Perirolandic Hypoperfusion on Tc-99m ECD Brain SPECT in Term Infants with Perinatal Asphyxia: Comparison with MRI and Clinical Findings

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= 국문초록 =

주산기아가 있는 환아에서 나타나는 Tc-99m ECD 뇌 단일광자 컴퓨터촬영에서의 플란도야의 혈류감소: 자기공명영상 및 임상소견과의 비교

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이선아·유영축·이종우·황윤준·김동익·윤영호·전평·문성우·박철일

뇌성마비는 뇌 발달시기 중 초기의 장애로 인하여 운동기능과 자세의 이상 등을 초래하는 질환으로 임상적으로 여러 유형으로 나뉘어진다. 뇌성마비 환자중에서 MRI상 플란도야의 이상소견을 보이는 경우 특이한 임상적 특징을 나타내다고 보고되어 있다. 본 논문에서는 이를 대상으로 하여 뇌 단일광자 컴퓨터촬영에서 나타나는 뇌혈류 이상 소견과 MRI소견, 그리고 임상양상을 비교해보고자 하였다.

임상적으로 뇌성마비로 진단된 80여명의 환자중 MRI상 플란도야에 이상소견 뇌혈류의 소견을 보인 7명을 대상으로 하였다. 이들중 5-10mCi의 Tc-99m-ECD를 정맥주사 후 뇌 단일광자 컴퓨터촬영을 하였다. 뇌 단일광자 컴퓨터촬영영상에서는 특이 뇌피질, 선조체, 시상, 시간 및 소뇌의 혈류이상소견을 분석하였고, 이를 MRI 소견 및 임상증상과 비교하였다.

모든 환자들은 만삭 또는 만삭에 가깝게 테어났고, 주산기 아사가 여섯병의 환자에서 있었다. 임상적으로는 건강성 사지마비로 나타났다. Tc-99m ECD를 이용한 뇌 단일광자 컴퓨터촬영영상 플란도야의 혈류감소는 모두에서 확인하게 나타났다. MRI상에서 플란도야의 이상소견은 5명에서는 확실하게 나타났고, 2명에서는 의심되었다. MRI상에서 이상소견을 보인것보다 더 광범위한 부분에서 뇌단일량자 컴퓨터촬영영상 이상소견이 보였다.

결론적으로, 플란도야의 이상소견을 보인 환자는 임상적, 구조적으로 그리고 기능적으로 특이한 소견을 보였다. Tc-99m-ECD를 이용한 뇌 단일광자 컴퓨터촬영은 매우 민감하게 반영하였고, MRI보다 뇌의 더 광범위한 부위에서 이상소견을 보였다.
INTRODUCTION

Cerebral palsy is a collection of nonprogressive disorders that manifest as abnormalities of motion and posture\(^1\). It results from CNS injuries sustained in the early period of brain development, one of its major causes being hypoxic-ischemic encephalopathy\(^2\). Magnetic resonance imaging of patients with hypoxic-ischemic encephalopathy has shown that the developing brain reacts to hypoxic-ischemic insults in a predictable manner, the pattern and topography of which depends on the state of maturation of the brain at the time of the insult\(^2,9\).

Perirolandic cortico-subcortical involvement on MRI has recently been described as a specific finding in term infants with perinatal asphyxia\(^10\). In addition, patients with such findings on MRI presented uniformly with spastic quadriplegia type of cerebral palsy in a previous study\(^10\). Thus patients with such findings on MRI represent a distinctive subset among patients with cerebral palsy, namely those with perinatal asphyxia at term and spastic quadriplegia.

In this study, correlative analysis of Tc-99m ECD ethyl cysteinate dimer brain SPECT in selected patients with perirolandic cortico-subcortical involvement on MRI is carried out, the purpose of which is to compare the MR and SPECT features of these infants, to correlate them with clinical features, and to evaluate the role of brain SPECT as a functional imaging method in comparison to that of a structural imaging method.

MATERIALS AND METHODS

The seven patients included in this study were selected from a population of over eighty patients who had been diagnosed as having cerebral palsy. The eighty patients had undergone a research protocol that included brain MRI and SPECT. Informed consent to be examined according to the protocol was given by the parents or legal guardian of each subject.

A summary of the clinical manifestations of the 7 patients included in this study are provided in Table 1. There were 5 boys and 2 girls. Their age ranged from 14 to 39 months (mean 26 months) at the time of the imaging studies. The intrauterine history of the patients were unremarkable and all were born at term or at near term, with birthweights ranging between 2.7 and 3.7kg (mean 3.18kg). Overt perinatal asphyxia was present in all but one of them. Cerebral palsy in the form of spastic quadriplegia was the uniform presenting clinical feature. There were no difference in the clinical manifestations or MR findings between the patients with a history of perinatal asphyxia and the one without.

1. MRI procedure

MR imaging was performed with a 1.5 signa unit (General Electrics Medical Systems, Milwaukee, Wis). A multisection T2 weighted fast spin echo (FSE) sequence (3333/114 TR/effective TE), 20cm FOV, 256×256 matrix, one excitation) was used to obtain axial images. A multisection T1 weighted sequence (400/12, 20cm field of view, 256×256 matrix, two excitations) was used to obtain axial and midline sagittal images. Slice thickness were 5mm, with a 2.5mm interslice gap. No intravenous contrast was used.

All MRI data were initially evaluated by two experienced neuroradiologists. Patients with the specific abnormalities of the area bordering the central sulcus were selected for inclusion in this study. Perirolandic cortico-subcortical involvement on MRI was defined as localized atrophy
of the cortex located in areas bordering the central sulcus, with additional gliosis, cystic changes, or tissue loss of the subcortical white matter. The central sulcus was identified according to a method formerly described by Sobel et al. The MR images of those included in this study were reevaluated to assess for tissue loss and evidence of tissue damage as demonstrated by areas of altered T1 and/or T2 relaxation. In particular, the perioicald cortex, basal ganglia, thalamus, cerebellum, corpus callosum, periventricular and subcortical white matter, and the frontal, temporal, and occipital cortex were scrupulously scrutinized. Additionally, the changes of the right and left perioicald area were qualitatively graded as either subtle or obvious.

2. SPECT procedures

After intravenous injection of 5–10mCi (185–370MBq) of Tc-99m-ECD, SPECT images were obtained with a brain dedicated annular crystal camera (Digital Scintigraphic Inc, Waltham, USA) equipped with low-energy, high-resolution parallel hole collimators. 120 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 Chang’s method, and coronal and sagittal slices were calculated from the original transaxial images (parallel to the orbitomeatal line). To ensure absence of motion during the SPECT examination, intramuscular injection of chlorpromazine was routinely used to sedate the patients prior to the procedure.

All SPECT scans were assessed initially by two experienced nuclear medicine specialists. SPECT data were reevaluated in patients exhibiting central cortical and subcortical involvement on MRI. An overall qualitative visual grading (as either increased, normal, or decreased perfusion) of the SPECT data by mutual consensus was recorded for the perioicald cortex, basal ganglia, thalamus, cerebellum, and the frontal, temporal, and occipital cortex. Abnormalities of the right and left perioicald cortex, where found, were qualitatively graded as subtle or obvious.

RESULTS

Atrophy and gliosis of the perioicald cortex were present in all 7 patients on MRI, subtly in 2, and obviously in 5 of them. It was depicted by decreased signal intensities on T1, and increased signal intensities on T2-weighted axial images. The lesions were band shaped in the left–right direction and distributed symmetrically along the
Fig. 1. A 14mo year old girl with spastic quadriplegia and perinatal asphyxia
A, Technetium-99m-ECD SPECT demonstrates bilaterally decreased perfusion around the periolandic
area, on both axial and sagittal reconstructed images. The cortical hypoperfusion is better dem-
strated on the sagittal reconstructed image. Decreased perfusion of the thalami and lentiform nuclei
bilateraly are present. The cerebellum and brain stem exhibits hypoperfusion as well.
B, Atrophy and gliosis of the periolandic cortex is present bilaterally. It presents as linear band
shaped area of decreased signal intensities on T1 and increased signal intensities on T2-weighted
images.
C, Midline sagittal T1-weighted images demonstrate thinning of the posterior body of the corpus
callosum.
D, T2 weighted axial image through the level of basal ganglia and thalami shows relatively normal
appearing thalami. Increased signal intensities at dorsolateral aspect of lentiform nuclei on both
sides are seen.
E, T2 weighted axial image of the cerebellum appears normal.

central sulcus (Fig. 1B). Subcortical white matter
bordering the central sulcus also demonstrated
atrophy in the 7 patients, with signal changes
compatible with gliosis. Cystic changes of the
periolandic cortex and subcortical white matter
were not observed. Bilaterally decreased perfu-
sion around the central sulcus were present in
all seven cases on Tc-99m-ECD brain SPECT

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Table 2. Abnormalities Detected on SPECT vs. MRI

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<tr>
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<td>7</td>
</tr>
<tr>
<td>subtle</td>
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</table>

Fig. 2. A 16 mo old boy with spastic quadriplegia and perinatal asphyxia
A, Tc-99m-ECD SPECT demonstrates bilaterally decreased perfusion of the perirolandic cortex, along with hypoperfusion of both thalami. The basal ganglia show normal perfusion. Cerebellum appears hypoperfused.
B, Subtle signal intensity changes of the perirolandic area are demonstrated on MRI.

(Fig. 1A). Hypoperfusion of the perirolandic cortex was judged to be obvious in all cases, even in the 2 cases with subtle findings on MRI (Fig. 2A, 2B).

SPECT revealed decreased cerebellar perfusion in 3 patients without corresponding anatomic abnormalities on MRI (Fig. 1A, 1E). Basal ganglia was hypoperfused in 5 patients, 3 of whom showed signal changes on MRI (Fig. 1A, 1D). Hypoperfusion of the thalami was a universal finding on SPECT, whereas MRI showed signal changes in 5 patients (Fig. 1A, 1D). Temporal lobe was hypoperfused in 1 case, in which MRI failed to reveal signal changes. Summaries of the SPECT and MRI findings are provided in Table 2.

DISCUSSION

Cerebral palsy, a nonprogressive disorder of movement and posture due to damage to the immature brain, represents a syndrome, rather than a specific etiologic diagnosis. It results from various kinds of injuries sustained in the early period of brain development. The clinical manifestations of cerebral palsy are varied as well, with several clinical subtypes. They are specifically spastic, athetoid, rigid, ataxic, tremor, atonic, and mixed types.

Attempts have been made to assign a specific imaging diagnosis according to the subtype\(^{12,13}\). Imaging diagnosis, i.e., the anatomic distribution of the cerebral lesions, largely determines the clinical picture of patients with cerebral palsy. For example, in spastic diplegia, the most common form of cerebral palsy, periventricular leukomalacia predominant around the occipital horns is the most frequent finding seen on MRI\(^{14}\); passage of motor fibers to the lower extremity in the white matter tracts affected by periventricular leukomalacia accounts for the clinical symptoms.

In addition, MR imaging provides clues to the timing of the brain injury. Although not as significantly as has previously been thought to be, the role of hypoxic ischemic encephalopathy
as the major causative factor of cerebral palsy holds\textsuperscript{15, 16}. And having documented the response patterns to hypoxic-ischemic injuries of the immature brain on MRI\textsuperscript{13-17}, the approximate timing of brain damage can be predicted by MRI in patients with cerebral palsy: the immature brain responds to hypoxic-ischemic insults in a predictable manner, the pattern and topography of which depends on the state of maturation of the brain at the time of the insult. Preterm infants manifest with periventricular leukomalacia as the predominant MR finding, whereas cortico-subcortical involvement mainly in the parasagittal watershed areas is seen in term infants. In the postterm infants, the cortex and subcortical white matter in the watershed regions are most severely involved, with relative sparing of the immediate periventricular white matter.

Perirolandic cortico-subcortical involvement has been described as a specific MR pattern in term infants with perinatal asphyxia, who, with spastic quadriplegia as the predominant clinical feature, represented a distinctive subset among patients with cerebral palsy\textsuperscript{10}. Perirolandic cortico-subcortical involvement was defined as localized atrophy of the cortex located in areas bordering the central sulcus, with additional gliosis and tissue loss of the adjacent white matter\textsuperscript{10}. It characteristically appeared as band-shaped (in the left-right direction) areas of decreased signal intensities on T1, and increased signal intensities on T2-weighted MR images.

Involvement of the perirolandic area in perinatal asphyxia at term may be explained in terms of it being an active zone of myelination at the time of birth\textsuperscript{18}. The susceptibility of specific regions of the brain to hypoxic insults depends to a certain extent on the level of metabolic activity exhibited, and the onset of myelination in specific white matter tracts is generally accepted to be related to the onset of essential functions\textsuperscript{17, 19-21}. The central sulcus represents an active zone of myelination at the time of birth, and hence its involvement in hypoxic insults to the brain in early life. Perirolandic involvement thus represents a pathophysiologicaly distinctive process causing cerebral palsy.

Patients with perirolandic cortico-subcortical involvement manifested uniformly with spastic quadriplegia in a previous study\textsuperscript{10}. The presenting feature in all the patients included in this study were spastic quadriplegia also. Involvement of the central sulcus, and thus the corticospinal motor tracts, accounts for such symptoms. Although the basal ganglia were involved in a number of cases on MRI, the symptoms expected from such anatomic lesions (i.e., choreoathetoid movements) were masked by the spasticity of the four limbs.

Functional studies such as cerebral blood flow or glucose metabolism studies of patients with cerebral palsy have been performed previously\textsuperscript{22-27}. Even attempts to describe the regional glucose metabolism abnormalities according to the subtype of cerebral palsy have been made\textsuperscript{28}. The results have not been consistently established, however. In the asphyxiated term newborn, parasagittal impairment of cerebral blood flow has been described\textsuperscript{27}, but the perirolandic hypoperfusion observed in our study has not been mentioned so far.

Decreased cerebral blood flow to the perirolandic area was demonstrated in all patients included in this study on Tc-\textsuperscript{99m} ECD brain SPECT scans. It represents cortical hypoperfusion, as the subcortical white matter with its relatively lower regional cerebral blood flow relative to the cortex, little contributes to the
results of the brain perfusion scans. In comparison to MRI which demonstrates structural alterations of the perirolandic cortex, Tc-99m-ECD brain SPECT scans demonstrates decreased cerebral perfusion, and therefore, decreased function.

Definite hypoperfusion was seen around the perirolandic area even in cases with subtly visualized alterations on MRI (Fig. 2A, 2B). In addition, the reduction in function was seen in a wider area of brain than was seen structural abnormalities. Tc-99m-ECD brain SPECT showed decreased perfusion of the thalamus and basal ganglia even in cases without demonstrable signal changes on MRI. Hypoperfusion of the cerebellum and temporal lobes were not accompanied by congruent structural changes: MRI failed to reveal structural alterations. The hypothesis that the distribution of metabolic impairment extends beyond the region of anatomic involvement as has been previously suggested is supported by these results.

The major limitation of brain SPECT is that it fails to show abnormalities of the subcortical white matter. The lower regional cerebral blood flow of white matter in comparison to the gray, and the lower spatial resolution of brain SPECT in comparison to MRI, does not allow brain SPECT scans to reveal hypoperfusion in these areas. MRI may however compensate for brain SPECT's limitations.

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