Retrograde Thalamocortical Diaschisis in Temporal Lobe Epilepsy

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측두엽 간질에서의 역행성 시상피질 해리현상

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목 적 : 측두엽 간질 환자의 발작간 뇌 스캔에서 관찰되는 측두엽 혈류 감소와 같은 쪽 시상 혈류 감소 소견의 빈도를 알아보고 이러한 소견이 간질 병소 국소화에 미치는 유용성에 대해 알아보고자 한다.

대상 및 방법 : Tc-99m-ECD를 이용하여 발작간 뇌 스캔을 시행한 67명의 측두엽 간질 환자에서 편측 측두엽과 같은 쪽 시상에 혈류 감소를 보인 12명의 환자를 대상으로 하였다. 간질 병소는 표면 뇌파 검사, 발작시 뇌파 검사, 심부 뇌파 검사, 자기 공명 영상 그리고 임상적 소견을 종합하여 국소화 하였다.

결 과 : 편측 측두엽과 같은 쪽 시상에 혈류 감소는 18%의 환자에서 관찰되었다. 7명의 환자는 왼쪽 측두엽과 시상에 혈류 감소를 보였다. 이들 7명중 4명은 자기공명영상 소견상 왼쪽 내측 측두엽 경화 소견을 보였다. 5명의 환자는 오른쪽 측두엽과 시상에 혈류 감소를 보였다. 이들 5명중 4명은 자기공명영상 소견상 오른쪽 내측 측두엽 경화 소견을 보였다.

결 론 : 발작간 뇌 스캔상 관찰되는 편측 측두엽과 같은쪽 시상의 혈류 감소 소견은 측두엽과 시상사이의 상호 연결에 의한 해리 현상으로 부분 발작의 병태 생리와 밀접한 연관이 있으리라 생각한다. 또한 이러한 소견은 간질 병소 국소화에 도움이 되리라 생각한다.

Key Words : Temporal lobe epilepsy, Diaschisis, Interictal brain SPECT

INTRODUCTION

Diaschisis is defined as hypoperfusion and hypometabolism in a portion of the brain distant from the site of damage due to an interruption of its afferent axonal supply[1]. Crossed cerebellar diaschisis(CCD) is a well known phenomenon of the hypometabolism in the contralateral cerebellum due to functional disconnection from supratentorial ischemic lesions or other clinical circumstances, including brain tumors, vascular malformation and hemorrhages[2, 3]. Baron et al reported bilateral depression of cortical metabolism after unilateral thalamic lesion on PET and called thalamocortical diaschisis[4]. In well documented cases of unilateral mesial temporal lobe epilepsy, extratemporal hypometabolism on interictal fluorodeoxyglucose (FDG) F-18 PET scan have been demonstrated[5-8]. However, the significance of extratemporal hypometabolism in temporal lobe epilepsy still remains unclear. Moreover, the characteristics of alteration of perfusion in the thalamus and basal ganglia in temporal lobe epilepsy patients had not been well documented.

We evaluated the prevalence of the decreased perfusion in the thalamus and basal ganglia on interictal brain SPECT in temporal lobe epilepsy patients. Also we assessed the usefulness of this findings for the lateralization of epileptic foci on the interictal scan.

MATERIALS AND METHODS

1. Clinical Data

The interictal brain SPECT using Tc-99m ECD of 67 patients suffering from medically intractable epilepsy were included in this study. 12 patients were chosen for inclusion in the final study group on the basis of findings of concomitant decreased perfusion in the temporal lobe and ipsilateral thalamus on interictal brain SPECT. The patients ranged in age from 10 to 34 years. All patients had partial seizure disorders; 4 of 12 patients had secondarily generalized epilepsy as a prominent clinical problem. An informed consent was obtained in all patients. MRIs were performed in all patients including fast spin echo T2 weighted coronal and oblique axial images but not quantitative volumetry. Selective intracarotid sodium amytal injection (WADA) test to assess hemispheric language dominance and memory and bilateral carotid and vertebral angiography were performed in 5 patients. Ictal EEG was performed in 5 patients. Electrocorticography was obtained in 4 patients. The localization of seizure foci was determined in conjunction with scalp EEG, ictal EEG, cortical EEG, MRI and clinical outcomes. The seizure foci were right temporal(n=5) and left temporal(n=7) origins. Five patients underwent surgical therapy for the epileptogenic focus and showed mesial temporal sclerosis in 4 patients and hippocampal microdysgenesis in one patient.

2. SPECT procedures

After an intravenous injection of 15-20mCi(555-740MBq) of Tc-99m ECD, interictal brain SPECT was performed by using a brain dedicated gamma camera(Digital Scintigraphic Inc. CERASPECT, Waltham, USA) equipped with high-resolution, low-energy parallel-hole collimators. 120 projections were acquired with 30 angular increment. Transaxial images were obtained by filtered back projection methods using a Butterworth filter(Nyquist frequency 1.1cycle/cm at an order No.10), and attenuation correction was performed by Changs method. The reconstructed slices were displayed on a 128×128 matrix(1.67×1.67mm) as a set of 64 slices(1.67mm slice thickness). Coronal and sagittal images were generated from the original transaxial images(parallel to orbitomeatal line). Additionally, transaxial images parallel to the long-axis of the temporal lobes were obtained for evaluation of the temporal lobes. The slice thickness was 1.67 or 3.34mm. Ictal scans were obtained in 5 out of the 12 patients.

SPECT findings were visually interpreted by two experienced nuclear medicine specialists blinded to EEG findings, clinical informations or other imaging findings, who evaluated cortical and subcortical regions including thalamus and basal ganglia.

Interictal PET was available in two patients and was compared with interictal SPECT findings.

RESULTS

Concomitant decreased perfusions in both temporal lobe and ipsilateral thalamus were observed in 12(18%) of 67 patients who had interictal brain SPECT.

Demographic data and MR findings were

Table 1. Demographic Data and MR and Interictal SPECT Findings

Pt. No	Sex/Age	Age of Onset	Seizure type	Surface EEG	MRI	interictal SPECT
1	F/26	1	CP to 2'GTC	LT	Lt.HA	LT & Th & BG
2	M/33	9	CP	LT	Lt.HA	LT & Th
3	F/23	10	CP to 2'GTC	RT	NL	LT & Th & BG
4	M/34	12	CP	BT	Rt.HA	RT & Th
5	F/17	14	CP to 2'GTC	RT	Rt.HA	RT & Th
6	M/35	14	CP	RT	Lt.HA	LT & Th
7	F/24	21	CP	BT	Lt.HA	LT & Th
8	F/30	22	CP	RT	Rt.HA	RT & Th & BG
9	M/10	8	CP	LT	NL	LT & Th
10	M/31	18	CP to 2'GTC	LT	NL	LT & Th & BG
11	F/22	9	CP	LT	Rt.HA	RT & Th
12	F/16	11	CP	NL	NL	RT & Th

CP : complex partial seizure, GTC : generalized tonic clonic seizure
LT : left temporal, RT : right temporal, BT : bitemporal, NL : normal, HA : hippocampal atrophy
Th : thalamu, BG : basal ganglia
Locations on interictal SPECT indicate the areas of decreased perfusion

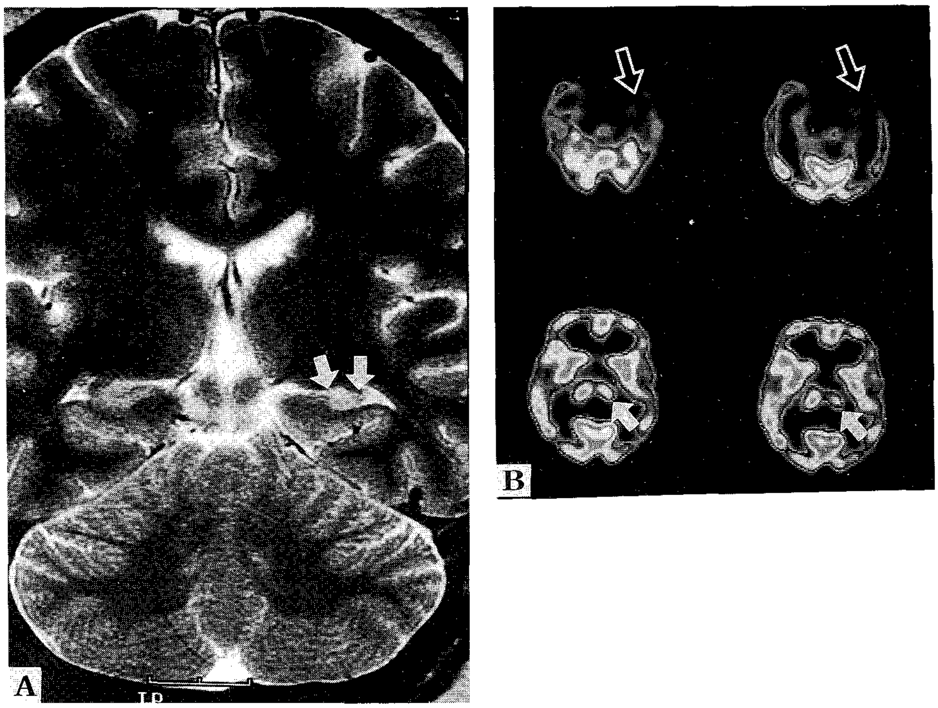

Fig. 1. 26 year-old female patient with left temporal lobe epilepsy.
a) Coronal T2 weighted MR image shows increased signal intensity and atrophy of the left hippocampus(arrow).
b) Transaxial reconstructed SPECT images show decreased perfusion of left temporal lobe(open arrow) and left thalamus(arrow).

summarized in Table 1. In view of MR and cerebral angiographic findings, no structural abnormalities were noted on both thalamus and basal ganglia. Seven patients revealed hypoperfusion in

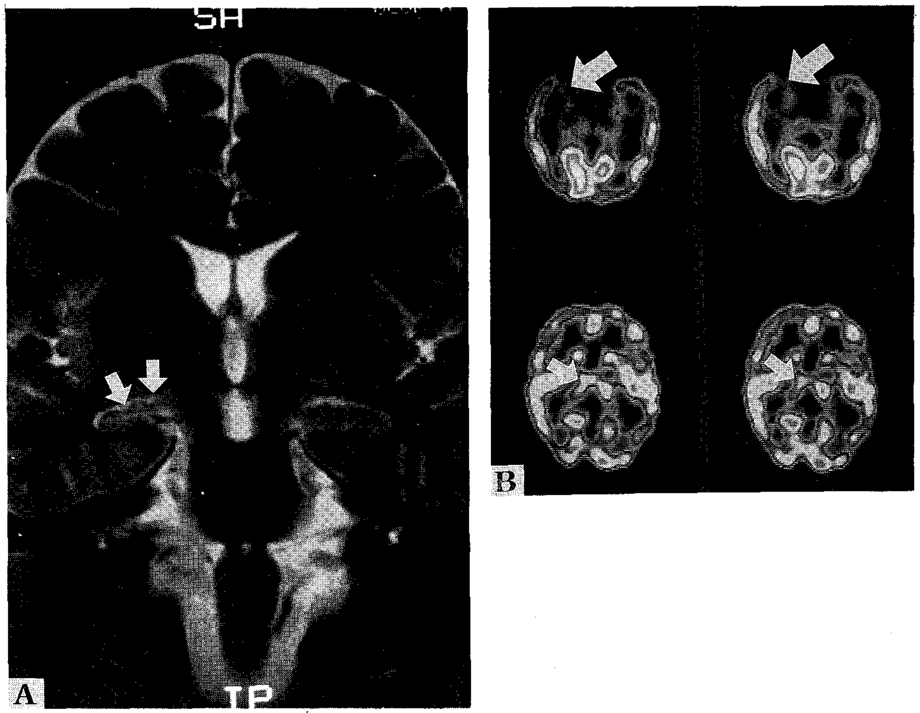

Fig. 2. 17 year-old female patient with right temporal lobe epilepsy.
a) Coronal T2 weighted MR image shows increased signal intensity and atrophy of the right hippocampus(arrow) which was consistent with mesial temporal sclerosis.
b) Transaxial reconstructed SPECT images show decreased perfusion of right temporal lobe(large arrow) and ipsilateral thalamus(small arrow).

both left temporal and ipsilateral thalamus(Fig. 1). Of those 7 patients, three patients also had hypoperfusion in ipsilateral basal ganglia. On MRI, mesial temporal sclerosis was found in four but regarded as normal in remaining three. In 4 of 7 patients, localization on the basis of interictal SPECT was concordant with surface EEG, discordant in 2 patients and unlocalized in 1.

Five patients had hypoperfusion in both right temporal lobe and ipsilateral thalamus(Fig. 2). On MRI, mesial temporal sclerosis was found in four but regarded as normal in one. Of those five patients, localization on the basis of interictal SPECT was concordant with surface EEG in 2 patients but discordant in 1 and unlocalized in 2.

Five patients also performed ictal SPECT, in which hypoperfused areas on interictal SPECT such as temporal lobe and thalamus revealed as hyperperfused areas on ictal SPECT(Fig. 3).

Interictal PET study using F-18 fluorodeoxyglucose (FDG) which was available in two patients revealed temporal and thalamic and/or basal ganglia hypometabolism, the PET findings were concordant with interictal SPECT findings.

DISCUSSION

Originally used by Von-Monakow in 1914, diaschisis implies an immediate decrease in neuronal activity in a region due to an interruption of its afferent axonal supply from the site of a primary brain lesion[9]. The classical definition of diaschisis requires a reversible, functional phenomenon without structural changes. Primary metabolic

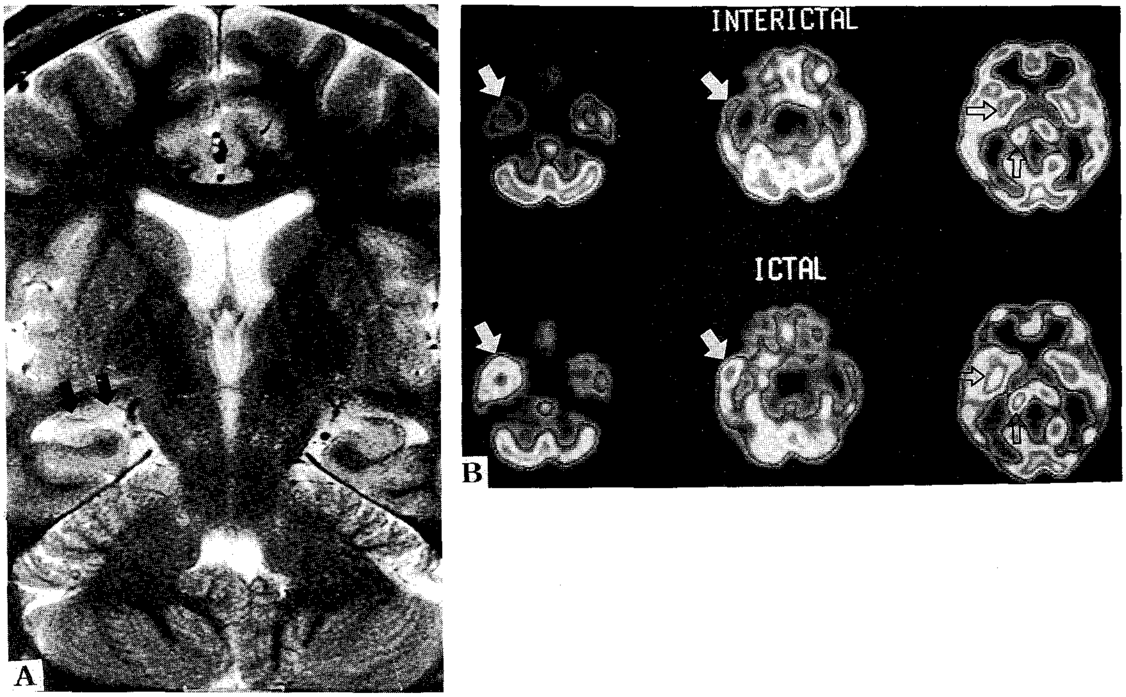

Fig. 3. 34 year-old female patient with right temporal lobe epilepsy.
a) Coronal T2 weighted MR image shows increased signal intensity and atrophy of the right hippocampus(arrow), suggesting mesial temporal sclerosis.
b) Transaxial reconstructed interictal SPECT images show decreased perfusion of right temporal lobe(arrow) and ipsilateral thalamus and basal ganglia(open arrow). On ictal SPECT, right temporal lobe(arrow) and right thalamus and basal ganglia(open arrow) reveal increased perfusion when compared to the left side.

suppression from diaschisis causes reduced the regional cerebral blood flow, oxygen metabolic rate and glucose metabolic rate. However, the normal oxygen extraction rate is crucial to differentiate primary metabolic suppression due to diaschisis from the ischemic condition[10].

Supratentorial ischemic lesions or other clinical circumstances, including brain tumors, vascular malformation and hemorrhages are well known to be associated with diaschisis. However, reports dealing with diaschisis in epilepsy are rare. Some of previous studies using interictal PET showed extratemporal hypometabolism[5-8]. Recently, hyperperfusion within the cerebellum contralateral to the seizure foci was reported on ictal SPECT[11-13]. Won et al reported this finding was common (75%) on ictal brain SPECT in seizure patients, and it might aid in the lateralization of epileptogenic foci despite the lack of typical uptake pattern on ictal SPECT or surface EEG[11]. Duncan et al also reported a patient with a focal epilepsy revealed crossed cerebellar hyperperfusion on ictal SPECT, slight hypoperfusion of the ictal focus and symmetrical normal uptake of the cerebellum on interictal SPECT[12].

Diaschisis and its clinical importance in the regions other than the contralateral cerebellum have yet to be documented. Wise et al observed 30-40% decrease of cerebral blood flow and cerebral metabolic rate for oxygen in the thalamus ipsilateral to cerebral infarction[14]. On the contrary, Baron et al reported the thalamocortical diaschisis, the depression in bilateral cortical metabolism after unilateral thalamic lesion on PET scan[4]. The mechanism of the thalamocortical diaschisis was thought to be an interruption of cortical afferents originating from the thalamus. Similar to crossed cerebellar atrophy observed in CCD[3], ipsilateral thalamic atrophy may be observed in patients with cerebral infarction in the territory of middle cerebral artery[15]. Matthews reported the thalamic neuronal degeneration following cortical ablation in rabbits and concluded that the thalamic degeneration resulted mainly from the retrograde degeneration in the axotomized thalamic neurons[16].

Several reports have found the evidence of thalamic hypometabolism ipsilateral to temporal hypometabolism in several subjects[5-8]. Henry et al reported the abnormal regional asymmetry of the thalami in 63% of 27 patients and basal ganglia in 41%. They suggested that subcortical hypometabolism is secondary to the decreased efferent activity from the temporal lobe structures, especially in amygdala and hippocampus to subcortical nuclei. Moreover, diminished subcortical activity may then lead to the defective regulation of cortical excitability in the temporal lobe, increasing the likelihood of seizure development and spread[7].

Studies of monosynaptic pathways in primates showed dense ipsilateral, reciprocal connections among the amygdala, hippocampal formation and entorhinal cortex[17-19]. The primate midline thalamic nuclei, including the nucleus reuniens, are reciprocally connected with ipsilateral amygdala and hippocampal formation; the hippocampal formation is also reciprocally connected with the lateral dorsal and anterior thalamic nuclei[17, 20, 21]. In the primate inferior and lateral temporal neocortex also has dense monosynaptic, reciprocal connections ipsilaterally with the amygdala and the hippocampal formation. Thus, the anterograde and retrograde axonal tracing techniques disclose unilateral monosynaptic, reciprocal projections among widespread mesial and lateral temporal areas, and the thalamus in primates[17, 19, 22]. Furthermore, the amygdala and anterior portions of the hippocampal formation (which are most often involved in both the electrographic ictal onset zone and the neuronal loss of mesial temporal lobe epilepsy) are included in all of these reciprocal connections[23].

In our study, we evaluated decreased perfusion in both temporal lobe and ipsilateral thalamus on interictal brain SPECT and observed hypoperfusion of thalamus ipsilateral to the hypoperfused temporal lobe in 12(18%) of 67 patients. Findings of the thalamic hypoperfusion ipsilateral to temporal hypoperfusion without any evidence of morphological abnormalities on MRI and cerebral angiography might reflect the decreased efferent activity from the temporal lobe structures as well as alteration of reciprocal connection between the temporal lobe structures and thalami. It is of interest to note that the hypoperfused thalamus and basal ganglia on interictal SPECT are changed into hyperperfused on ictal SPECT, and these findings are related to the functional alteration of subcortical structures. We considered this hypoperfusion of the thalamus ipsilateral to the hypoperfusion of the temporal lobe on interictal SPECT as retrograde thalamocortical diaschisis. This retrograde thalamocortical diaschisis had not been reported in the study of interictal brain SPECT, up to now, although several PET studies reported the subcortical alteration of metabolism on interictal study. Our results of interictal PET studies in two patients, were almost identical with that of earlier PET studies. Therefore, improved detection of the thalamic hypoperfusion on interictal SPECT might be due to improved spatial resolution of brain-dedicated annular crystal gamma camera used in our study[24].

Although this retrograde thalamocortical diaschisis was too small to assist in seizure localization, hypoperfusion of the thalamus ipsilateral to the hypoperfused temporal lobe on interictal SPECT may be relevant to the pathophysiology of partial epilepsy and may aid in the localization of seizure foci.

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