Case Report

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Epileptic nystagmus with different localization of lesions in magnetic resonance imaging in a patient with MELAS

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Abstract

Mitochondrial myopathy, encephalopathy, lactic acidosis, and stroke-like episodes (MELAS) is a syndrome which is characterized as mitochondrial myopathy, encephalopathy, lactic acidosis and recurrent stroke-like episodes. Recurrent attacks of prolonged migrainous headache, different types of epileptic seizures and repeated cerebral lesions are the main clinical features of the disease. Cerebral lesions can cause different seizure types in this syndrome according to affected brain areas. Herein, we are reporting a case of MELAS who experienced recurrent neurologic deficits, confusional states and epileptic seizures with ictal epileptic nystagmus. Ictal electroencephalogram (EEG) recordings and magnetic resonance imaging (MRI) lesions also supported to the ictal focus of epileptic nystagmus. With this case, we would like to take attention to this rare ictal event.

Keywords: Seizure, epileptic nystagmus, MELAS

INTRODUCTION

Mitochondrial myopathy, encephalopathy, lactic acidosis, and stroke-like episodes (MELAS) covers a range of symptoms: encephalopathy frequently presenting with seizures and progressive cognitive decline, stroke-like episodes at a young age, and biochemical or morphologic evidence for mitochondrial defects such as lactic acidosis or ragged-red fibers (RRF) in muscle biopsies (1). Epilepsy in MELAS is associated either with complex partial or generalized seizures, which mostly evolve to status epilepticus (2). Seizures occur primarily in patients who have stroke-like lesions, and are often associated with migraine-like headache. Stroke-like lesions are usually located at the occipital and temporal lobes, and seizure semiology often reflects involvement of these locations.

We report a patient with recurrent headaches, confusion, focal neurologic deficit, and epileptic seizures who was diagnosed as having MELAS. Epileptic nystagmus, a rarely seen ictal event, accompanied two seizure episodes.

CASE PRESENTATION

A 23-year-old woman was admitted to our clinic with sudden-onset headache and difficulty in comprehension, which she had for 2 days. She had two preeclampsia episodes in her medical history and reported no recurrent headache or other previous neurologic problems. Her family history was also unremarkable. On neurologic examination, perceptive aphasia was detected. A diffusion hyperintensity with corresponding apparent diffusion coefficient (ADC) hypointensity was observed in the left temporal lobe. An acute ischemic infarction on the posterior division of the left temporal lobe was revealed on brain magnetic resonance imaging (MRI) (Figure 1). MR-venography, biochemical tests (liver-renal function tests, erythrocyte sedimentation rate, C-reactive protein), and complete blood count were within normal limits.

In the ischemic stroke analysis, there were no abnormal findings in vasculitic markers (dsDNA, ANA, ANCA, anti-Ro, anti-La), thyroid function tests, serum pyruvate-lactate level and serum viral serology (anti-HIV, Hepatitis-B, Hepatitis-C, CMV, and VZV). MR-angiography of neck and cranium, electrocardiography and echocardiography were also normal. Due to temporal lobe involvement, lumbar puncture was also performed to exclude herpes encephalitis

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and there was no finding of infection in cerebrospinal fluid (CSF) analysis. During clinical follow-up, the patient reported seeing colorful objects in relatively small or large scales. Therefore, electroencephalogram (EEG) was performed upon clinical suspicion of an epileptic seizure. During the EEG recording, the patient reported blindness and experienced right-beating horizontal nystagmus. EEG showed fast activity (12-13 Hz) in the occipital electrodes with evolution of spike and wave activity in the left occipito-temporal region (Figure 1). The episode lasted a couple of minutes with a recurrence every 3 minutes. An injection of intravenous (IV) 10 mg diazepam reduced the frequency of seizures and a 1500 mg IV levetiracetam infusion was administered afterwards. Her long term treatment was continued with 1500 mg/day levetirac-

Figure 1. Fast spike activity is seen on occipito-temporal region on scalp EEG, bipolar, double banana montage (red arrow). Cranial MRI (diffusion with ADC scans) showed left temporo-occipital lesion

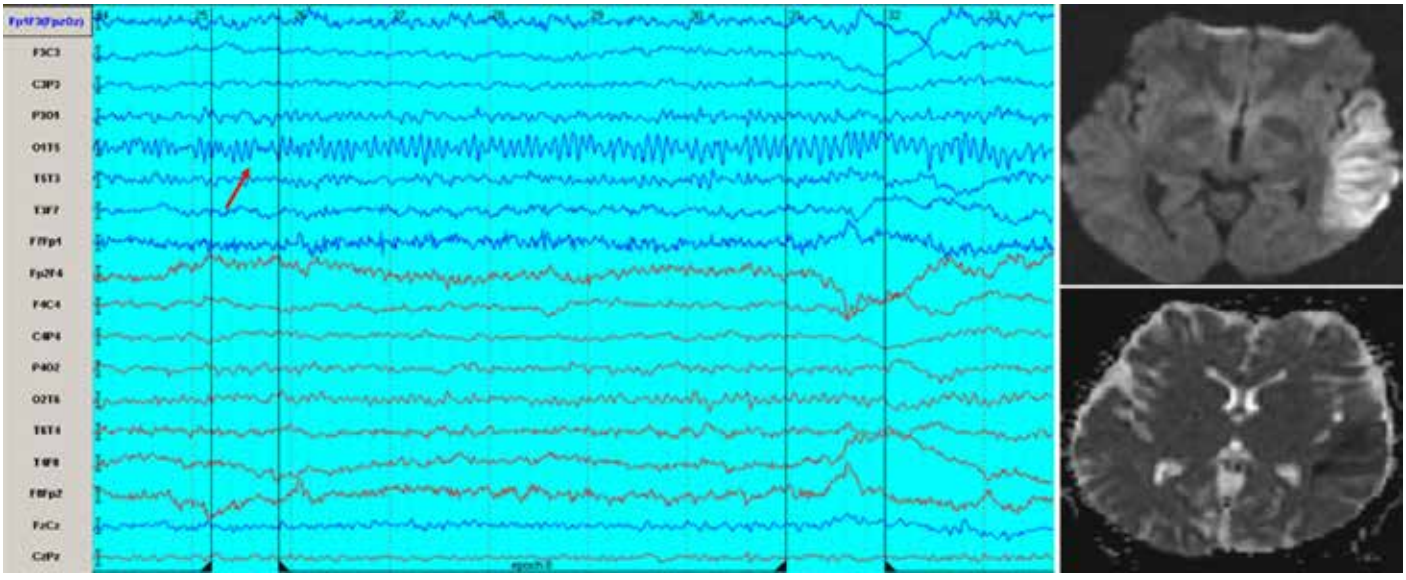
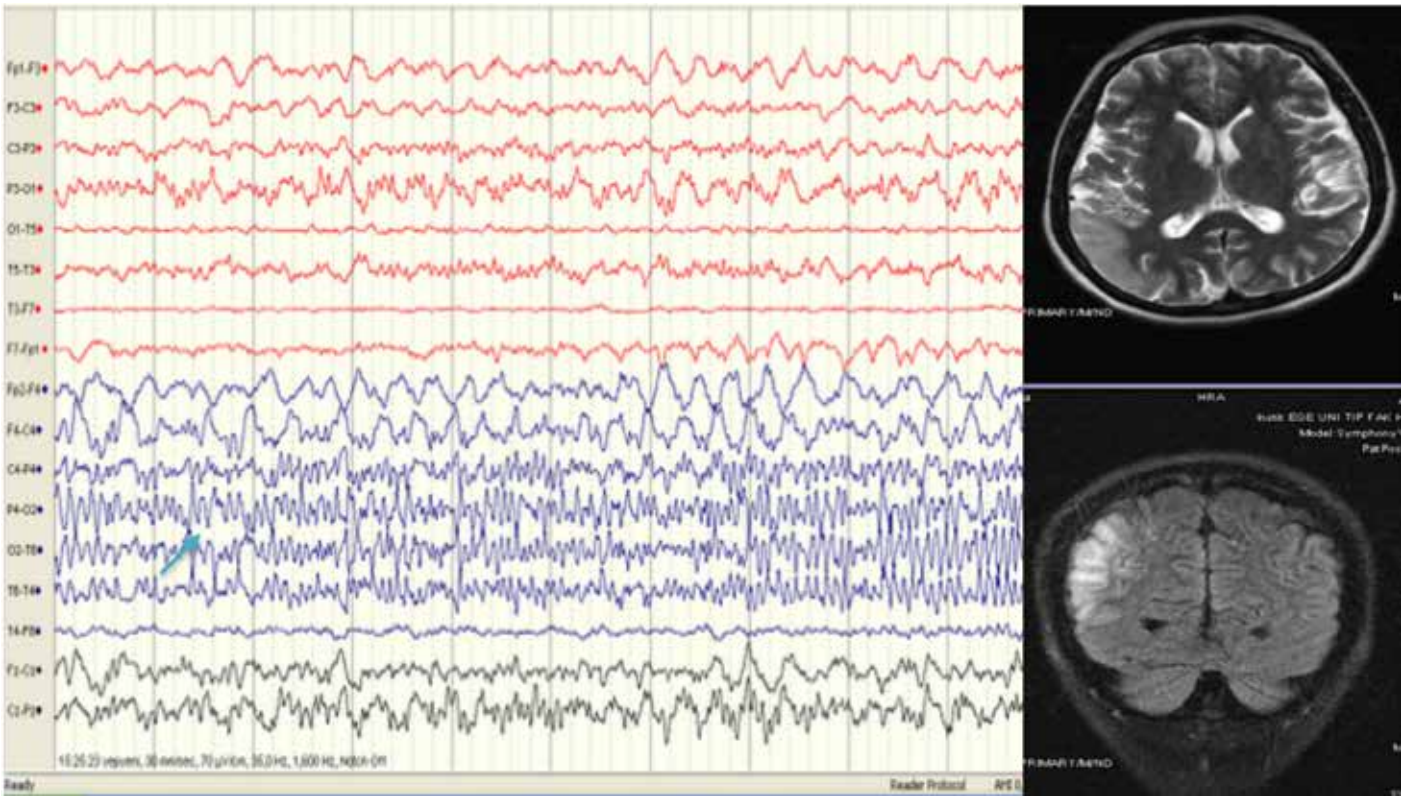


Figure 2. On scalp EEG (double banana, bipolar montage), ictal fast activity is prominently seen on right temporo-parieto-occipital region. Cranial MRI (T2-flair) showed right parieto-occipital hyperintensity



etam. She was free of seizures under the levetiracetam treatment and also her aphasia regressed. A follow-up EEG was normal. During clinical follow-up, her speech and comprehension completely recovered and she was discharged with 1500 mg/day levetiracetam treatment.

The patient was re-admitted to hospital after 2 months with an episode of headache, vomiting, and loss of vision in the left visual field. Left homonymous hemianopia was detected and brain MRI revealed a new lesion in the right occipital lobe; resolution was observed in the previous left hemispheric lesions. EEG showed slow (6-7 Hz) background activity in the right hemisphere with no epileptiform discharges. After 20 days of the second episode, a follow-up brain MRI was obtained and the right occipital lesion was also resolved. She was discharged from the hospital with 2000 mg/day levetiracetam treatment and her symptoms regressed.

One year after the first episode, the patient experienced a third attack with symptoms of headache, vomiting and focal motor seizure in the left arm. There were no motor or sensory deficits, but she was confused and her reaction time was prolonged.

A new lesion in right parieto-occipital area was detected on brain MRI (Figure 2). EEG showed fast spike activity (10-12 Hz) in the right parieto-occipital region that spread to the same hemisphere (Figure 2), and a seizure episode with left-beating horizontal nystagmus, and clonic movements in left hand and left side abdominal muscles were observed. Seizure was stopped with administration of IV diazepam and a 3500 mg levetiracetam infusion. In her third attack, an elevated serum lactic acid level was detected (40 mg/dL; normal range: 5-20 mg/dL) and an increased lactic acid level was also seen in CSF analysis (48 mg/dL; normal range: 10-22 mg/dL). Needle, myogenic motor unit potentials, which show myopathy, were demonstrated in the proximal upper extremity muscles. To verify a mitochondrial pathology, a muscle biopsy was taken from the left deltoid muscle. Ragged-red fibers were seen using modified Gomori trichrome staining. Genetic analysis revealed an A3243G mitochondrial mutation associated with MELAS. In terms of systemic involvement, only bilateral sensorineural hearing loss was detected.

L-carnitine and coenzyme Q10 were added to her current treatment. Under this treatment, she experienced complex partial seizures once per month. The patient is being regularly monitored for seizure frequency and systemic complications, which could possibly be seen in the future.

DISCUSSION

In our case, the clinical presentation, brain MRI findings, biochemical test results, and muscle biopsy findings supported the diagnosis of MELAS. MELAS may be associated with partial or generalized seizures, including progression to status epilepticus (2). In a study on 31 patients with a mitochondrial disorder and epilepsy, five patients were classified as having MELAS-syndrome (3). Seizure onset began between the ages of 14 and 39 years in these patients. Prior to onset of seizures, these patients developed stroke-like episodes, migraine, diabetes or psychomotor retardation (3). Four patients developed partial seizures and one patient had tonic-clonic seizures. EEG recordings in these patients showed diffuse slowing, unilateral slowing, focal posterior sharp waves, and symmetrical sharp waves or photosensitivity (3). Recurrent complex partial seizures and non-convulsive status epilepticus have been reported in other patients with MELAS-syndrome (4).

Our patient predominantly experienced complex partial seizures and we recorded rare clinical ictal seizure activity as epileptic nystagmus. Before the seizure episodes, she had migraine-like headache episodes, focal neurologic deficits, and signs of encephalopathy. Non-convulsive status epilepticus could also be considered in these cases because of confusion. However, EEG did not support non-convulsive status epilepticus during the confusional episode in our patient.

The findings in the literature regarding epileptic nystagmus can be summarized as follows: in almost all patients, the nystagmus beat is on the opposite side of that ictal discharges. Seizures are mostly symptomatic and mostly originate from the posterior part of the brain (5). Epileptic nystagmus is infrequent; it was reported in only 10% of 42 patients with occipital lobe epilepsy (6). In the literature, there is only one case of epileptic nystagmus associated with MELAS. The ictal activity of that case was detected in the temporo-occipital region corresponding to diffusion restriction in that area (7). In our case, we observed epileptic nystagmus beating on different sides in two different attacks, which correlated with the epileptic focus and clinical seizure activity. Ictal EEG recording indicated the occipital origin and MRI revealed temporo-occipital or parieto-occipital lesions. Lesions tend to appear in different locations for different episodes, which is particularly characteristic of MELAS syndrome (8). Brain MRI in patients with MELAS show changes predominately in the occipital, parietal and temporal lobes that could simulate ischemic stroke (9). The exact mechanism of the disease predilection for certain locations in the central nervous system has not yet been clarified, but the possibility of heteroplasmy in brain tissue was ruled-out by genetic studies when comparing tissue from different brain areas (9). These brain lesions can be unilateral or bilateral. However, these areas do not fit to specific vascular territories. Angiographic studies show that vessels in the affected regions have increased blood flow and are sometimes dilated (10). The temporal, parietal, and occipital lobes were also the most affected brain parts in our patient. Furthermore, different localizations of MR lesions showed concordance with clinical ictal seizure events in each episode of our patient.

In conclusion, MELAS is a rare cause of epilepsy and can present with different seizure types. Other accompanying neurologic deficits and neuroimaging findings are major clues in the diagnosis of this syndrome. Early diagnosis with adequate seizure control in MELAS must be the main goal of physicians to prevent or reduce neurologic sequelae because this is a disease that affects young adults.

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