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Seizure Propagation on Ictal Brain SPECT : A Pitfall in the Localization of the Seizure Focus

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발작기 뇌혈류 스캔에서의 간질 확산에 관한 연구 : 간질 병소 국소화의 오류

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김만득 · 이종두 · 유영훈 · 김도중 · 김재근 · 문성욱 · 윤평호 · 이창훈 · 이병인*

본 연구는 간질 병소의 국소화에 있어 발작기 및 발작간 뇌스캔의 정확도를 알아보고 발작기 뇌스캔에서 나타나는 간질 확산이 정확한 간질 병소를 국소화 하는데 어떠한 영향을 미치는가에 대하여 알아보고자 하였다.

15명의 복잡 부분 발작 환자를 대상으로 하였으며, 간질 병소의 최종적인 국소화는 두피 및 발작 뇌파, 피질 뇌파, 자기 공명 영상, 임상양상 및 병리 소견을 종합한 근거로 하였다. 발작기 뇌스캔은 뇌파상 발작 중 또는 환자가 aura를 호소할 때 Tc-99m HMPAO 20mCi(740 MBq)를 정맥 주입후 시행하였으며 발작간 뇌스캔은 발작기 뇌스캔 후 3일 이내 임상적으로 발작 증상이 없는 기간에 시행하였다. 간질 병소는 우측 측두엽이 8예, 좌측 측두엽이 6예, 측두엽 이외의 기원이 1예였다.

발작기 뇌스캔상, 모두 11예(73.3 %)에서 단발성 또는 다발성 섭취 증가가 간질 병소 및 간질 확산 부위에서 관찰되었으며, 간질 병소에만 국한된 섭취 증가는 4예(26.7%)에 불과 하였다. 발작간 뇌스캔에는 모두 11예(73.3 %)에서 간질 병소에만 섭취가 감소되었다. 자기 공명 영상에서는 8예(53.3 %)에서 hippocampal sclerosis를 포함한 간질 병소가 확인 되었다.

본 연구로 복잡 부분 발작 환자에서, 간질 확산이 발작기 뇌 스캔 중 자주 관찰 됨을 알 수 있었으며, 이러한 간질 확산에 따른 다발성 방사능 섭취가 발작기 뇌스캔상, 간질 병소의 국소화에 있어 한계가 있음을 결론내릴 수 있었다.

Key Words : Seizure, Propagation, Tc-99m HMPAO, brain, Emission tomography Ictal, Interictal

INTRODUCTION

In complex partial seizure, 30 to 60% of the patients ultimately become refractory to medical treatment and will be referred for surgical treatment[1]. Therefore precise localization and removal of epileptogenic brain tissue is the ultimate goal in these patients. However, to date, no single test is accurate for the localization of the surgical sites.

Functional brain imaging using technetium-99m-hexamethyl propyleneamine oxime (Tc-99m HMPAO) has been used as a non-invasive method in the localization of seizure foci since single photon emission computed tomography

(SPECT) can image regional cerebral blood flow. It has been well known that blood flow is increased in the areas of epileptic foci in ictal phase, however, blood flow is decreased in interictal phase. So far, in terms of sensitivity in the localization of seizure foci, ictal SPECT was known superior to interictal SPECT. Interictal brain SPECT has a sensitivity in the range between 50 to 70%[2-4], whereas the sensitivity of the ictal studies ranges between 65 and 97%[2, 5, 6]. The accuracy of ictal and interictal SPECT are 56 ~73% and 44~56%, respectively, in patients with temporal lobe epilepsy[7-9]. Therefore, ictal brain SPECT is commonly used for the accurate localization of epileptic foci.

However, false localization of epileptic region leads to 20 to 40% failure rates of surgical treatment[4, 5]. The exact cause of false localization is unknown, but increased uptake within the sites of seizure propagation might be an important factor in the false localization. The purpose of our study was to assess how the seizure propagation impacts on the seizure focus localization on ictal brain SPECT.

MATERIALS AND METHODS

Fifteen patients with complex partial seizure were included. The localization of seizure foci was determined in conjunction with scalp EEG, ictal EEG, cortical EEG, MRI and clinical outcomes. Temporal lobectomy(n=13) and occipital lobectomy(n=1) were undertaken. For ictal brain SPECT, the patients were monitored by video and EEG. When seizure or aura developed, HMPAO was immediately reconstituted in 20mCi (740MBq) of Tc-99m pertechnetate and injected intravenously. The time from seizure onset on EEG to the injection of Tc-99m HMPAO was also monitored. Within one hour of injection, the patients were transported to the nuclear medicine unit for brain SPECT. The scanning procedure was performed by using a dual-headed gamma camera (ADAC, Milpitas, CA) or brain dedicated gamma camera(Digital Scintigraphic Inc, CERA-SPECT) equipped with high-resolution, low-energy parallel-hole collimators. Sixty-four projections with an acquisition time of 40 sec/ view for dual-headed camera or 120 projections with an acquisition time of 20 sec/view with CERA-SPECT. Transaxial images were obtained by filtered back projection method using a Butterworth filter(Nyquist frequency 0.38 cycle/cm at an order No 5 or 1.1 cycle/cm at an order No[10] and the coronal and sagittal images were reconstructed using the transaxial images. Ictal SPECT was followed by interictal brain SPECT within three days of seizure free period. The SPECT findings were qualitatively evaluated by two experienced nuclear medicine specialists who were blind to the clinical data, EEG findings or MRI, but were informed regarding whether the tracer was injected ictally or interictally.

The foci of increased uptake on ictal SPECT were compared with those of decreased uptake on

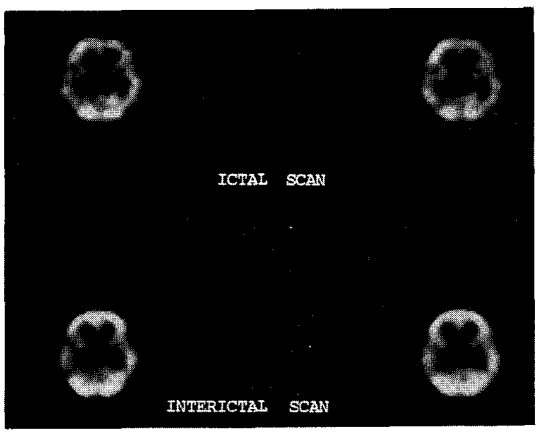

Fig. 1. Ipsilateral frontal lobe propagation.
Right temporal epilepsy in a 11-year-old male.
Ictal SPECT shows increased uptakes on right frontal lobe, and interictal SPECT shows decreased uptake on the same site.

interictal brain SPECT. The tentative localization on brain SPECT was also compared with the epileptic foci which were finally diagnosed by EEGs, semiology and surgical outcomes. MRI were performed in all patients including fast spin echo T2 weighted coronal and oblique axial images and compared with the SPECT findings.

RESULTS

The seizure foci were right temporal(n=8), left temporal(n=6) and extratemporal(n=1) origins. On ictal SPECT, increased uptake was seen within epileptic area as well as extraepileptic regions in nine patients (60%).

However, only four patients (26.7%) had increased uptake confined to seizure foci. Increased uptake only in the extraepileptic region without uptake of epileptic foci were seen in two patients (13.3%). On interictal brain SPECT, decreased uptake confined to the epileptic regions were seen in eleven out of fifteen (73.3%) patients. Increased uptakes within the seizure propagation sites were seen at ipsilateral frontal (Fig. 1) (n=4, 28.6%), parietal (n=4, 28.6%), parietooccipital (n=2, 14.3%), occipital(n=1, 7.1%) and contralateral temporal

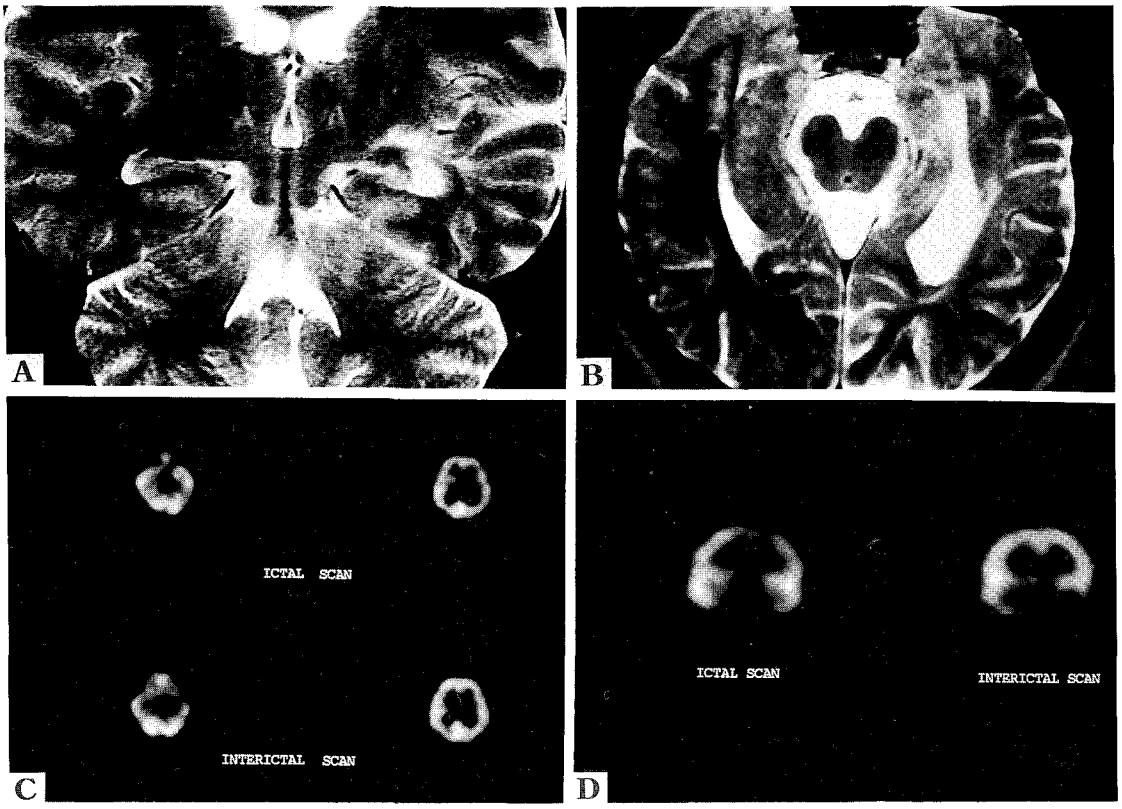

Fig. 2. Contralateral temporal lobe propagation without uptake within the seizure foci.
Left temporal epilepsy in 25-year-old male.
a and b : On T2 weighted coronal and oblique axial image, left hippocampus shows high signal intensity and atrophic change consistent with mesial temporal sclerosis.
c and d : On ictal SPECT ,increased uptakes are noted on right temporal and temporoparietal area, but no increased uptake on left temporal lobe. Interictal SPECT shows decreased uptake on left temporal lobe. The patient became seizure free after left temporal lobectomy.

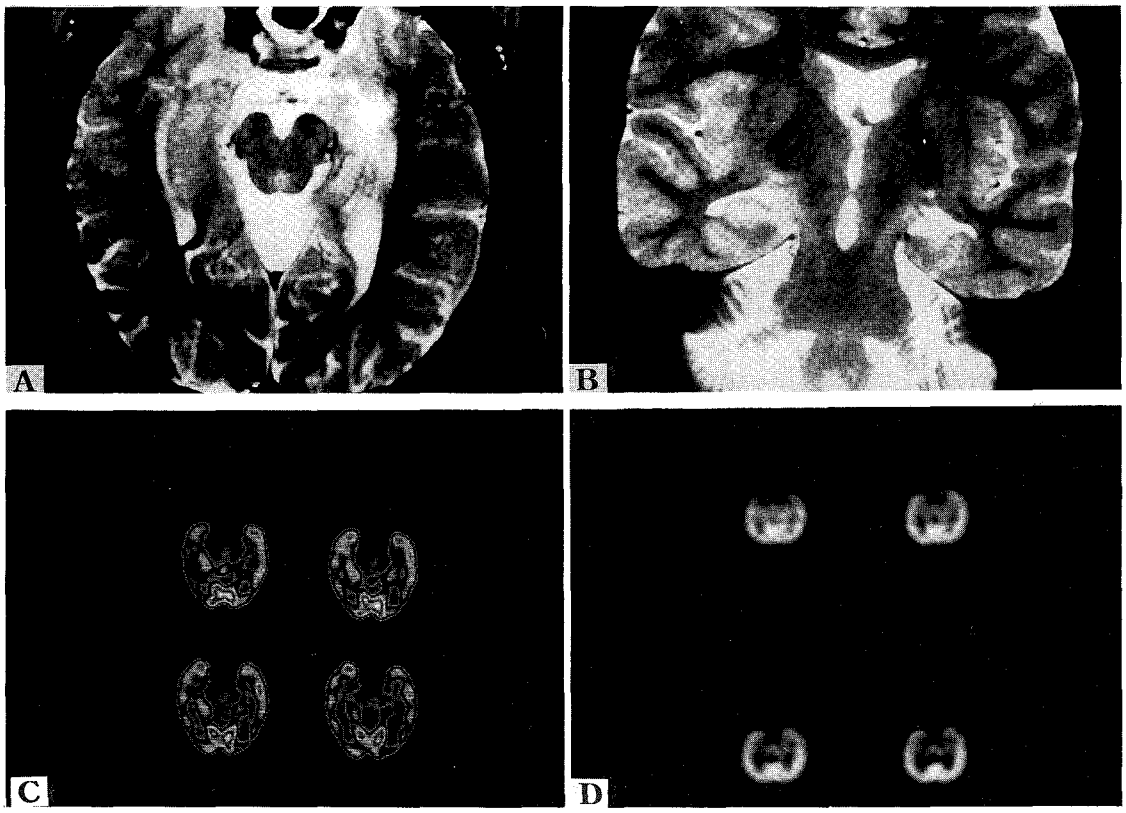

Fig. 3. Contralateral temporal lobe propagation with increased uptake within seizure foci.
Left temporal epilepsy in a 36-year-old female.
a and b : On T2 weighted MR imaging, atrophy and high signal intensity of left hippocampus is seen.
c: Ictal SPECT shows increased uptakes on bilateral temporal lobes.
d: In this case, interictal SPECT shows normal symmetrical uptakes on bilateral temporal lobes.

(n=3, 21.4%) regions. Among three cases with contralateral increased uptake, seizure foci depicted normal uptake in two cases (Fig. 2) and the other one showed increased uptakes within both epileptogenic and propagation sites (Fig. 3). In addition, diffuse increased uptake within entire ipsilateral cerebral hemisphere was seen in one patient (Fig. 4). MRI revealed high signal intensity of hippocampus on T2 weighted image with atrophic change consistent with mesial temporal sclerosis in eight patients (53.3%), which were concordant with epileptogenic foci. When compared with interictal and ictal SPECT, patients with mesial temporal sclerosis on MRI had decreased uptake on the same sites in seven patients on interictal SPECT and increased uptake in five patients on ictal SPECT. The other case presenting hippocampal abnormality on MRI, interictal brain SPECT was normal, while ictal SPECT showed increased uptake at the same site.

Mean injection time from the onset of seizure on EEG to Tc-99m HMPAO injection of the group presenting seizure propagation was 53 seconds (ranged between 34 seconds and 96 seconds), while time for the group showing focal uptake confined to seizure foci was 70 seconds (ranged between 39 seconds and 101 seconds).

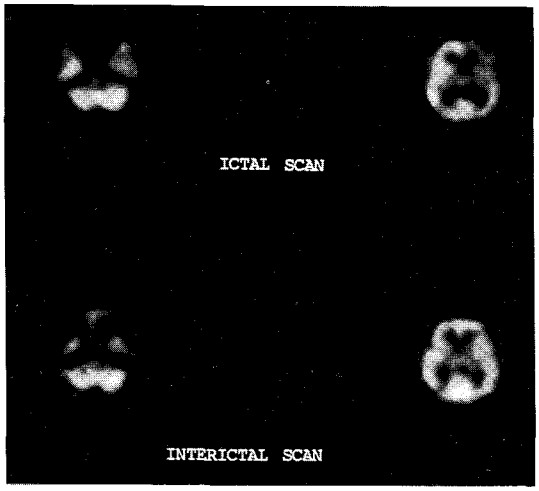

Fig. 4. Diffuse propagation to ipsilateral cerebral hemisphere
Right temporal epilepsy in a 31-year-old female.
On ictal brain SPECT, diffusely increased uptake is seen within right cerebral hemisphere. However, interictal SPECT shows decreased uptake on right temporal lobe.

DISCUSSION

Seizure propagation is defined as a spread of epileptic activity from the seizure foci to potentially epileptic region during the seizure. Adam et al, using stereo-EEG, proved occurrence of rapid and widespread diffusion of seizure propagation in patients resistant to neurosurgery and suggested that a seizure of extratemporal origin can appear to have temporal origin if the activity always propagated first to temporal lobe[12]. The propagation sites could also appear as increased uptake on ictal brain SPECT, which could sometimes mimic epileptic foci[5]. The propagation patterns have been known to be variable both within and among patients. But the most common mode of spread studied on EEG is initiating temporal lobe ipsilateral frontal lobe contralateral frontal lobe contralateral temporal lobe[12]. Prefrontal region, especially orbitofrontal cortex has been well known to be strongly influenced by mesial temporal ictal activity and may play a role in the interhemispheric propagation[13]. In fact, the frontal lobes are closely interconnected with mesial temporal lobe structures[14, 15]. Propagation is also multidirectional, sometimes to the contralateral temporal lobe for initial propagation site without involving the frontal lobe.

Our ictal SPECT study showed that multiple sites of increased uptake within the extraepileptic region may be due to seizure propagation. In our study, the seizure propagations were observed in eleven (73.3%) out of fifteen patients. Ipsilateral frontal, parietal and contralateral temporal lobes were most frequently affected sites of seizure propagation. All propagation sites mimic epileptic region. There were two cases of increased uptake only on the contralateral temporal lobe without uptake within epileptic foci (i.e. purely contralateral seizure propagation) on ictal SPECT. Therefore, in patients with complex partial seizure, increased uptake at frontal lobe on ictal SPECT should be considered as a possible seizure propagation site even though the primary seizure foci cannot be detected. However, interictal brain SPECT showed hypoperfusion confined to epileptic region in most cases.

In the study of Rowe et al, in some cases, interictal SPECT made it possible to localize the seizure foci when multiple increased uptakes were on ictal SPECT[9]. When comparing MRI with interictal SPECT, in most of the cases which showed hippocampal abnormality on MRI, the lesions were detected on interictal SPECT and consistent with epileptic region.

In terms of injection time of Tc-99m HMPAO, Stefan et al. reported that postictal hyperperfusion on SPECT might lead to false lateralization due to spread of epileptic activity. So the injection of radiopharmaceutical agent should be administered as quickly as possible after seizure onset[5]. In contrast to our expectation, our study showed

that mean injection time with propagation group was 53 seconds, which was shorter than 70 seconds of group without propagation. Therefore, injection time in our study did not influence on false localization. Basically, injection time is important for the true localization of epileptogenic foci. However, sometimes it is very difficult to inject the tracer in time since propagation may occur less than 7 seconds after onset of seizure[12]. Adam et al reported that fast ictal progression is also associated with resistance to epilepsy surgery. Very short propagation times and diffuse ictal onsets on EEGs indicate the anteromedial temporal lobectomy might indicate less effective epilepsy surgery[6]. So ictal SPECT findings should be interpreted only with simultaneous EEG recordings. Recognition of seizure spread pattern and seizure propagation will facilitate better localization of seizure foci.

In conclusion, seizure propagation was frequently observed in complex partial seizures on ictal brain SPECT. Ictal brain SPECT has a limitation in the localization of seizure foci due to seizure propagation. Therefore ictal SPECT findings should be interpreted with simultaneous EEG recordings to facilitate a better localization of seizure foci.

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