MELAS 증후군과 미토콘드리아 근육병에서의 Tc-99m ECD 뇌 단일 광전자방출 전산화단층촬영 소견: 자기공명영상과의 비교

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Tc-99m ECD Brain SPECT in MELAS Syndrome and Mitochondrial Myopathy: Comparison with MR findings

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Abstract

Purpose: We evaluated brain perfusion SPECT findings of MELAS syndrome and mitochondrial myopathy in correlation with MR imaging in search of specific imaging features. **Materials and Methods:** Subjects were five patients (four females and one male; age range, 1 to 25 year) who presented with repeated stroke-like episodes, seizures or developmental delay or asymptomatic but had elevated lactic acid in CSF and serum. Conventional non-contrast MR imaging and Tc-99m-ethyl cysteinate dimer (ECD) brain perfusion SPECT were performed and imaging features were analyzed. **Results:** MRI demonstrated increased T2 signal intensities in the affected areas of gray and white matters mainly in the parietal (4/5) and occipital lobes (4/5) and in the basal ganglia (1/5), which were not restricted to a specific vascular territory. SPECT demonstrated decreased perfusion in the corresponding regions of MRI lesions. In addition, there were perfusion defects in parietal (1 patient), temporal (2), and frontal (1) lobes and basal ganglia (1) and thalami (2). In a patient with mitochondrial myopathy who had normal MRI, decreased perfusion was noted in left parietal area and bilateral thalami. **Conclusion:** Tc-99m ECD SPECT imaging in patients with MELAS syndrome and mitochondrial myopathy showed hypoperfusion of parieto-occipital cortex, basal ganglia, thalamus and temporal cortex, which were not restricted to a specific vascular territory. There were no specific imaging features on SPECT. The significance of abnormal perfusion on SPECT without corresponding MR abnormalities needs to be evaluated further in larger number of patients. **(Korean J Nucl Med 1998;32:6:490-6)**

Key Words: Mitochondrial encephalomyopathy, MELAS, Tc-99m ECD, Brain, Emission tomography, Magnetic resonance imaging

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Introduction

MELAS (mitochondrial myopathy, encephalopathy, lactic acidosis, and stroke-like episodes) syndrome is a group of inherited mitochondrial abnormalities that, in some patients, has been found to be caused by an A-G transition mutation at nucleotide position 3243 of mitochondrial DNA (mtDNA),[1-3] but the pathogenesis is still not fully understood. Patients can present at any age, most commonly in the second decade. MELAS syndrome was first described in 1984 by Pavlakis et al., who found it to be characterized by lactic acidosis and recurrent stroke-like episode.[4] The hallmarks of this syndrome are ragged red fibers in the muscle biopsy that are due to an accumulation of ultrastructurally abnormal mitochondria. These morphologic abnormalities together with the elevated lactate levels in the venous blood indicate a defect of the oxidative mitochondrial metabolism.[5]

Imaging studies including CT and MRI demonstrate fluctuating abnormalities of gray and white matter predominantly in the parieto-occipital regions. However, these findings are nonspecific and in the absence of clear-cut symptoms and laboratory results, the imaging features can not be considered pathognomonic.[1,5-8] Recent clinical and histopathological reports concerning MELAS suggest that certain cerebral circulatory and/or metabolic disorders refer to manifestations of stroke-like episodes.[9-12] Few studies have used PET and SPECT to examine the functional aspects of cerebral hemodynamics for MELAS.[13-17]

We conducted this study to evaluate SPECT findings of MELAS syndrome and mitochondrial myopathy and correlate them with MR findings in search of specific imaging features and to assess the role of SPECT in MELAS syndrome.

Materials and Methods

Five patients (four females and one male, age range; 1 to 25 years) who presented with repeated stroke-like episodes or seizures or developmental delay or were asymptomatic but had elevated lactic acid in CSF and serum were evaluated with conventional noncontrast MR imaging and SPECT. Diagnosis of MELAS syndrome (four patients) and mitochondrial myopathy (one patient) was done by skeletal muscle biopsy and laboratory data and clinical course. Clinical features are summarized in Table 1.

MR imaging was performed with a 1.5T signa unit (General Electrics Medical Systems, Milwaukee, Wis.). A multisection T2 weighted fast spin echo (FSE) sequence (3333/114 [TR/effective TE], 20 cm FOV, 256×256 matrix, one excitation) was

Table 1. Clinical Features in 5 Patients with MELAS Who Had Ragged Fibers on Muscle Biopsy

Case	Age/Sex	Clinical symptom	Lactic acidosis
1	25/F	TIA	(+)
2	4/F	D.D	(+)*
3	13m/M	D.D	(+)
4	2/F	D.D and seizure	(+)*
5	4/F	bilateral SNHL	(+)*

(Abbreviations TIA, transient ischemic attack; m, month; D.D, delayed development; SNHL, sensory neural hearing loss); *, Elevated serum lactic acid level but normal in CSF.

used to obtain axial images. A multisection T1 weighted sequence (400/12, 20 cm field of view, 256×256 matrix, two excitations) was used to obtain axial and midline sagittal images. Slice thickness were 5 mm, with a 2.5 mm interslice gap. No intravenous contrast was used.

SPECT images were obtained after an intravenous injection of 370-740 MBq of Tc-99m-ECD with a brain dedicated annular crystal camera (Digital Scintigraphic Inc., Waltham, USA) equipped with low-energy, high-resolution parallel hole collimators. One hundred twenty projections were acquired with 3-degree angular increments. The matrix size was 128×128. Transaxial images were obtained by the filtered back projection method using a Butterworth filter (Nyquist frequency 1.1 cycle/cm at an order no. 10) Attenuation correction of the transaxial images was performed by the

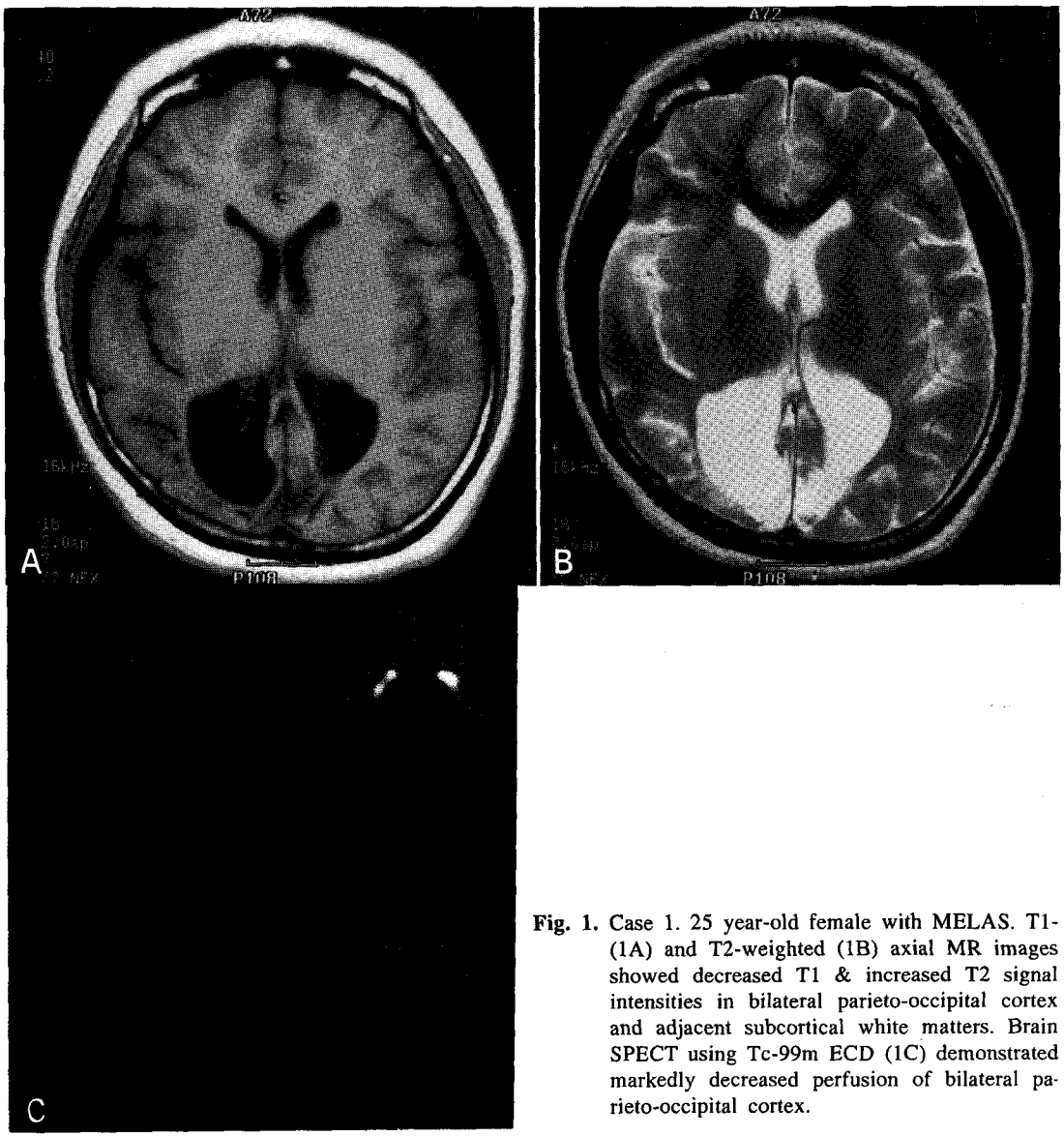

Fig. 1. Case 1. 25 year-old female with MELAS. T1-(1A) and T2-weighted (1B) axial MR images showed decreased T1 & increased T2 signal intensities in bilateral parieto-occipital cortex and adjacent subcortical white matters. Brain SPECT using Tc-99m ECD (1C) demonstrated markedly decreased perfusion of bilateral parieto-occipital cortex.

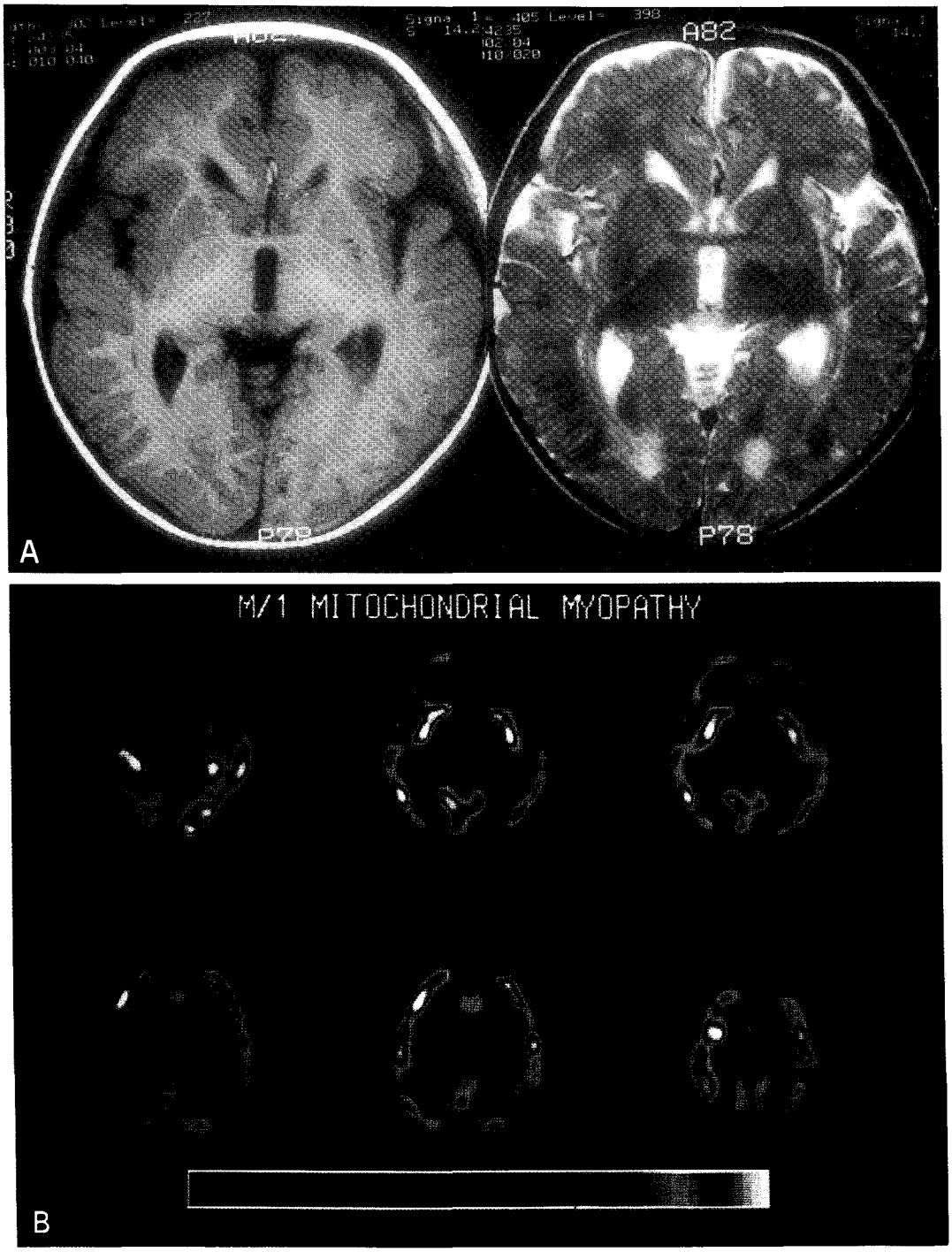

Fig. 2. Case 3. 13 month-old male with mitochondrial myopathy who showed no clinical sign of encephalopathy. T1- and T2-weighted axial MR images (2A) showed no abnormal signal intensity or morphologic changes. Brain SPECT using Tc-99m ECD revealed (2B) decreased perfusion of left parietal cortex and bilateral thalami.

Chang's method and coronal and sagittal slices were calculated from the original transaxial images (parallel to the orbitomeatal line).

All SPECT scans were assessed initially by two experienced nuclear medicine specialists who were blinded to the results of the MRI. An overall qualitative visual assessment of the SPECT data by mutual consensus was recorded.

Results

MRI demonstrated increased T2 signal intensities in the affected areas of gray and white matters mainly in the parietal (4/5) and occipital lobes (4/5) and in the basal ganglia (1/5), which were not restricted to a specific vascular distribution(Fig. 1A). No abnormal signal intensity changes were noted on thalami and cerebellum in all patients. In a patient with mitochondrial myopathy (case 3), brain MRI was completely normal(Fig. 2A).

SPECT demonstrated perfusion impairments in the corresponding regions of MRI lesions. In addition, there were perfusion defect in parietal (1 patient), temporal (2), and frontal (1) lobes and basal ganglia (1) and thalami (2). Additionally, in a patient with mitochondrial myopathy who had normal MRI, decreased perfusion was noted on left parietal area and bilateral thalami (Fig. 2B). Areas of decreased perfusion on SPECT were more numerous than conventional MR imaging.

Discussion

MELAS refers to a group of disorders that are characterized by episodes of nausea, vomiting and stroke-like episodes (hemianopsia and hemiparesis) in conjunction with some of the signs and symptoms of generalized mitochondrial disease. The abnormal mitochondria are not solely confined to skeletal muscle but are also found in various other tissues including central nervous tissue and endothelial cells of the brain vessels, indicating that the disease is not only a myopathy but also an encephalopathy.[16] Stroke-like events, probably the results of a proliferation of dysfunctional mitochondria in the smooth muscle cells of small arteries, may give rise to permanent or reversible deficits.

MRI shows increased water in the affected areas of the brain, primarily in parietal and occipital lobes. Sequential scans may show resolution and subsequent reappearance of the abnormal areas, which are not restricted to a specific vascular distribution.[1,5-8]

MR spectroscopy shows high lactate and decreased phosphocreatinine in the affected areas of brain.[18,19] However, as infarcts of any cause seem to result in local increases in lactate, the presence of lactate in a patient with acute onset of neurologic deficit is not specific for MELAS.[20]

SPECT has been known to be useful for demonstrating the lesions in MELAS. Decreased perfusion in the affected brain areas, mainly parieto-occipital lobe, can be explained by a hypoperfusion due to reduced cerebral function.[13,14] Hyperperfusion was also observed before and during a stroke, which may be the result of focal lactic acidosis or epileptic activity.[15,16]

In our study, decreased perfusion was noted mainly in parieto-occipital cortex, which was consistent to abnormalities demonstrated on MRI. Whereas, in a patient with mitochondrial myopathy with normal MR findings, SPECT demonstrated decreased perfusion of parietal lobe and thalami. Thalamic and temporal hypoperfusion seen in 2 patients with MELAS was not evident on MRI. The significance of hypoperfusion without MRI abnormalities was uncertain, but could be attributed to metabolic disturbances or cortico-thalamic diaschisis. Fujii et al also reported decreased perfu-

sion of frontal and occipital area on SPECT without corresponding MRI or CT abnormalities and suggested that SPECT was more sensitive than CT or MRI for detecting stroke-like lesions in MELAS patients.[21]

On constellation of above findings, SPECT may be a sensitive method in demonstrating metabolic abnormalities with mitochondrial encephalomyopathy than other imaging studies including conventional MRI. However, this should be confirmed by a further study in larger number of patients. Moreover, we compared SPECT findings only with conventional MRI. Diffusion or perfusion weighted MR imaging might be better in demonstrating subclinical abnormalities which were not evident on conventional MRI.

PET have demonstrated a marked decrease in cerebral metabolic ratio of oxygen with relatively preserved cerebral blood flow and cerebral metabolic ratio of glucose, supporting a disturbance of mitochondrial oxidative metabolism of the brain.[17] However, PET remains a relatively expensive and complicated procedure that is not widely available.

In conclusion, SPECT demonstrated hypoperfusion of parieto-occipital cortex, basal ganglia, thalamus and temporal cortex, which were not restricted to a specific vascular distribution and showed more numerous areas of abnormalities than MRI. However, the significance of abnormal perfusion on SPECT without corresponding MR abnormalities needs to be evaluated further in larger number of patients. Brain perfusion SPECT may play a role in evaluating pathophysiology of metabolic disturbances in MELAS.

요 약

목적: 본 연구의 목적은 MELAS 증후군과 미토콘드리아 근육병의 뇌 SPECT 소견을 알아보고 SPECT 소견과 자기공명영상 소견을 비교 분석하여 MELAS증후군의 특징적인 영상 소견을 찾아보고자 하였고 MELAS 증후군에 있어서 뇌 SPECT의 역할을 평가해 보고자 하였다. **대상 및 방법**: 뇌졸중 유사 증상이나 경련 또는 발달 지연을 주소로 하였고, 혈청 또는 뇌척수액의 lactic acid치가 상승되어 있는 1세에서 25세의 5명의 환자를 대상으로 하였고 남녀비는 4:1이었다. 모든 환자에서 Tc-99m ECD를 이용한 뇌혈류 단일광전자방출 전산화 단층촬영술(SPECT)와 자기공명영상을 시행하여 영상 소견을 분석하였다. **결과**: 자기공명영상에서는 주로 두정엽(4/5)과 후두엽(4/5), 그리고 기저핵(1/5)에 백질과 회백질에 증가된 T2 신호강도를 나타내었는데, 특정한 혈관 영역에는 부합하지 않는 병변의 분포양상을 보였다. SPECT상에서는 자기공명영상에서 이상소견을 보인 모든 부위에서 관류 저하를 보였으며 추가적으로 두정엽(1예), 측두엽(1예), 전두엽(1예), 기저핵(1예)와 시상(2예)에서도 감소된 Tc-99m ECD의 섭취를 나타내어서, 자기공명영상과 SPECT에서 이상 소견을 보인 수를 비교하면 자기공명영상에서 나타난 해부학적인 이상소견보다 SPECT에서 보인 관류 저하가 더 광범위하였다. **결론**: MELAS 증후군의 SPECT에서는 특정한 혈관 영역에는 부합하지 않는 두정엽과 후두엽, 기저핵, 시상, 측두엽 등의 관류저하를 보여 주었는데, 본 연구의 여러 제한점으로 인하여 MELAS 증후군에서만 나타나는 특징적인 소견이라고 할 수는 없었다. 자기공명영상에서 상응하는 이상 소견이 없이 SPECT에서만 관류 저하를 보이는 경우의 중요성은 좀 더 많은 수의 환자를 대상으로한 연구를 통해 평가되어져야 할 것으로 생각한다.

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