HE MELAS syndrome, first described in 1984, presents as a combination of mitochondrial myopathy, encephalopathy, lactic acidosis, and strokelike episodes. The disease shares some features with two other mitochondrial diseases, Kearns–Sayre syndrome and MERRF (myoclonus epilepsy and ragged-red fibers) syndrome, and all three manifest as ragged-red fibers on skeletal muscle biopsy. Clinically, MELAS syndrome is characterized by strokelike episodes, nausea, vomiting, encephalopathy, seizures, short stature, headaches, muscle weakness, exercise intolerance, neurosensory hearing loss, hemiparesis, hemianopsia, cortical blindness, lactic acidemia, occasional elevated levels of muscle enzymes, and myopathy. The MELAS syndrome was identified by its distinct clinical features and by morphological and biochemical studies of muscle. Recent advances in molecular genetic analysis have provided a more reliable method for the identification of the causative point mutations, most commonly found at the nucleotide pair of 3243 or 3271.

A 28-year-old woman presented with mitochondrial myopathy, encephalopathy, lactic acidosis, and strokelike episodes (MELAS). The diagnosis was based on the results of molecular genetic analysis, which indicated a typical point mutation at the nucleotide pair 3243. Xenon computerized tomography scans obtained during the strokelike episodes revealed the lesion responsible for the symptoms to be an area of focal hyperperfusion, and scans obtained after the episodes revealed an area of hypoperfusion. Pathogenesis of the strokelike episodes appears to be metabolic dysfunction, although the involvement of a vascular event cannot be excluded.

Case report

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A 28-year-old woman presented with mitochondrial myopathy, encephalopathy, lactic acidosis, and strokelike episodes (MELAS). The diagnosis was based on the results of molecular genetic analysis, which indicated a typical point mutation at the nucleotide pair 3243. Xenon computerized tomography scans obtained during the strokelike episodes revealed the lesion responsible for the symptoms to be an area of focal hyperperfusion, and scans obtained after the episodes revealed an area of hypoperfusion. Pathogenesis of the strokelike episodes appears to be metabolic dysfunction, although the involvement of a vascular event cannot be excluded.

Case Report

History. This 28-year-old woman was admitted to our hospital because of subacute onset of recent memory and speech disturbance. The patient had suffered from generalized convulsion when she was 23 years of age. At that time, cerebral CT scans obtained at another hospital had demonstrated calcification in the bilateral basal ganglia.

Focal hyperperfusion in a patient with mitochondrial myopathy, encephalopathy, lactic acidosis, and strokelike episodes

Case report

Abbreviations used in this paper: CBF = cerebral blood flow; CT = computerized tomography; MELAS = myopathy, encephalopathy, lactic acidosis, and strokelike episodes; MR = magnetic resonance.
Bilateral sensorineural hearing loss was noted when the patient was 26 years of age. Her sister had died suddenly at the age of 19 years.

Examination. On admission, neurological examination demonstrated agraphia, finger agnosia, right–left disorientation, and acalculia, which indicated Gerstmann syndrome. The patient also had ideomotor apraxia and amnestic aphasia. No motor paresis was present, but her speech and gait were moderately disturbed and she was unable to perform simple actions such as operating a television, using chopsticks, and screwing bottle caps on and off. She could not select appropriate words during conversation and was disoriented as to place and date. The patient’s height was 146 cm, and mild atrophy was found in her upper and lower extremities bilaterally.

Computerized tomography scans revealed bilateral hemispheric atrophy with calcification in the bilateral basal ganglia and an isodense area in the left parietooccipital region (Fig. 1). A T2-weighted MR image demonstrated a hyperintense area in a similar location (Fig. 2). No enhancement was found on MR images after administration of contrast medium. Ischemic stroke was suspected, but cerebral angiography revealed dilation of the cortical arteries and capillary blush without occlusive lesions in the left parietooccipital region (Fig. 3 left). Concurrent xenon CT scans revealed increased regional CBF in the region that corresponded to the lesion (Fig. 3 right).

Laboratory examinations yielded normal results, except for a high level of glucose in the serum (210 mg/dl) and urine. Blood gas analysis of an arterial blood sample obtained while the patient was breathing room air revealed metabolic acidosis compensated by hypocapnia (pH 7.366, PCO2 29 mm Hg, PO2 114 mm Hg, base excess −7.6 mmol/L, and HCO3 − 16.2 mmol/L). Concentrations of lactate and pyruvate were high in the serum (66.2 mg/dl, normal range 4–16 mg/dl and 3.72 mg/dl, normal range 0.3–0.9 mg/dl, respectively) and in the cerebrospinal fluid (61.9 mg/dl, normal range 8.7–13.5 mg/dl and 2.93 mg/dl, normal range 0.37–0.75 mg/dl, respectively). Electrocardiography and ultrasonic cardiography revealed no abnormalities. Subsequent molecular analysis of mitochondrial DNA disclosed mutation from A to G at the nucleotide pair 3243 of the mitochondrial transfer RNA Leu (UUR) gene in the blood. The diagnosis was determined to be MELAS syndrome.

Additional symptoms of dysarthria, dysphasia, facial seizure, and mild dementia emerged during admission, and progression of muscle atrophy in the limbs was observed.

Treatment and Posttreatment Course. The patient was treated with corticosteroid therapy for a short period after admission and, thereafter, with anticonvulsant medication and 60 mg/day of coenzyme Q10. Within a month the patient’s neurological status improved, except for the muscle atrophy and mild dementia. Metabolic acidosis improved and serum lactate and pyruvate levels decreased to ranges of 15.9 to 35.3 mg/dl and 0.78 to 1.32 mg/dl, respectively, during the patient’s hospital stay. Follow-up MR imaging performed 2 months after admission demonstrated reduction of the lesion in the parietooccipital region (Fig. 4), and repeated angiography and xenon CT scanning, which were performed concurrently, revealed slightly decreased perfusion in the previously hyperperfused area (Fig. 5). After rehabilitation, the patient was able to walk and was discharged from the hospital.

Discussion

Xenon CT scans demonstrated focal hyperperfusion in our patient during the stroke-like episode and hypoperfusion thereafter. Neuroimaging of our patient performed during the stroke-like episode revealed typical CT scanning, MR imaging, and angiography findings. Repeated studies performed after the stroke-like episode revealed reduced lesions on MR images and decreased local CBF on angiograms and xenon CT scans. We think that the hyperperfusion may have been responsible for the acute stroke-like episode during which the infarct-like lesions developed. In contrast, the hypoperfusion, which was accompanied by subtle CT or MR imaging changes, was probably associated with old lesions that may have been symptomatic or asymptomatic. Consequently, the increased and decreased CBF values reported in previous
cerebral circulation studies of patients with MELAS indicate different stages of the disease. The inconsistency in the acute and long-term findings in our case suggest that cerebral metabolism studies are the preferred modality to evaluate such lesions. The various stages of the clinical course of MELAS syndrome should be considered during neuroimaging evaluations, and examinations should be repeated in patients with clinical symptoms indicative of the disease.

The pathogenesis of the strokelike episodes in patients with MELAS has not been determined. Changes in CBF may represent an active vascular disorder because mitochondrial angiopathy can impair autoregulation, leading to hyper- or hypoperfusion. On the other hand, the cause may be nonvascular because the lesions usually do not correspond to anatomical vascular distributions. Lactic acidosis may be the basis for the cerebral manifestations and vascular changes could represent the passive response to metabolic imbalance. Recent cerebral circulation studies tend to support a metabolic basis for the strokelike episodes that occur in cases of MELAS syndrome. Findings in our case clearly demonstrated that the strokelike episode reflected hyperperfusion rather than ischemic events; however, the pathophysiology of the hyperperfusion remains unclear. We assume that a vasogenic cause still cannot be excluded because some evidence of vasoparalysis has been reported in cases of MELAS syndrome, and such impaired autoregulation could possibly result in vasogenic edema. Magnetic resonance imaging results of reversible areas of hyperintensity in the cortical or subcortical regions associated with hyperperfusion are similar to the radiological findings of hypertensive encephalopathy, which results in vasogenic edema. Biopsy sampling of lesions performed during the strokelike episodes may lead to a greater understanding of this disease.

Effective therapies for MELAS syndrome have not been established. Administration of coenzyme Q10, which provides protection for the mitochondrial respiratory function in ischemic heart muscle, sometimes achieves both biochemical and clinical improvement in patients with Kearns–Sayre or MELAS syndrome. Recently, idebenone, a molecule that is similar to coenzyme Q10, but more readily enters the brain, has been somewhat effective when given alone or with coenzyme Q10. Our patient was treated with corticosteroid medication for a short period and 60 mg coenzyme Q10 daily thereafter. Improvements in both her clinical symptoms and the chemical environment were observed. Because the dosage of coenzyme Q10 seemed to be minimal for this disease, we doubt that the coenzyme Q10 was beneficial in this case. Further study is necessary to develop an effective treatment for this disease.

Neurosurgeons should be aware of MELAS syndrome because of the variable clinical presentation. Further investigation of mitochondrial disorders will lead to more effective intervention for these patients.
Fig. 5. Left carotid artery angiogram, late arterial phase (left), and xenon CT scan (right) obtained concurrently 2 months after the initial studies. In the angiogram relative hypovascularization in the parieto-occipital region can be identified. The xenon CT scan, which was obtained at the same anatomical level as the angiogram, confirms reduction in uptake in the left parietal region.

References

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