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Case Report

Repeated Attacks of Dizziness Caused by a Rare Mitochondrial Encephalomyopathy

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Cases of dizziness caused by multiple sclerosis are commonly reported, but those caused by mitochondrial encephalomyopathy have been rarely reported. Particularly, the description of eye nystagmography (ENG) using caloric and optokinetic nystagmus tests has not been reported to date. We encountered the case of a 40-year-old woman with mitochondrial encephalomyopathy who visited us with the chief complaint of dizziness. At first, we considered multiple sclerosis based on the magnetic resonance imaging (MRI) findings and dizziness. Repeated attacks of dizziness and serum lactic acid levels suggested mitochondrial encephalomyopathy. A muscle biopsy confirmed the diagnosis. ENG findings suggested central vestibular disorder of the cerebellum and brainstem. This case suggests that we should not rule out the differential diagnosis of a very rare mitochondrial encephalomyopathy in patients who experience dizziness with MRI findings indicative of multiple sclerosis.

KEYWORDS: Mitochondrial encephalomyopathy, multiple sclerosis, dizziness, eye nystamography (ENG), MRI

INTRODUCTION

Mitochondrial encephalomyopathy is a rare disease. With regard to consultation in the field of otolaryngology, there are very few reports of hearing impairment and dizziness. In particular, there have been no reports describing eye nystagmography (ENG). In contrast, multiple sclerosis is a rare disorder, but known to cause dizziness, and it is often diagnosed based on MRI findings and dizziness. Here, we report a case of dizziness thought to be caused by multiple sclerosis but later diagnosed as mitochondrial encephalomyopathy with crucial ENG findings of nystagmus.

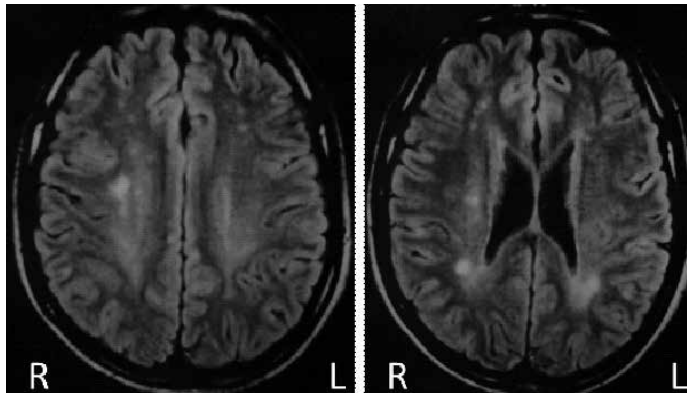

Figure 1. MRI findings (horizontal): T2 FLAIR showed a high-signal area in the bilateral cerebral deep white matter

CASE PRESENTATION

A 40-year-old female patient experienced dizziness with a floating sensation and gait difficulties in X 25th, 20YY. She visited hospital "A" in X+1month 1st and was hospitalized. In the MRI performed on X+1month 2nd, T2 and FLAIR imaging revealed high-intensity regions in the deep white matter on both sides of the brain (Figure 1).

Multiple sclerosis was suspected and steroid pulse therapy was started in the Department of Neurology at that hospital. Subsequently, she was transferred to the Department of Neurology of the hospital "B" on X+1month 27th. The blood test at the previous hospital on X+1month 14th showed a high lactic acid level of 24.2 mg/dL (normal range: 3.3-14.9) and a high pyruvic acid level of 2.02 mg/dL (0.3-0.94).

This study was preseted at 15th Korea-Japan Joint Meeting of Otorhinolaryngology, Head and Neck Surgery, 3-5 April 2014, Seoul, Korea.

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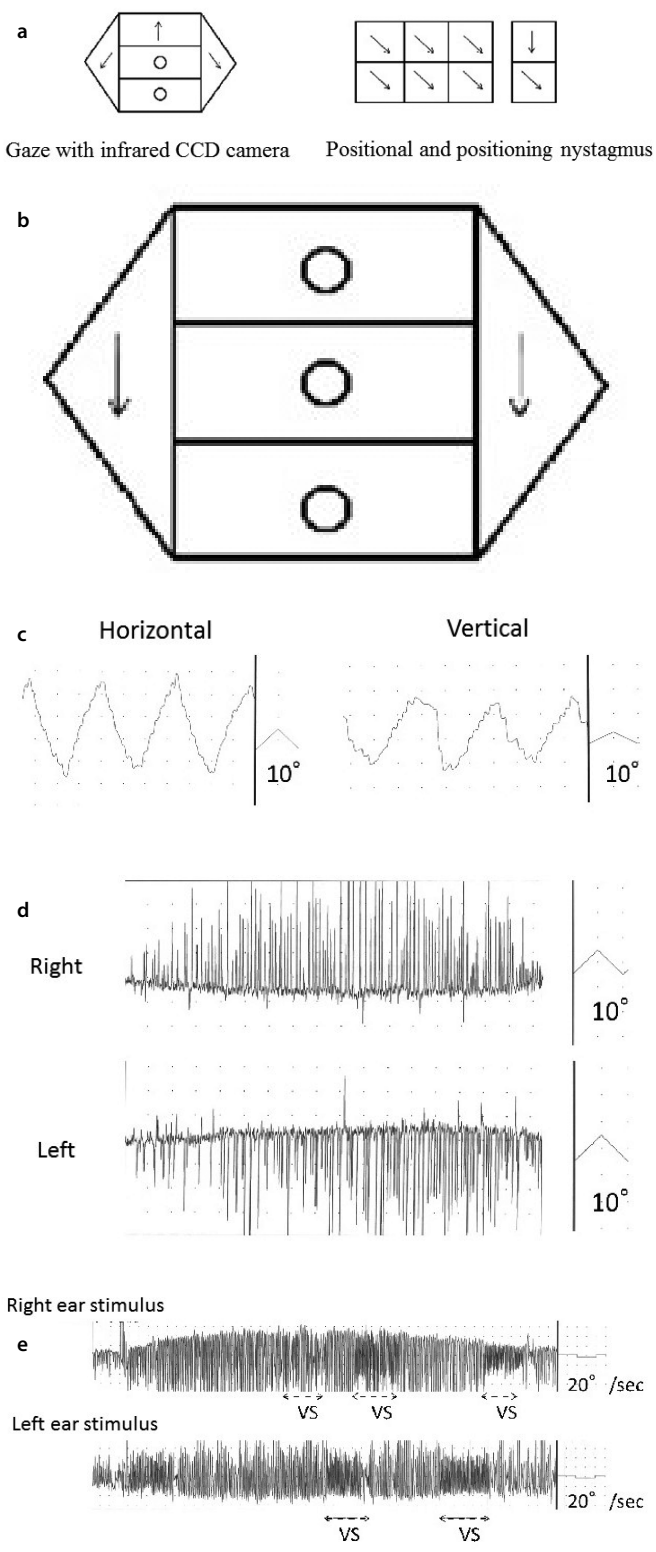

Figure 2. a-e. (a) Diagonal and verticality nystagmus were observed in a infrared CCD camera, (b) spontaneous downward nystagmus was observed in the rightward and leftward gaze in the dark, (c) eye-tracking test (ETT): Both horizontal and vertical ETT showed slightly saccadic patterns, (d) optokinetic nystagmus pattern test (OKNP): A decrease in maximum slow phase velocity was observed, and the degree of blackening was also decreased, (e) caloric test (12°C air caloric); right ear stimulus; nystagmus duration 3 minutes and 25 seconds, maximum slow phase velocity 60°/s. Left ear stimulus; nystagmus duration 4 minutes 00 seconds, maximum slow phase velocity 50°/s

Upon admission, the patient's height was 153 cm and weight was 49 kg. She was conscious and clear, with mild mental retardation. Hyperreflexia was seen in the tendons of the four limbs. Babinski and Chaddock signs were observed in the left extremities. The finger-to-nose and diadochokinesis test results were normal. Impaired interlimb coordination, particularly in the left leg and difficulties with standing and walking were noted. In the blood test at admission to our hospital on X+1month 28th, lactic acid level was 8.9 mg/dL and pyruvic acid was 0.89 mg/dL, which were in the normal ranges. A cerebrospinal fluid test on X+1month 28th showed a colorless and transparent appearance, with protein level 46 mg/dL (normal range: 10-40 mg/dL); lactic acid level 10.9 mg/dL (normal range: 9-16 mg/dL); pyruvic acid level 0.78 mg/dL (normal range: 0.3-0.5); and myelin basic protein and oligoclonal band were negative.

Thereafter, she was referred to the ENT department for neurotological tests. The pure-tone audiometry test result was in the normal range for both ears. Diagonal and vertical nystagmuses were observed using an infrared CCD camera (Figure 2a). The ENG findings on X+2months 11st showed downward nystagmus on both rightward and leftward gaze (Figure 2b). An eye-tracking test (ETT) indicated saccadic eye movements in both horizontal and vertical directions (Figure 2c). An optokinetic nystagmus pattern test (OKNP) indicated poor responses under the stimuli in both right and left directions (Figure 2d). The time and amplitude of the caloric test were normal in both the ears and retention time was >3 min. However, the visual suppression test revealed poor responses, suggesting the disorder of central inhibitory controlling by the cerebellum (Figure 2e).

According to the findings above, multiple sclerosis was considered as the most probable cause and steroid pulse therapy was continued. The symptoms mildly reduced and she was transferred to rehabilitation on X+2months 3rd.

However, on X+5months 30th, she experienced dizziness again and was hospitalized to the previous hospital on the suspicion of recurrence of multiple sclerosis, and steroid pulse therapy was administered. She was discharged after the recovery of symptoms.

Furthermore, dizziness and nausea occurred again on X+9months 29th. Therefore, the patient was admitted to the hospital B, Department of Neurology, and again underwent steroid pulse therapy. On X+10months 4th, we again performed an ENG. The results are presented in Figure 3 a-c.

The patient was repeatedly admitted to hospitals because of dizziness and MRI revealed a spatial distribution of multiple lesions as a clinical feature of multiple sclerosis (Figure 3d). However, another spinal fluid test revealed no oligoclonal bands, which are typically detected in multiple sclerosis. Moreover, the high lactic acid and pyruvic acid levels suggested mitochondrial encephalomyopathy. Subsequently, on X+11months 1st, a muscle biopsy was performed and histopathology revealed ragged-red muscle fibers and confirmed the diagnosis of mitochondrial encephalomyopathy (Figure 4). The oral administration of coenzyme Q10 was started as treatment, and the patient was transferred to rehabilitation. Written informed consent for the medical study was obtained from the patient.

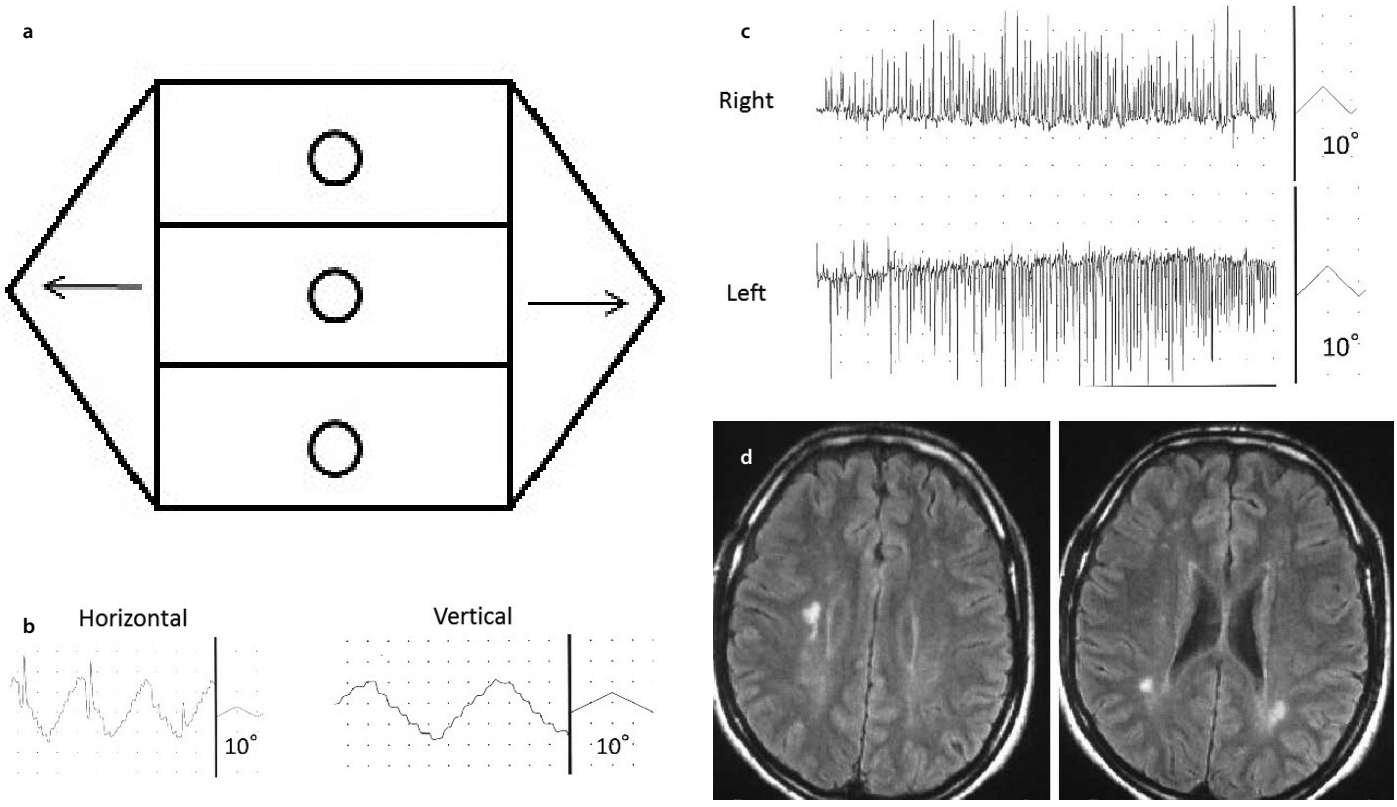

Figure 3. a-d. Electronystagmography (ENG) on X+10months 4th, (a) Nystagmus in the dark: rightward viewing rightwards, leftward viewing leftward viewing nystagmus, (b) Eye-tracking test (ETT): Both horizontal and vertical showed slightly saccadic patterns, (c) Optokinetic nystagmus pattern test (OKNP): A decrease in maximum slow phase velocity was observed, and the degree of blackening was also decreased, (d) MRI findings (horizontal) of T2 FLAIR showed a high-signal area in the bilateral cerebral deep white matter

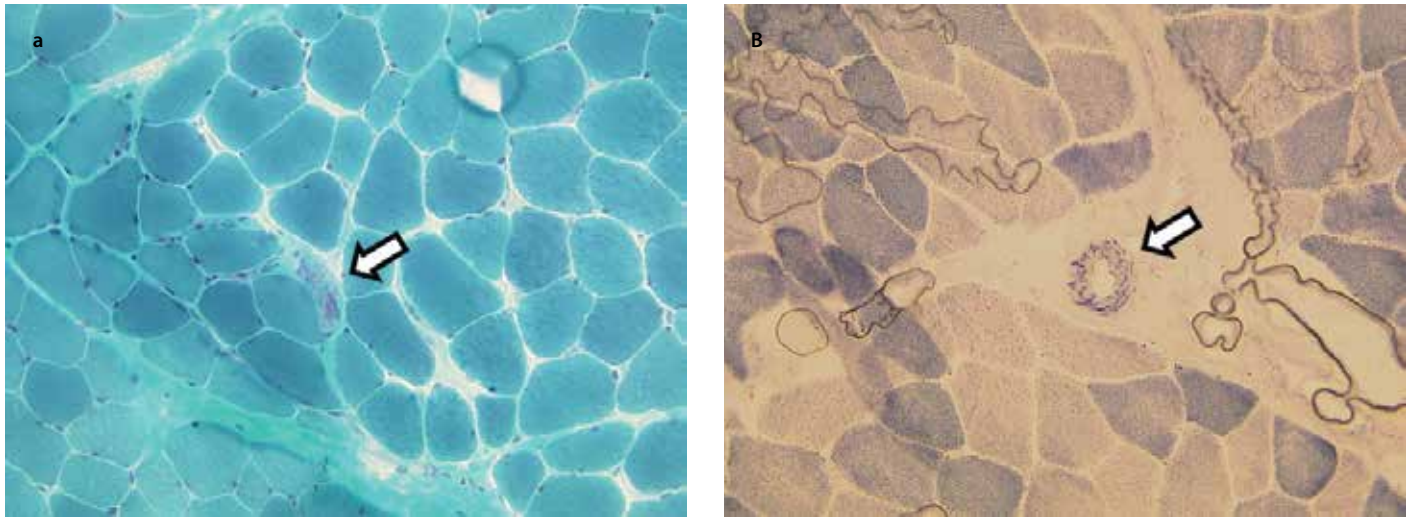

Figure 4. a, b. Histopathological findings of muscle biopsy. (a) Gomori trichrome stain (20× times). Ragged-red fiber was recognized (white arrow), (b) COX staining (20× times). SSV (strongly SDH-positive vessels) was recognized (white arrow)

DISCUSSION

Dizziness in mitochondrial encephalomyopathy is rarely reported, and this report is the first that shows ENG findings, including ETT, OKNP, and caloric test.

Mitochondrial encephalomyopathy is a generic term for syndromes that exhibit skeletal muscle and central nervous system symptoms due to intracellular mitochondrial DNA abnormality [1]. Blood tests show elevated lactic acid and pyruvic acid levels. Myopathology reveals an increasing number of abnormal mitochondria; in particular, increasing muscle fibers are observed as ragged-red fibers in microscopy. MRI shows T2 high-intensity areas in the deep bilateral cerebrum [2]. Regarding treatment, symptomatic therapy and rehabilitation are the focus. Oral coenzyme Q10 and intravenous cytochrome preparation are administered [3, 4].

However, multiple sclerosis sometimes causes dizziness and shows similar MRI findings as mitochondrial encephalomyopathy. In present case, we initially diagnosed the patient with multiple sclerosis based on the dizziness symptoms and MRI findings. However, due to repeated symptoms and blood tests, we suspected mitochondrial encephalomyopathy, and muscle biopsy confirmed the diagnosis. This clinical course was educational.

In the field of otolaryngology, case reports of mitochondrial encephalomyopathy with hearing impairment have been reported, but only a few cases of dizziness have been reported. Regarding deafness, Pavlakis et al. [5] reported 43 patients (61%) with Kearns-Sayre syndrome of the CPEO type and three cases (27%) of the MELAS type.

There are very few reports on nystagmus and vertigo. Iwasaki et al. suggested a relationship with the vestibular dysfunction of the mitochondrial A3243G mutation [6]. In addition, there are only reports from Shinmei et al. [7] and Choi et al. [8] for eye movement abnormality; thus, our report is the first one describing ENG. Shidara et al. [9] explained that there is less vestibular damage compared to hearing impairment because it is resistant to an ischemic condition or is anatomically likely to obtain blood flow from the collateral circulation.

About nystagmus and ENG, mitochondrial encephalomyopathy and multiple sclerosis seemed to be similar because they are both central vestibular disorders. Thus, oblique nystagmus was observed through the infrared CCD camera, which is hardly considered peripheral. In addition, an ETT in ENG revealed a saccadic pattern, which is said to be exhibited by the brainstem/cerebellar single lobe disorder, and OKN showed a decrease in nystagmus velocity caused by a brainstem lesion [10]. With regard to the caloric test, in previous reports, there were various findings, and bilateral nonresponsive cases were also observed, but an apparent caloric response was seen in this case [7]. Therefore, at the least, the neural transmission and function remained via the lateral semicircular canals, superior vestibular nerves, and vestibular nuclei. However, the ETT and OKN, which showed poor responses at that time, supposed that unrevealed lesions using MRI in the brainstem or cerebellum already occurred pathologically. Alternatively, there could be a site involved in these vestibule-ocular abnormalities somewhere in the brain lesion that was depicted in the MRI, although the data are still unknown.

Informed Consent: Written informed consent was obtained from the patient who participated in this study.

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Author Contributions: Concept - S.S., H.I., Y.N.; Design - Y.N., S.S.; Supervision - T.O., S.K.; Materials - T.T., Y.N., S.S., H.I.; Data Collection and/or Processing - T.T., Y.N., A.K., S.S., H.I.; Analysis and/or Interpretation - T.T., Y.N., S.S., H.I.; Literature Review - T.T., Y.N., A.K., H.M.; Writer - T.T., Y.N.; Critical Review - T.O., H.M.

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