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Brain Perfusion SPECT in Patients with Herpex Simplex Virus (HSV) and Non-HSV Encephalitis

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Symptoms and signs of temporal lobe origin associated with central nervous system (CNS) infection suggests Herpes simplex virus encephalitis (HSVE) (1). However, about 50% of cases of suspected HSVE have other diseases (1–4). Brain biopsy, previously considered the most accurate method of demonstrating HSVE (1, 2, 5, 6), is known to give false negative results occasionally (7).

In HSVE, therapy with acyclovir is known to be most effective when started immediately (1) after first symptoms of encephalitis. However, at an early stage of HSVE a reasonable diagnostic accuracy may be gained only using combined clinical, laboratory, EEG, CT, MRI and brain scintigraphy data, especially if brain biopsy is unobtainable (1, 6, 8, 9). Therefore, a specific and sensitive method for detecting HSVE would be of great value.

We have examined the brain perfusion of patients with HSVE and non-herpetic encephalitis by single photon emission computed tomography (SPECT). We report here, that SPECT demonstrates characteristic findings in HSVE and is therefore capable of distinguishing HSVE from non-herpetic encephalitides. SPECT seems to be superior to CT in the diagnosis of early HSVE.

Patients, diagnosis and imaging

We studied 19 patients with viral encephalitis, remitted to the Department of Neurology, Helsinki University Central Hospital by SPECT. Either ^{123}I-iodoamphetamine (IMP) or ^{99m}Tc-hexamethylpropyleneamine oxime (HM-PAO) was used as the brain perfusion tracer. The time between initial encephalitis symptoms and the first SPECT varied from 4 to 11 days. Altogether 32 SPECTs were performed. All patients were treated with acyclovir (30 mg/kg/day).

CT, EEG and lumbar CSF investigations were performed on all patients within the first 48 hours in the hospital. Follow-up CT, SPECT, EEG and CSF studies were also performed. CSF and serum antibody screening tests, microbial cultivation and staining and other blood tests were done to uncover the virological diagnosis and to exclude underlying systemic diseases.

The criteria for viral encephalitis were: (1) an acute or a subacute onset of signs and symptoms to be found in encephalitides, (2) EEG findings suggesting encephalitis, (3) CSF findings indicating CNS infection, and (4) exclusion of bacterial and systemic diseases.

The criteria for HSVE were: (1) typical clinical findings and course of disease, (2) at least a fourfold increase of CSF HSV antibody titres in repeated CSF specimens or a constantly very high CSF antibody level (10) (case 1 in Table 1), (3) EEG consisting of focal sharp and slow wave complexes in the affected temporal lobe during the early phase of the encephalitis, and (4) exclusion of other CNS diseases.

A summary of clinical data and neuroimaging findings is presented in Table 1.

SPECT was performed using a General Electronic 400T large field-of-view rotating gamma camera equipped with a low-energy parallel hole collimator. Either 4.9–6.0 mCi ^{123}I-IMP and 64 frames with frame per 40 seconds or 10.0–14.5 mCi ^{99m}Tc-HM-PAO and 64 frames with frame per 30 seconds was used. Only one type of tracer was used in studies on a single patient. For analysis of side-to-side differences regions of interest (ROI) were drawn on 42 predefined sites on 6 tomographic slices of each study. Scaling was done by dividing mean counts/pixel/minute (cpm) from each ROI with the mean cpm rate of all other ROIs.

CT scannings were performed with a General Electric 8080 or Siemens Somatom 2 scanners and contrast enhancement was used. MRI was performed with Instrumentarium Acutscan^{r} 0.02 T field scanner.

Results

All patients with HSVE had an area of increased perfusion in the affected temporal lobe (Fig. 1a, c, e) in the first SPECT. This hyperperfusion was seen to increase in two patients (cases 4 and 6 in Table) between 4 and 13 days after first encephalitis symptoms. The initial hyperperfusion was followed by progressing hypoperfusion (Fig. 3) in the affected area in all HSVE cases. Hypoperfusion appeared between 37 and 165 days after the first symptoms (Fig. 3).

None of the patients with non-herpetic encephalitis had any perfusion abnormalities during the first two weeks of disease and no hypoperfusion was seen to develope in the patients followed up (Figs. 2 and 3).

Conventional brain scintigraphy was performed on two patients with HSVE and one with non-HSV encephalitis. The scintigrams were normal in both patients with HSVE when SPECT showed hyperperfusion. In the non-herpetic encephalitis case both SPECT and scintigraphy were normal.

Table 1. Clinical and neuroimaging data of patients with HSVE and non-herpetic encephalitis.

Case	Virus	Symptoms	Initial SPECT	Follow-up SPECT	Initial CT	Follow-up CT	MRI	^{99m}Tc Scan	Outcome
1 F 57 Y	HSVE	L focal	RT hyper	RT hypo	normal	RT atrophy	normal	normal	moderate
2 F 32 Y	HSVE	L focal	RT hyper	RT hypo	normal	RT atrophy	NT	NT	poor
3 M 40 Y	HSVE	R focal	LT hyper	LT hypo	normal	normal	LT lesion	NT	moderate
4 F 63 Y	HSVE	L focal	RT hyper	RT hypo	normal	RT atrophy	NT	NT	moderate
5 F 22 Y	HSVE	R focal	LT hyper	LT hypo	normal	normal	normal	NT	poor
6 F 54 Y	HSVE	L focal	RT hyper	LT hypo	normal	RT atrophy	RT lesion	normal	poor
1 M 17 Y	Rubella	R focal	normal	normal	normal	normal	NT	NT	good
2 M 18 Y	Adenovirus	L focal	normal	NT	normal	normal	normal	NT	good
3 F 16 Y	SSPE	diffuse	normal	normal	normal	atrophy	NT	NT	poor
4 F 69 Y	?	diffuse	normal	NT	normal	normal	NT	NT	moderate
5 F 57 Y	?	diffuse	normal	NT	normal	normal	NT	NT	moderate
6 F 38 Y	?	diffuse	normal	NT	normal	normal	NT	NT	good
7 M 54 Y	?	L focal	normal	NT	normal	normal	NT	NT	good
8 M 53 Y	?	R focal	normal	normal	normal	atrophy	NT	normal	moderate
9 F 19 Y	?	R focal	normal	NT	normal	normal	NT	NT	good
10 M 58 Y	?	R focal	normal	NT	normal	LT lesion	LT lesion	NT	moderate
11 F 18 Y	?	diffuse	normal	normal	normal	atrophy	WM lesion	NT	poor
12 M 13 Y	?	diffuse	normal	NT	normal	normal	NT	NT	moderate
13 M 17 Y	?	R focal	normal	NT	normal	LP atrophy	LP lesion	NT	moderate

F = female; L = left; R = right; LT = left temporal; RT = right temporal; LP = left parietal; WM = white matter; NT = not done; hypo = hypoperfusion; hyper = hyperfusion.

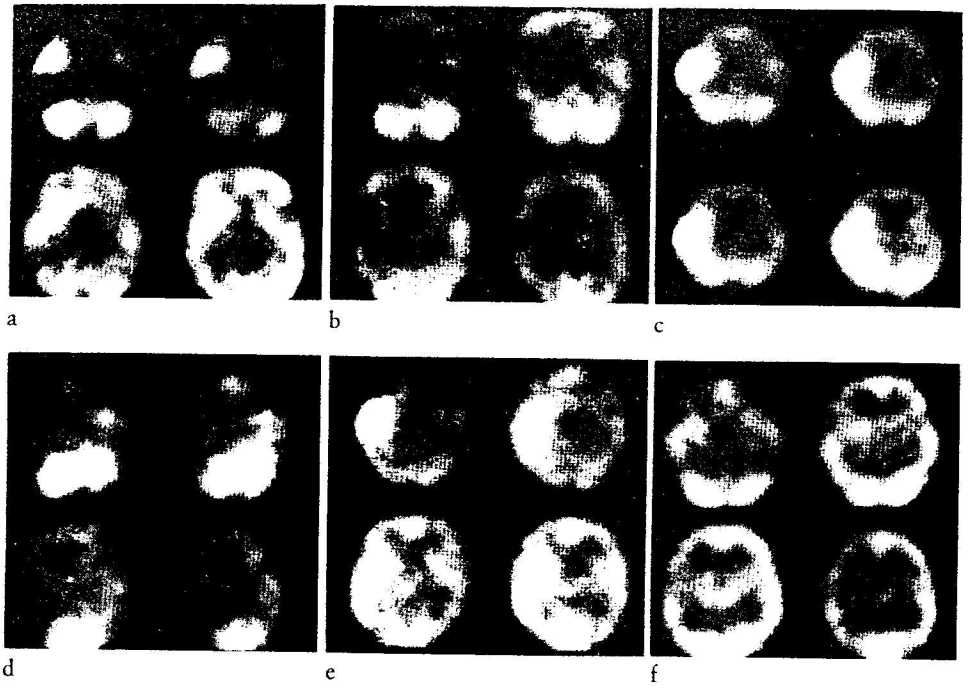

Fig. 1. SPECT in HSVE. *Case 3* in the Table imaged with HM-PAO. a) A hyperperfused area is seen in the right temporal lobe 39 days after onset of encephalitis. b) The hyperperfusion has changed into hypoperfusion 91 days after the onset of encephalitis. *Case 1* in the Table imaged with IMP. c) An intensely hyperperfused area is seen in the right temporal lobe 8 days after onset of encephalitis. d) The area of hypoperfusion covers right frontal and temporal lobes 232 days after onset. This patient was also 59 and 163 days after onset, and gradual decrease of the hyperperfusion was seen. *Case 6* in the Table imaged with HM-PAO. e) An hyperperfused area in the right anterior and middle temporal lobe 4 days after onset of encephalitis. f) Hypoperfusion is seen 55 days after onset in the corresponding area where initial hyperperfusion was seen.

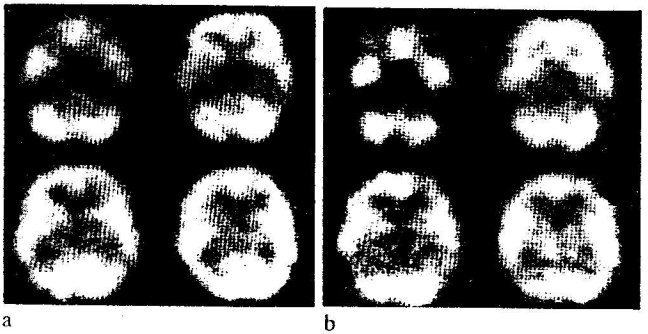

Fig. 2. SPECT in non-herpetic encephalitis. *Case 9* in the Table imaged with HM-PAO. a) SPECT 10 days after first symptoms of encephalitis. No perfusion abnormalities are present. b) SPECT 193 days after onset. No hyperperfusion or other abnormalities present.

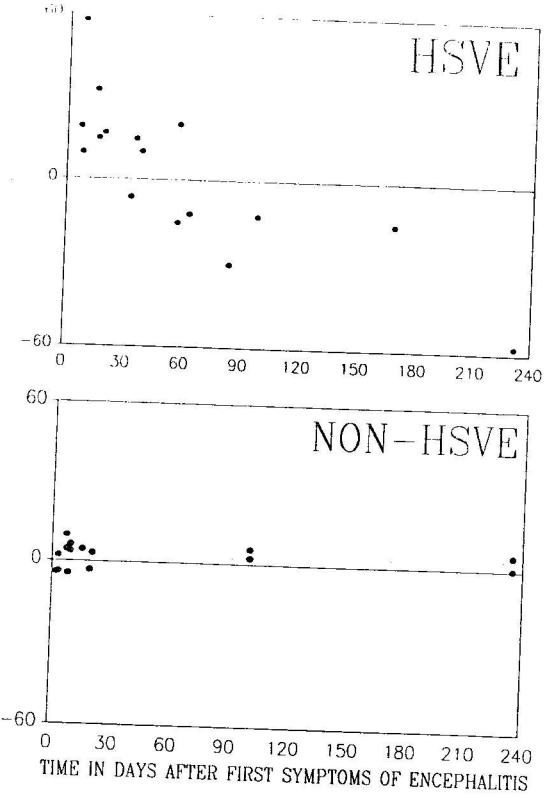

Fig. 3. Per cent side-side differences of temporal lobes in initial and follow-up SPECT in patients with HSVE and non-HSVE. The dotted line represents linear regression of findings. Note the remarkable differences between the HSVE and non-HSVE group.

Discussion

We have found focal unilateral hyperperfusion of this magnitude only in association with early HSVE among the 510 SPECT imagings performed in our laboratory so far. None of the patients with non-herpetic encephalitis had similar initial or late findings although focal neurological symptoms or focal EEG findings were found. Regional hyperperfusion is known to occur in focal epilepsy ictally (11) and the luxury perfusion phase of stroke (12, 13). According to our experience so far, the magnitude and duration of hyperperfusion in these conditions have been markedly less than in HSVE. Thus, the finding appears fairly specific.

Conventional brain scintigraphy was negative in two HSVE patients, while at the same time SPECT demonstrated hyperperfusion. Thus, the increased tracer accumulation is not related to disruption of the blood brain barrier.

Without treatment HSVE causes death in about 70% of cases and moderate or severe neurologic impairment in about 90% of the survivors (14). Treatment with acyclovir is known to improve the prognosis dramatically (1). As acyclovir does not have serious side-effects, all suspected cases of HSVE should be treated with acyclovir immediately after the clinical suspicion has arisen. About 46% of suspected HSVE cases, however, have other diseases, the diagnosis of which may require brain biopsy (6). HM-PAO and IMP SPECT seem to be both sensitive and specific in differentiating between HSVE and other clinically HSVE-like diseases. Therefore, either IMP or HM-PAO SPECT should be added to the diagnostic assortment when HSVE is suspected.

Summary

We studied brain perfusion using ^{123}I-iodoamphetamine or ^{99m}Tc-hexamethylpropyleneamine oxime and single photon emission computed tomography (SPECT) in 19 patients with acute encephalitis. All six patients with Herpes simplex virus encephalitis (HSVE) had a strongly increased radiotracer accumulation in the affected temporal lobe. The time interval between the onset of encephalitis symptoms and the first SPECT varied from 4 to 11 days. At the time of the first SPECT CT was normal in each patient. The SPECT appearance gradually converted within 4 to 10 weeks into an area of markedly decreased tracer accumulation. We have seen such an intense tracer accumulation only in early HSVE. Also, the combination of increased uptake followed by a decreased uptake in the temporal lobe was observed only in patients with HSVE. SPECT was normal in all 13 patients with non-HSVE. Thus, brain perfusion SPECT is both sensitive and specific for the early diagnosis of HSVE.

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