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Case report

Adult-onset of mitochondrial myopathy, encephalopathy, lactic acidosis and stroke-like episodes (MELAS) syndrome with hypothyroidism and psychiatric disorders

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ABSTRACT

Mitochondrial myopathy, encephalopathy, lactic acidosis and stroke-like episodes (MELAS) is a clinical syndrome associated with mitochondrial disorders (MIDs). This report illustrates a case of MELAS syndrome with hypothyroidism and psychiatric disorders, which is different from the common clinical manifestations of MELAS syndrome, such as exercise intolerance, migraine-like headaches, hearing loss and seizures etc. There are considerable interests in the possibility that mitochondrial dysfunction may play a role in the pathogenesis of endocrine dysfunctions and psychiatric disorders in MELAS syndrome.

1. Introduction

Mitochondrial disorders (MIDs), presenting as multi-system affected, such as the central and peripheral nervous system, eyes, ears, endocrine glands, heart, kidney etc., single or multiple combination, are clinically, biochemically and genetically highly variable [1]. MIDs may onset at any age since birth until adulthood with acute or progressively chronic manifestation [2]. Mitochondrial encephalopathy, lactic acidosis and stroke-like episodes (MELAS) is a subtype of MIDs. Approximately 80% of patients with MELAS carry the A3243G mutation in the mitochondrial DNA [3,4]. An adult MELAS patient with a mutation at A3243G point, characterized by hypothyroidism and psychiatric disorders simultaneously is presented in this article.

2. Case report

The patient was a 37-year-old female, of 157 cm in height and 45 kg in weight. She was transferred to our department from a local hospital due to psychiatric features (both agitated behavior and auditory hallucinations), alexia and apraxia that had begun 10 days ago, followed by disorientation and generalized tonic-clonic seizures. She had a long history of episodic migraine-like headaches and progressive bilateral hearing loss for 3 years. However, she did not take any medication.

Her vital signs showed a normal body temperature of 36.8 °C, a hypotension of 90/56 mm Hg and pulse at 72 beats per minute. Because of the patient's psychiatric symptoms and application of sedative after seizure attacks, she could not cooperate with physical examination.

The laboratory data showed high anion gap metabolic acidosis with elevated levels of lactate and pyruvate. Serum levels of thyroid-stimulating hormone (TSH) and free thyroxine (FT4) were decreased. Her TSH level was low at 0.26 mU/L (normal range 0.35–5.5 mU/L), and FT4 concentration was 7.56 pmol/L (normal range 10.2–31 pmol/L). Both serum free and total triiodothyronine (FT3 and TT3) were significantly lower than normal range. FT3 concentration was 2.28 pmol/L (normal range 3.5–6.5 pmol/L), and TT3 concentration was 0.6 nmol/L (normal range 1.2–3.4 nmol/L). Moreover, elevated titers of serum anti-thyroglobulin and anti-thyroid microsomal antibodies were detected. Cerebral spinal fluid (CSF) studies were normal for cell counts and biochemistry, and negative for culture. CSF IgG index was 0.48 (normal range ≤ 0.7), and oligoclonal bands (OB) was negative.

Computed tomography (CT) scan showed lesions of hypodense in the left temporal and parietal lobe, with brainstem and cerebellar atrophy (Fig. 1A). No evidence of subarachnoid or intracerebral hemorrhage. Vascular imaging of the cervical and cerebral arteries by CT angiography excluded the possibility of cerebrovascular disease (Fig. 1B). However, CT images were not conclusive to differentiate between the infectious or metabolic lesion. On day 5, brain magnetic resonance

Abbreviations: MELAS, mitochondrial myopathy, encephalopathy, lactic acidosis and stroke-like episodes; MIDs, Mitochondrial disorders; MRC, mitochondrial respiratory chain; ATP, adenosine triphosphate; CT, Computed tomography; MRI, magnetic resonance imaging; ROI, region of interest; CSF, Cerebral spinal fluid; OB, oligoclonal bands; NAA, *N*-acetyl aspartic acid; Cr, creatine; BAEP, Brainstem auditory evoked potential; DWI, diffusion-weighted image; ADC, apparent diffusion coefficient; FLAIR, fluid-attenuated inversion recovery; DNA, deoxyribonucleic acid; RFLP, restriction fragment length polymorphism.

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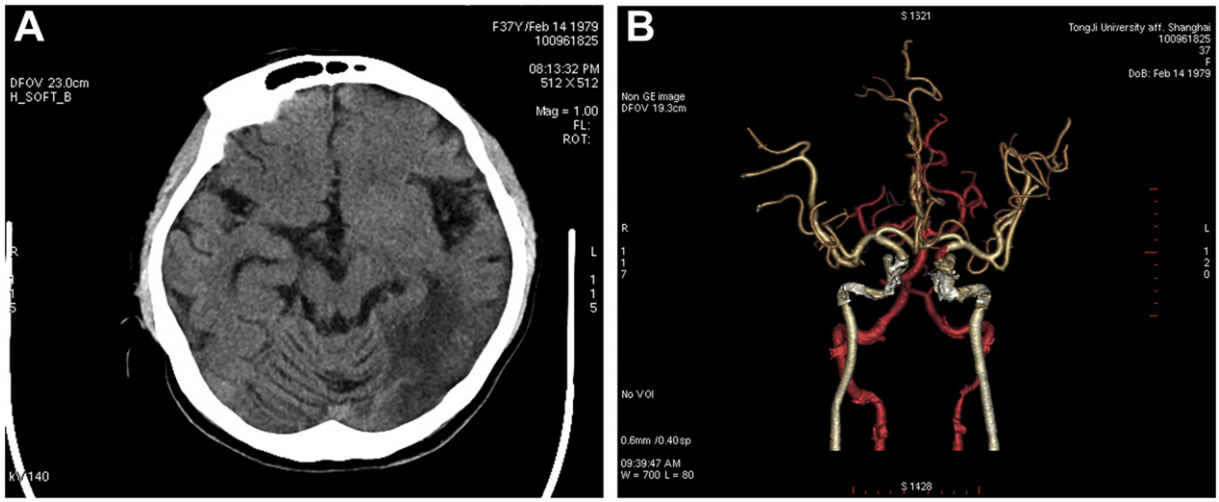

Fig. 1. CT scan showed lesions of hypodense in the left temporal and parietal lobe (Panel A). Three-dimensional reconstruction of CT vessel images (Panel B).

imaging MRI (3.0 T) revealed a hypointensity lesion in the left temporal-parietal lobe on T1 weighted image (Fig. 2A), and increased signal intensity in the same region on FLAIR sequences (Fig. 2B) with a clearly restricted diffusion (Fig. 2C). The signal intensity on ADC sequence was mildly reduced (Fig. 2D). No obvious enhancement was found on Gd-DTPA enhanced images (Fig. 2E). MR spectroscopy was carried out as well. Compared to the ipsilateral normally appearing area (Fig. 2F), there was a significantly elevated lactate peak at 1.3 ppm in region of interest (ROI) with decreased NAA spectrum and reduced NAA/Cr ratio (Fig. 2G). The change of the spectrum reflected the severity of metabolic disorders, suggesting the local accumulation of lactic acid and disturbance of hypoxic processes.

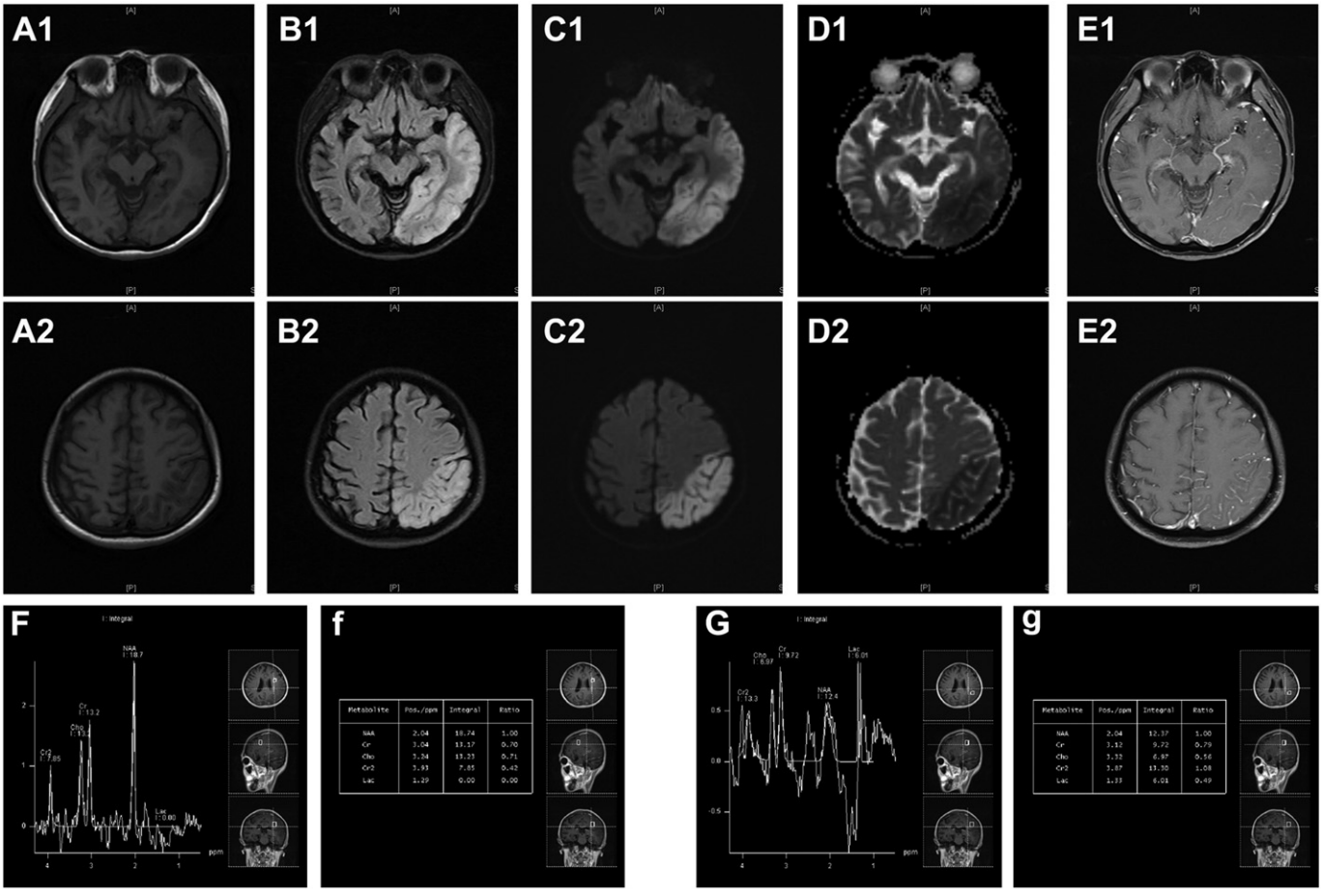

Fig. 2. Brain MRI (3.0 T) revealed a hypointense lesion in the left temporal and parietal lobe on T1 (Panel A), and increased signal intensity in the same region on Flair (Panel A) image with a clearly restricted diffusion (Panel C). The signal intensity on ADC sequence is mildly reduced (Panel D). No obvious enhancement was found on Gd-DTPA enhanced images (Panel E). Compared to the ipsilateral normally appearing area (Panel F), MR spectroscopy presented a significantly elevated lactate peak at 1.3 ppm in region of interest (ROI) (Panel G). Panels f and g are the molecular findings of metabolites respectively.