to the hyperglycaemia or oxidative stress is an important aetiological issue, but is difficult to be determined by a case report. Hence, we are in the process of solving this question by trying to find similar patients.

Morphologically distinct cataract in young patients with newly diagnosed diabetes is a rare complication. According to a study, after following up 600 paediatric diabetic patients, the prevalence of diabetic cataract is around 1% in the paediatric diabetic population in Finland [2]. To our knowledge (on Medline), this is the first young patient with acute cataract as a first manifestation of diabetes in the Japanese population. The fact that clinically significant cataracts develop in only a small percentage of diabetic children suggests that the degree of hyperglycaemia alone is not the only factor involved in cataract formation.

Mitochondrion is a key organelle in producing oxidative stress. Juvenile cataract in patients with mitochondrial diseases has been well documented. For example, a study reported that one in three patients with MELAS showed juvenile cataract [3]. Another study reported an autopsy case of MLEAS with *3243 mtDNA* mutation, with juvenile cataract but not diabetes [4]. The *3243 mtDNA* mutation itself increases intra-cellular reactive oxygen species production [1]. Therefore, excess free radical production due to mitochondrial dysfunction could amplify oxidative stress in the lens, thereby developing cataract formation in patients with mitochondrial diseases. On the other hand, the *3243* mutation in the $tRNA^{Leu(UUR)}$ gene causes a lack of uridine-modification in $tRNA^{Leu(UUR)}$ at the first letter of the anticodon [5]. The defect disturbs the interaction between tRNA and mRNA, stopping protein synthesis, thereby generating a small but significant amount of premature proteins even in the case of a very small amount of the mutant *mtDNA*. In turn, the premature proteins may interrupt efficient respiration, causing the generation of oxidative stress. Alternatively, oxidative stress may increase mutation in *mtDNA* and develop cataract formation independent of the mutation. However, not all patients with mitochondrial diseases show juvenile cataract. Therefore, even among patients with mitochondrial diseases, there could be a subset of patients with a different susceptibility to cataract formation.

In conclusion, juvenile cataract is a previously unreported feature of mitochondrial diabetes. Hence, this report may improve the understanding of the pathogenesis of juvenile cataract in diabetic patients. In addition, this is the first study to suggest the practical importance of a new technology using real-time PCR with a TaqMan Probe.

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