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A Case of MELAS With the m.3243A>G Variant of the MT-TL1 Gene Mimicking Acute Intermittent Porphyria

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Dear Editor,

The syndrome of mitochondrial encephalopathy, lactic acidosis, and stroke-like episodes, commonly called MELAS, is one of the family of mitochondrial diseases.[1] We report a MELAS patient who carried a pathogenic variant (m.3243A>G) in the mitochondrial tRNA leucine 1 (MT-TL1) gene. The patient presented with seizures, peripheral neuropathy, and acute abdominal pain. Acute intermittent porphyria (AIP) was initially suspected due to his symptom constellation. This case report highlights the difficulty of diagnosing a mitochondrial disorder presenting with porphyria-like syndromes, which has not been broadly described in MELAS.

A 23-year-old previously healthy male with no relevant medical history presented to the emergency room with new onset of status epilepticus. He deteriorated with cardiac arrest requiring cardiopulmonary resuscitation. He was successfully resuscitated and then transferred to an intensive-care unit, where sodium valproate and other supportive treatments were administered. On day 10 he was extubated. Once stable, he was transferred to Huashan Hospital affiliated with Fudan University for further diagnosis and treatment. Detailed history-taking showed that his family history was unremarkable, including non-consanguineous parents. His height was 173 cm but he had a low body mass index of 13.4 kg/m^2, with his body weight decreasing from 52 kg to 40 kg during the present admission. There was no significant evidence of deafness or visual deficits. In a neurological examination he was alert and oriented. He had bilateral facial palsy (Fig. 1A) with associated dysarthria and dysphagia. There was evidence of generalized muscle atrophy (Fig. 1B). He exhibited significant weakness in his arms and legs, with both upper and lower limbs having a strength of 4/5 proximally, while distally his arms had a strength of 3/5 and his legs had a strength of 0/5. Muscle tone was reduced throughout. The Babinski sign was absent bilaterally. He had decreased pain, temperature, and proprioceptive sensations in the distal lower limbs.

He continued to experience episodes of sudden, severe abdominal pain with vomiting and constipation during his hospitalization. During the attacks of pain, his abdomen was soft and nontender, with normal bowel sounds. The pain could be rapidly relieved by gastrointestinal decompression.

He was noted to have anemia with a hemoglobin level of 102 g/L (normal 130−175 g/L). His erythrocyte sedimentation rate level was elevated, at 60 mm/h (normal <15 mm/h). The creatine kinase level was 35 U/L (normal 50−310 U/L). The blood lactic acid level was high, at 3.1 mmol/L (normal 0.7−2.1 mmol/L). Lumbar puncture was performed, which revealed a cerebrospinal fluid (CSF) pressure of 60 mmH_20 (normal 80−180 mmH_20). The CSF white cell count, protein level, and glucose level were normal. The CSF lactic acid level was higher than the normal range (1.1−2.4 mmol/L), at 3.2 mmol/L. A 4.5-hour sunlight urine test was ordered due to concern about porphyria, but it was negative (Fig. 1C).

Electromyography revealed multiple peripheral neuropathies, mainly affecting the motor

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axons. Mild myogenic damage was revealed in some muscles. Brain magnetic resonance imaging (MRI) revealed multiple enhanced lesions in the right occipital cortices (Fig. 1D). Susceptibility-weighted imaging (SWI) showed abnormal low signal intensities in the subcortical right occipital lobe (Fig. 1E). Abdomen computed tomography did not reveal any abnormality. The only abnormal finding in MRI of the lower limb muscles was mild atrophy in the left biceps brachii. A muscle

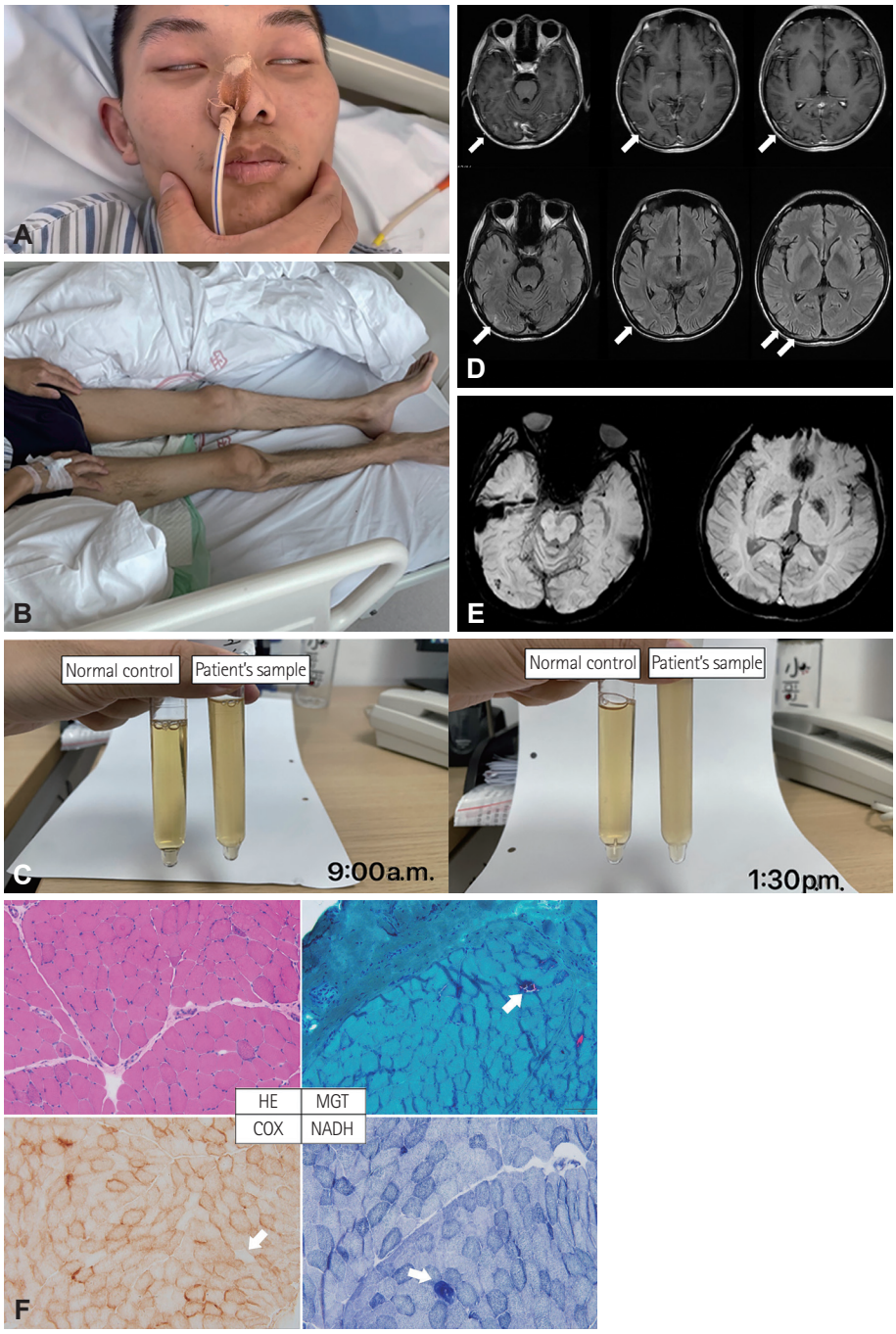

Fig. 1. Clinical phenotype, sunlight urine test result, brain magnetic resonance imaging (MRI), susceptibility-weighted imaging (SWI), and muscle biopsy results. A, B: Patient showed bilateral facial palsy and obvious muscle wasting in both lower limbs. C: A sunlight urine test of the patient produced a negative result. D: T1-weighted post-gadolinium imaging (upper row) and T2-weighted fluid attenuated inversion recovery (FLAIR) imaging (lower row) revealed multiple enhanced lesions in the right occipital lobe (arrows). E: SWI showed abnormal low signal intensities in the subcortical right occipital lobe. F: The skeletal biopsy revealed suspicious ragged-red fibers, COX-negative fibers and ragged blue fibers (white arrows). Original magnification: ×150 in HE, ×100 in MGT, and ×150 in COX and NADH. COX, cytochrome C oxidase stain; HE, hematoxylin and eosin stain; MGT, modified Gomori trichrome; NADH, nicotinamide adenine dinucleotide stain.

biopsy and genetic testing were also ordered.

Levetiracetam, L-carnitine, arginine, coenzyme Q10, and vitamin E were administered. The limb strength, dysarthria, dysphagia, and abdominal pain of the patient gradually improved over about 1 week. After 2 weeks he could stand without any assistance, and 1 month later he was discharged from Huashan Hospital affiliated with Fudan University. The results of the muscle biopsy and genetic testing were available at 40 days after his initial admission. The histopathological examination revealed suspicious ragged-red fibers, cytochrome C oxidase (COX)-negative fibers and ragged blue fibers (Fig. 1F). The genetic testing of blood mtDNA mutations detected the m.3243A>G variant in the MT-TL1 gene.

The typical symptoms of AIP include severe and colicky abdominal pain,[2] psychiatric symptoms,[3] peripheral neuropathies, and central nervous system signs including seizures.[4] Our patient's presentation was broadly consistent with AIP. However, repeated sunlight urine tests produced negative results. Our patient showed an acute pseudo-obstruction symptom. Although there are several cases reports of severe acute abdominal pain and chronic or subacute pseudo-obstruction among those with the m.3243A>G pathogenic variant,[5-8] there is still little evidence of acute pseudo-obstruction symptom in m.3243A>G-related mitochondrial disease. The present case indicates that individuals with the m.3243A>G pathogenic variant can present with a porphyria-like syndrome. A differential diagnosis should be made between mitochondrial disorders and porphyria when patients present with seizures, acute axonal neuropathy, and severe acute abdominal pain.

Ethics Statement

Informed consent was obtained from the patient for the publication of this report, including the photographs.

Availability of Data and Material

All data generated or analyzed during the study are included in this published article.

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Conflicts of Interest

The authors have no potential conflicts of interest to disclose.

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