Dandy–Walker Malformation and Mitochondrial Encephalopathy, Lactic Acidosis, and Stroke-like Episode Syndrome: Is There a Causal or Coincidental Association?

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To the Editor: The syndrome of mitochondrial encephalopathy, lactic acidosis, and stroke-like episode (MELAS) is one of the most frequently occurring mitochondrial disorders. Dandy–Walker malformation (DWM) is a rare posterior fossa malformation. We report a 21-year-old male with DWM and MELAS syndrome.

This report focuses on a 21-year-old Chinese male who is the only child of nonconsanguineous parents. His family history was unremarkable. Developmental milestones were achieved at the appropriate ages. The patient presented with his fourth stroke-like event within a 2-year period. The primary clinical manifestations were aphasia, recurrent headache, muscular weakness, cortical blindness, and seizures. Neurological examination showed anomic aphasia, right visual field deficits, left hemiparesis (muscle power was 4/5), gait ataxia, and cognitive impairment (mini-mental state examination score of 16). The cerebrospinal fluid examination was unremarkable. At 8 h after the event, the lactic acid levels were 200 mg/L. A significant increase in lactic acid levels in the serum was observed during the stroke-like event. They increased to 700–1200 mg/L during the event and decreased to 250 mg/L afterward.

Several magnetic resonance imaging (MRI) results revealed infarcts in the bilateral temporal lobes and the parietal and occipital lobes, which were inconsistent with any vascular distribution [Figure 1]. Meanwhile, there was demonstrated hypoplasia of the cerebellar vermis and cystic dilatation of an enlarged fourth ventricle, which are consistent with a diagnosis of DWM [Figure 2]. Repeated cerebrovascular disease tests were negative for stenosis and abnormalities.

During his admission in May 2014, polymerase chain reaction was used to sequence the patient's DNA. An AG mutation (A3243G) was found in the tRNA-Leu gene of the mitochondrial DNA, confirming MELAS syndrome. Therefore, he was diagnosed with MELAS syndrome and DWM.

The last stroke-like period was treated with coenzyme Q10 (CoQ10, 100 mg, 3 times/day), butylphthalide soft capsules (0.2 g, 3 times/day), and levetiracetam tablets (1000 mg, 2 times/day). At 6-month follow-up, the symptoms of aphasia, headache, cortical blindness, and seizures were disappeared, but his cognitive impairment and left hemiparesis remained unaltered. Unfortunately, we were unable to perform follow-up brain MRI.

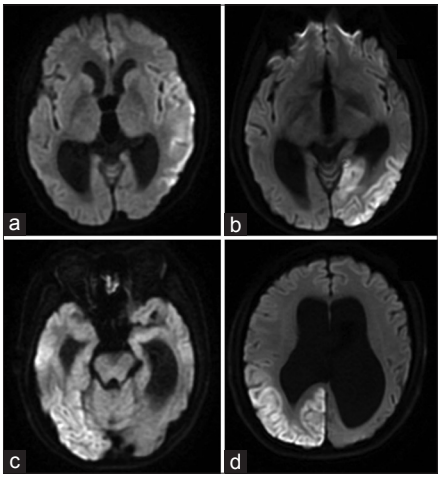

Figure 1: Magnetic resonance imaging results (diffusion weighted imaging) from the patient suffered four "stroke-like" accidents showing lesions at (a) left temporal lobe, (b) left temporal and occipital lobe, (c) right temporal lobe, (d) right parietal and occipital lobe.

DWM is characterized by hypoplasia or agenesis of the cerebellar vermis, involving the cortex and deep cerebellar nuclei, enlargement of the fourth ventricle in continuity with a posterior fossa cyst. It has been shown to be associated with multiple congenital anomalies or other diseases including down syndrome, Wisconsin syndrome, neurocutaneous melanosis, and schizophrenia.[1-4] However, to the best of our knowledge, there are few reports of a DWM diagnosis associated with mitochondrial diseases. MELAS

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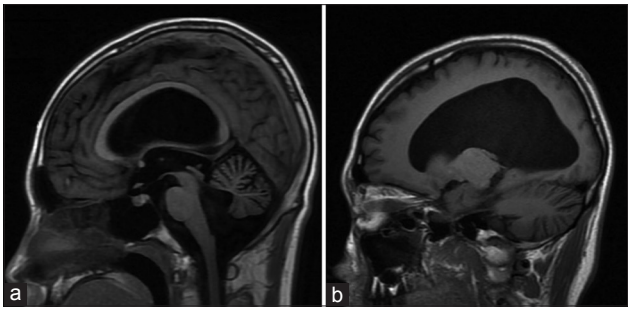

Figure 2: Axial T1-weighted brain magnetic resonance imaging results. It demonstrates the (a) hypoplasia of cerebellum and enlarged fourth ventricle and (b) hydrocephalus findings of characteristics of Dandy–Walker malformation.

syndrome is one of the most frequently occurring mitochondrial disorders and is most commonly caused by an A-to-G transition mutation at the 3243 position of the mitochondrial genome. However, mutations in the nuclear DNA may also contribute to this disorder. Many findings suggest that DWM is primarily due to a nuclear genome alteration. Unfortunately, we were unable to perform autosomal DNA tests on the patient because of cost. It is unclear that whether the coincidence of MELAS and DWM is coincidental or causal, further researches are needed to elucidate this possible association.

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Conflicts of interest

There are no conflicts of interest.

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