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MELAS Syndrome in a Child: CT and MR Findings

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— Abstract —

MELAS (mitochondrial myopathy, encephalopathy, lactic acidosis, and stroke-like episodes) is one of the mitochondrial encephalomyopathy, A rare disease caused by a disturbance of the mitochondrial chain of respiration.

MELAS is confirmed by typical light and electron microscopic findings: ''ragged red fibers'' by modified Gomori trichrome stain on light microscope and numerous abormal mitochondria on electron microscope.

We experienced a boy with the characteristic clinical and pathologic findings of MELAS. Our patient demonstrated bilateral basal ganglia calcifications and infarction at right parieto-occipital and thalamic areas on CT and MR. We found that MRI was more sensitive and represented the infarcted lesions better than CT.

Detection of cerebral insults of MELAS by MRI is important in making decision on patient treatment and also in predicion of the patient prognosis.

Index Words: Brain, MR studies
Brain, CT
Brain, diseases
Muscles, diseases
Children, cevtral uerous system

INTRODUCTION

We experienced a boy with MELAS which is characterized by mitochondrial myopathy, encephalopathy, lactic acidosis, and stroke-like episodes. The patient demonstrated following cardinal characteristics of MELAS:normal early development, short stature, seizures, hemiparesis and ''ragged red fibers'' on muscle biopsy. MELAS represents a syndrome distinct from two other clinical disorders that are also associated with mitochondrial myopathy and cerebral disease:Kearns-Sayre syndrome and the myoclonus epilepsy with ragged red fiber (MERRE) sydrome.

MELAS was confirmed by demonstrating ''ragged red fibers'' by modified Gomori trichrome stain on light microscope and numerous abnormal mitochondria contained with paracrystalline or osmophilic inclusion bodies on electron microscopic examination.

The computed tomographic (CT) findings of MELAS have been reported in the recent

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literatures. but not the MRI findings. CT & MRI of our patient showed calcifications in both basal ganglia and infarction in right parieto-occipital and thalamic areas. However, MRI was more sensitive and clearly defined the lesion better than CT. We report a case of a child with characteristic clinical, pathologic and radiologic findings of MELAS.

CASE REPORT

A 8-year-old boy was admitted with fever, vomiting, poor consiousness, and involuntary myoclonic jerk in his left arm. One day before admission, he complained right sided headache and eye pain. He also presented with visual and speech disturbance. This boy had a normal prenatal and perinatal period, and had ordinary family history. At the age of 6, he was first admitted with left facial paralysis and frequent headache, leg pain, and low exercise tolerance. At that time, his growth and development had been slowed down resulting in short stature and underweight. Brain CT performed with CT/T 9800 (General Electric, Milwaukee, Wisconsin) showed no sighificant abnormalities.

On his second admission 2 yrs later, blood lactate level was elevated to 48 mg/dl (normal, 10-20 mg/dl), EEG showed epileptic and ischemic nature, and EMG was compatible with myopathic process. Brain CT showed low density lesion in the right parieto-occipital areas and calcifications in both basal ganglia (Fig. 1a). T1-weighted image (T1WI) obtained in a 1.5T MR unit (Signa, General Eletric, Milwaukee, Wisconsin) showed low signal intensity in right parieto-occipital and thalamic areas,

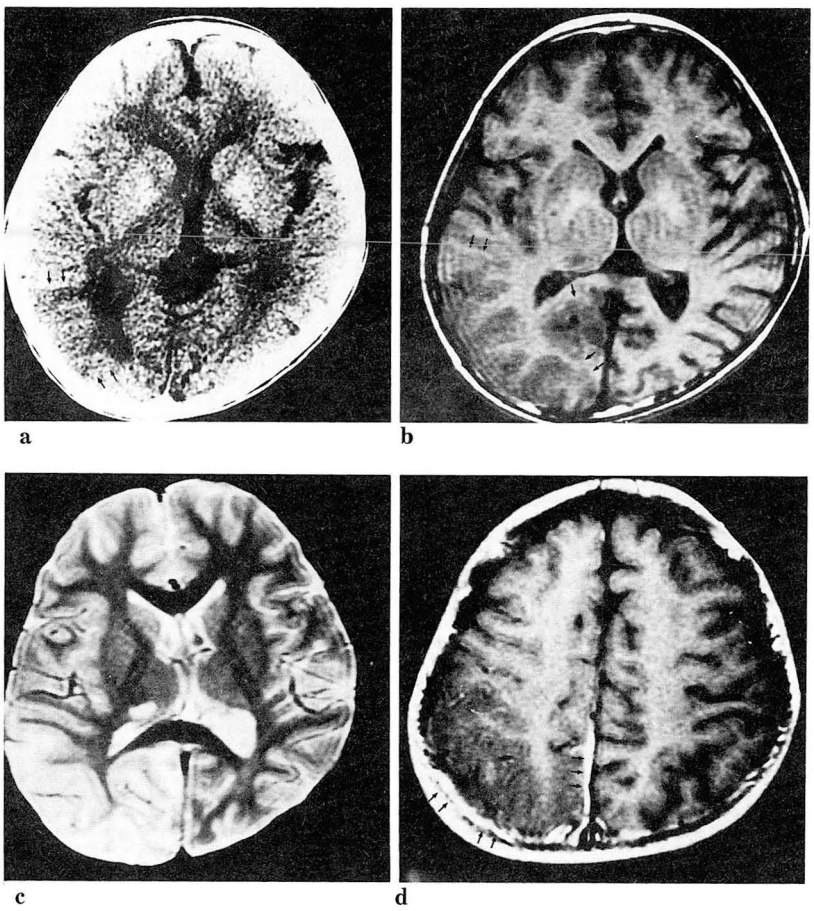

Fig. 1. a. Axial non-enhanced CT scan shows bilateral basal ganglia calcifications and low density infarction in right parietal region (arrows).
b. T1 weighted axial MR image shows high intensity calcifications in both basal ganglia and low intensity infarction in right thalamus and parieto-occipital parenchyma (arrows).
c. T2 weighted axial MR image shows high intensity in right thalamus and parieto-occipital parenchyma.
d. Gd-enhanced T1 weighted MR image shows linear enhancement at leptomeninges of the right parieto-occipital lesion (arrows).

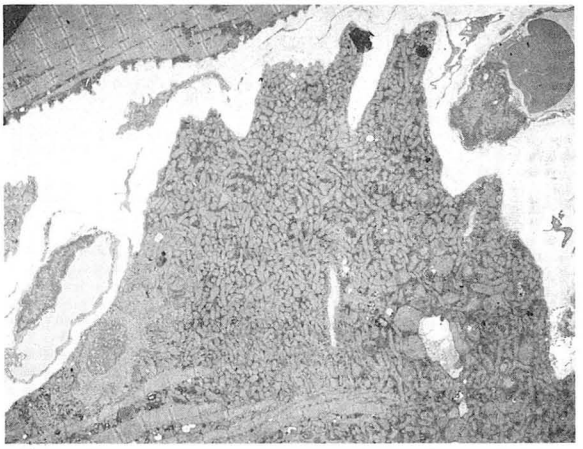

Fig. 2. Electron microscopic findings of muscle biopsy. An atrophic fiber shows proliferative dysmorphic mitochondria in the subsarcolemmal and interfibrillary space (°ϕ4000).

and focal high signal intensities in both basal ganglia (Fig. 1b). T2-weighted image (T2WI) revealed high signal intensity in right parieto-occipital and thalamic lesions (Fig. 1c). However bilateral basal ganglia lesions were not definitely identified in T2WI. Gd-enhanced T1WI revealed definite linear enhancement within the right parieto-occipital lesion (Fig. 1d). High signal intesities in the both basal ganglia on T1WI corresponded to the areas of calcifications on brain CT.

Electron microscopic findings of muscle biopsy specimen included an atrophic fiber with heavy accumulation of dysmorphic mitochondria in the subsarcolemmal and interfibrillary spaces and abnormal arrangement of cirstae and osmophilic inclusions in the highly polymorphic mitochondria (Fig. 2).

DISCUSSION

Mitochondrial encephalopathies are rare diseases caused by a disturbance of the mitochondrial chain of respiration. This prevents pyruvate from being completely integrated into the tricarboxylic acid (Kreb's) cycle, and hence there is an accumulation of lactate. The clinical pattern can vary greatly and ranges from ophthalmoplegia via mainly myopathic to encephalopathic froms. The patterns of signs and symptoms enable subclassification into three main syndromes. Three of them are the Kearns-Sayre syndrome (KKS, defined by the invariant triad:onset before age 20, ophthalmoplegia, and pigmentary retinopathy), MERRF (characterized by cerebellar ataxia and myoclonus), and MELAS (1). Pavlakis et al. have recently described the syndrome of MELAS since Luft introduced the concept of mitochondrial myopathies with multiorgan involvement. The classic clinical findings of MELAS were myopathy, short stature, seizures, hemiparesis, hemianopsia, cortical blindness, and migrane-like headache (1,2). Our patient also demonstrated early normal development, myopathy, short stature, stroke with hemiparesis, and headache.

Histologically, mitochondrial myopathies are characterized by "ragged red fibers" which were pathologic accumulation of mitochondria on light microscope with Gomori trichrome stain modified by Engel and Cunningham and ultrastructural mitochondrial disorders, such as megaconial (enlarged mitochondria with disoriented cristae) and pleoconial (proliferation of normal-looking mitochondria) myopathy on electron microscope which was explored systematically by Shy and Gonatas (1,3). Our case was also confirmed by showing structural morphological abnormalities of mitochondria in tissue from muscle biopsy on both light and electron microscope.

The CT findings of mitochondrial myopathies included focal low density lesions, basal ganglia calcification, ventriculomegaly and cortical atrophy. Many other reported cases also revealed bilateral low density lesions in temporo-parieto-occipital areas with or without basal ganglia calcifications especially in patients with MELAS (2,3,4). In our patient, initial CT showed no significant abnormalities, but CT obtained 2 years later revealed lower density lesion in right parietooccipital regions and bilateral basal

ganglia calcifications which did not correspond to vascular territories. Angiographic findings of MELAS were focal areas of capillary blush and early venous filling in the regions of low density seen on CT which did not correspond to vascular territories (5). MRI findings in our patient were consistent with CT findings, but MRI was more sensitive and nicely demonstrated the lesions in the right thalamic and parieto-occipital areas and bilateral basal gnaglia abnormality. The thalamic lesion was detected only by MRI. These findings are compatible with other recent reports on MRI findings of mitochondrial myopathies: one case with multiple migrating infarcts in posterior temporal, parietal and occipital regions without basal ganglia calcification (6) and another with high signal intensity of basal ganglia calcification (7). The pathogenesis of these manifestations of central nervous system (CNS) still remains unclear. According to Oldendorf et al (8), CNS capillaries have more abundant mitochondria compared with those of other organs. It may be assumed that CNS capillaries and blood-brain barriers might be especially vulnerable to mitochondrial dysfunction. Pavlakis et al (4). have speculated that mitochondrial dysfunction involving the endothelium of brain capillaries may contribute to the development of stroke-like events. The neuropathological characteristics of these syndromes are spongy degeneration with microcystic liquefaction and vascular proliferation, neuronal loss, and demyelination, but microcystic liquefaction or focal softening and basal ganglia calcifications are most prominent in MELAS (1,4).

The course of MELAS is variably progressive, punctuated by acute cerebral insults. We conclude that early detection of CNS abnormalities by MRI is important for treatment of the patients with mitochondrial myopathies.

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〈국문 요약〉

소아에서 MELAS 증후군의 CT와 MR소견

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MELAS 증후군은 미토콘드리아의 이상에 의해서 여러 장기가 침범되어 다양한 증상을 야기하는 드문 질환이다. MELAS 증후군의 진단은 특징적인 여러 임상증상과 더불어 근육생검에서 특이한 "ragged red fibers"와 비정상적인 미토콘드리아가 보여야 가능한 것으로 되어있다.

저자들도 8세된 남아가 MELAS시 보일 수 있는 여러 임상증상과 더불어 특징적인 병리학적 소견을 나타내면서 CT와 MR에서도 특징적인 소견인 양측 기저핵의 석회화 병변 및 두정후두부와 시상에 경색 소견을 나타내는 것을 경험하였으며 특히 MR이 CT보다 더 확실하고 예민하게 병변의 위치와 범위를 보여주는 것을 알 수 있었다.

MELAS시 MRI로 두부병변을 빨리 알아내는 것은 치료의 결정과 환자의 예후를 예견하는데 중요하다고 생각한다.