

原著論文

Usefulness of ^{99m}Tc -ECD Brain SPECT in Acute Onset Pediatric CNS Diseases : in Comparison with CT and MRI

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Abstract **PURPOSE** : To assess the usefulness of regional cerebral blood flow (rCBF) measured by ^{99m}Tc -L, L-ethyl cysteinyl dimer (ECD) brain SPECT in the acute onset type of pediatric central nervous system (CNS) diseases.

MATERIALS and METHODS : Thirteen children (7 girls, 6 boys, 4 month-12 years of age) who were diagnosed with 9 cases of viral encephalitis, two cases of febrile convulsion and one each of migraine and metabolic disorder underwent ^{99m}Tc -ECD brain SPECT, CT and/or MRI within one week interval.

RESULTS : The incidence of abnormal findings in the 13 patients was 96.4% (30/31) on ^{99m}Tc -ECD brain SPECT, 17.6% (3/17) on CT and 63.6% (14/22) on MRI. The positive detection rate of ^{99m}Tc -ECD brain SPECT was statistically ($P < 0.01$ by a χ^2 and/or Fisher's exact probability test) higher than those of CT and MRI. And the changes in rCBF were demonstrated.

CONCLUSION : ^{99m}Tc -ECD brain SPECT is a useful examination for the diagnosis and follow up management in patients with the acute onset type of pediatric CNS diseases.

Keywords ^{99m}Tc -ECD brain SPECT, MRI, CT, Acute onset type of pediatric CNS diseases

INTRODUCTION

Recent progress in neuroimaging studies has thrown much light on the etiology of acute hemiplegia syndrome (AHS). Early diagnosis and therapy during the first 2 or 3 days of symptomatic illness are essential if high mortality and serious neurologic sequelae are to be avoided^{1, 2)}. For the early diagnosis, estimation by ^{99m}Tc -L, L-ethyl cysteinyl dimer

(ECD) brain SPECT can be helpful but reported cases are rare³⁾. In this paper, we present 13 cases of acute onset type of pediatric CNS diseases estimated by ^{99m}Tc -ECD brain SPECT, and compared with CT and/or MRI.

MATERIALS and METHODS

Thirteen children (7 girls, 6 boys, 4 month-12 years of age) who were diagnosed with 9 cases of viral encephalitis, two cases of febrile

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Table 1 Breakdown of the 13 patients

Encephalitis	9
Influenzal encephalitis	2
HHV-6 (human herpes virus type-6) encephalitis	2
Herpes simplex virus (HSV) encephalitis	1
Measles encephalitis	1
Limbic encephalitis	1
Other encephalitis (etiology unknown)	2
Febrile convulsion	2
Migraine	1
Metabolic disorder	1
Total	13

convulsion and one each of migraine and metabolic disorder, underwent ^{99m}Tc -ECD brain SPECT, CT and/or MRI within one week interval. The breakdown of the patients is shown on **Table 1**. ^{99m}Tc -ECD brain SPECT to evaluate the regional cerebral blood flow (rCBF) was performed 20 minutes after an intravenous injection of 310-800 MBq of ^{99m}Tc -ECD. Thirty-one rCBF SPECT studies were done in 13 patients. SPECT was performed using a triple-head system (Toshiba GCA-9300A/HG) equipped with ultra-high-resolution fanbeam collimators and interfaced to a dedicated computer. Data were collected for continuous 5 rotations (3 minutes for one rotation) in a 128×128 matrix. Acquired data were reconstructed using 3-dimensional Butterworth-Wiener filter (order, 8.0 ; cutoff frequency, 0.13 cycle per pixel) after applying a Shepp & Logan back projection filter. Plain and/or post contrast enhancement CT was performed 17 times in 13 patients. Brain MR with or without Gd-DTPA enhancement was done 22 times in 13 patients. MR examinations were performed at 1.5 T (SHIMADZU MAGNEX150). MR imaging parameters included a 256×256 matrix and 6-mm-thick sections (with a 1.5-mm intersection gap) and axial scanner spin-echo (SE) T1-weighted sequence of 600-710/15/1 (TR/TE/ excitations) and a T2-weighted sequence of 3800-4600/110/1.

RESULTS

Thirty-one rCBF SPECT studies were performed in 13 patients with acute onset type of pediatric CNS diseases. In two of 13 patients marked regional high uptake was shown. And, in three of them, faint regional high uptake in the acute phase within a week after onset. Twenty-five studies showed regional low uptake in the subacute and chronic phases. One study showed normal regional uptake. Five lesions with regional high uptake changed to low uptake, and two lesions improved to normal uptake on follow up studies. On the comparative studies with MRI, 14 of 22 studies showed cortical thickness, high intensity area on T2 weighted images. In 3 of 17 studies, CT scan showed brain edema and brain atrophy. The incidence of abnormal findings in the 13 patients was 96.4% (30/31) on ^{99m}Tc -ECD brain SPECT, 17.6% (3/17) on CT and 63.6% (14/22) on MRI. The positive detection rate of ^{99m}Tc -ECD brain SPECT was statistically ($P < 0.01$ by a χ^2 and/or Fisher's exact probability test) higher than those of CT and MRI, as shown in **Table 2** and **Table 3**.

CASE REPORTS

<Case 1>A 6-year-old girl with herpes simplex virus (HSV) encephalitis. On the day of admission she exhibited high fever, repeated vomiting and slight weakness of the right upper limb. Nuchal rigidity was present. Patellar tendon reflex was reduced and Babinsky reflex was positive on the same right side. CT scan on admission and MRI obtained on the 5th day revealed no remarkable abnormality (**Fig.1a,b**). ^{99m}Tc -ECD brain SPECT on the 8th day after admission showed markedly increased rCBF on the left cerebral hemisphere (**Fig.1c**). ^{99m}Tc -ECD brain SPECT performed on the 27th day disclosed larger areas of decreased rCBF in the left cerebral hemisphere (**Fig.1d**). MRI obtained 4 and 19 month later also revealed no remarkable abnormality. On the follow-up ^{99m}Tc -ECD brain SPECT performed 19 month later, decreased

Table 2 Positive detection rate of ^{99m}Tc -ECD SPECT and CT

	Positive detection rate%		
	SPECT	CT	p-value
Encephalitis	100.0 (21/21)	21.4 (3/14)	P<0.01
HSV encephalitis	100.0 (7/7)	0.0 (0/3)	P<0.01
Influenzal encephalitis	100.0 (4/4)	0.0 (0/2)	N.S.
HHV-6 encephalitis	100.0 (4/4)	66.7 (2/3)	N.S.
Measles encephalitis	100.0 (2/2)	50.0 (1/2)	N.S.
Limbic encephalitis	100.0 (1/1)	0.0 (0/1)	N.S.
Others	100.0 (3/3)	0.0 (0/3)	N.S.
Febrile convulsion	100.0 (4/4)	0.0 (0/1)	N.S.
Migraine	100.0 (2/2)	0.0 (0/1)	N.S.
Metabolic disorder	0.0 (0/1)	0.0 (0/1)	N.S.
Total	96.4 (27/28)	17.6 (3/17)	P<0.01

Table 3 Positive detection rate of ^{99m}Tc -ECD SPECT and MRI

	Positive detection rate%		
	SPECT	MRI	p-value
Encephalitis	100.0 (21/21)	66.7 (10/15)	P<0.01
HSV encephalitis	100.0 (7/7)	66.7 (2/3)	N.S.
Influenzal encephalitis	100.0 (4/4)	0.0 (0/2)	N.S.
HHV-6 encephalitis	100.0 (4/4)	100.0 (4/4)	N.S.
Measles encephalitis	100.0 (2/2)	0.0 (0/1)	N.S.
Limbic encephalitis	100.0 (1/1)	100.0 (1/1)	N.S.
Others	100.0 (3/3)	100.0 (3/3)	N.S.
Febrile convulsion	100.0 (4/4)	100.0 (3/3)	N.S.
Migraine	100.0 (2/2)	0.0 (0/2)	N.S.
Metabolic disorder	0.0 (0/1)	0.0 (0/1)	N.S.
Total	96.4 (27/28)	61.9 (13/21)	P<0.01

rCBF in the left cerebral hemisphere had returned to almost normal (Fig.1e).

<Case 2>An 11-year-old girl with migraine. Her family history was positive for migraine in her brother, father and paternal uncle. On the day of admission she complained of right temporal headache and right neck pain after which unconsciousness, left hemiplegia and eye deviation to the right side developed. CT scan on admission and MRI obtained on the 4th day revealed no remarkable abnormality (Fig.2a). ^{99m}Tc -ECD Brain SPECT on the 4th day after admission showed markedly increased rCBF on the right cerebral hemisphere (Fig.2b). MRI

obtained 40 days after admission revealed no remarkable abnormality either. ^{99m}Tc -ECD Brain SPECT performed on the 40th day disclosed larger areas of decreased rCBF in the right cerebral hemisphere (Fig.2c).

DISCUSSION

Acute hemiplegia syndrome (AHS) is a generalized name for sudden onset of an acute hemiplegia in infants and children, caused by acute encephalopathy, cerebral vascular diseases, brain tumor and central nervous infectious diseases and so on. The acute encephalopathy type of acute hemiplegia syndrome frequently

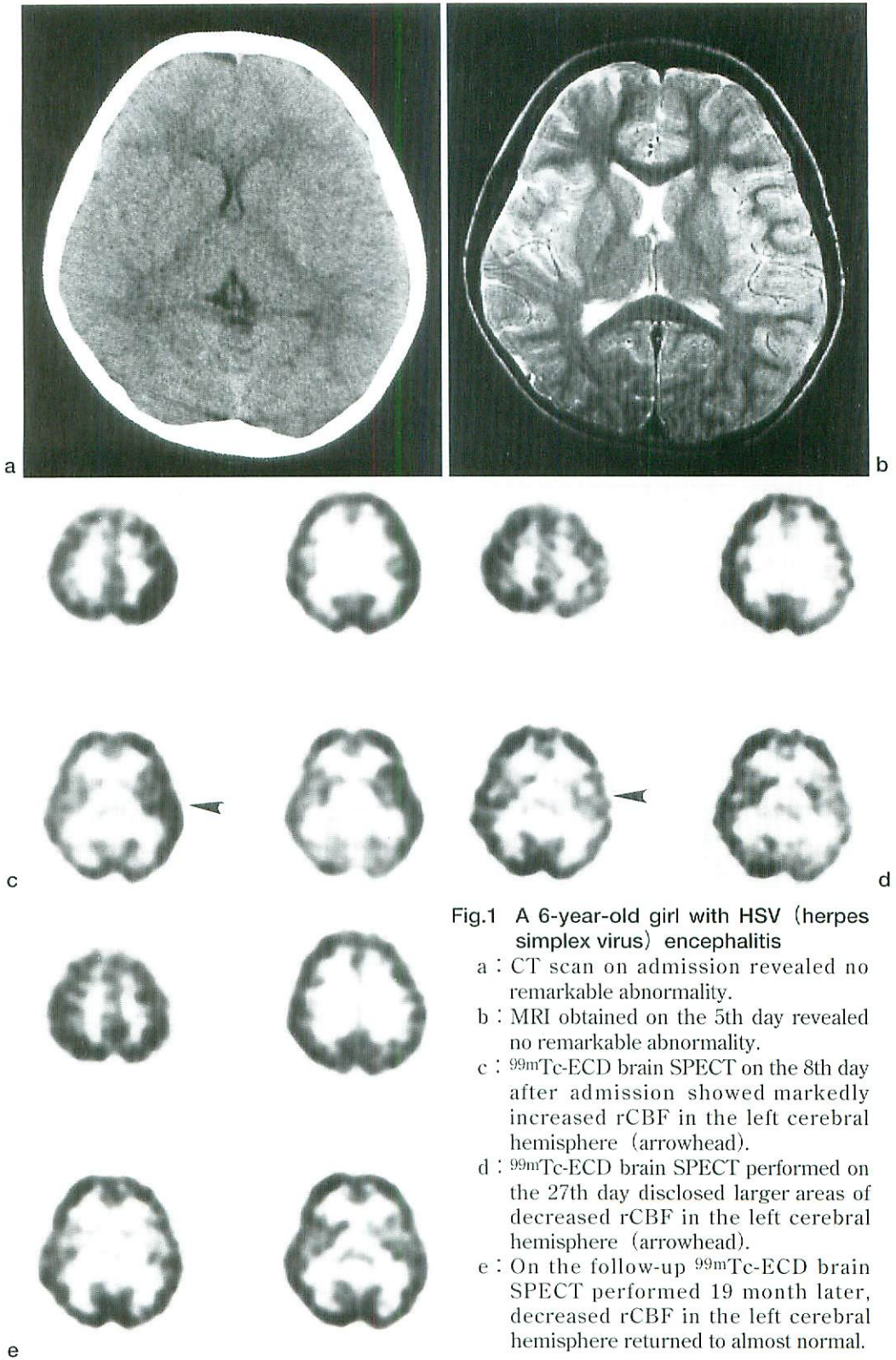


Fig.1 A 6-year-old girl with HSV (herpes simplex virus) encephalitis

- a : CT scan on admission revealed no remarkable abnormality.
- b : MRI obtained on the 5th day revealed no remarkable abnormality.
- c : ^{99m}Tc-ECD brain SPECT on the 8th day after admission showed markedly increased rCBF in the left cerebral hemisphere (arrowhead).
- d : ^{99m}Tc-ECD brain SPECT performed on the 27th day disclosed larger areas of decreased rCBF in the left cerebral hemisphere (arrowhead).
- e : On the follow-up ^{99m}Tc-ECD brain SPECT performed 19 month later, decreased rCBF in the left cerebral hemisphere returned to almost normal.

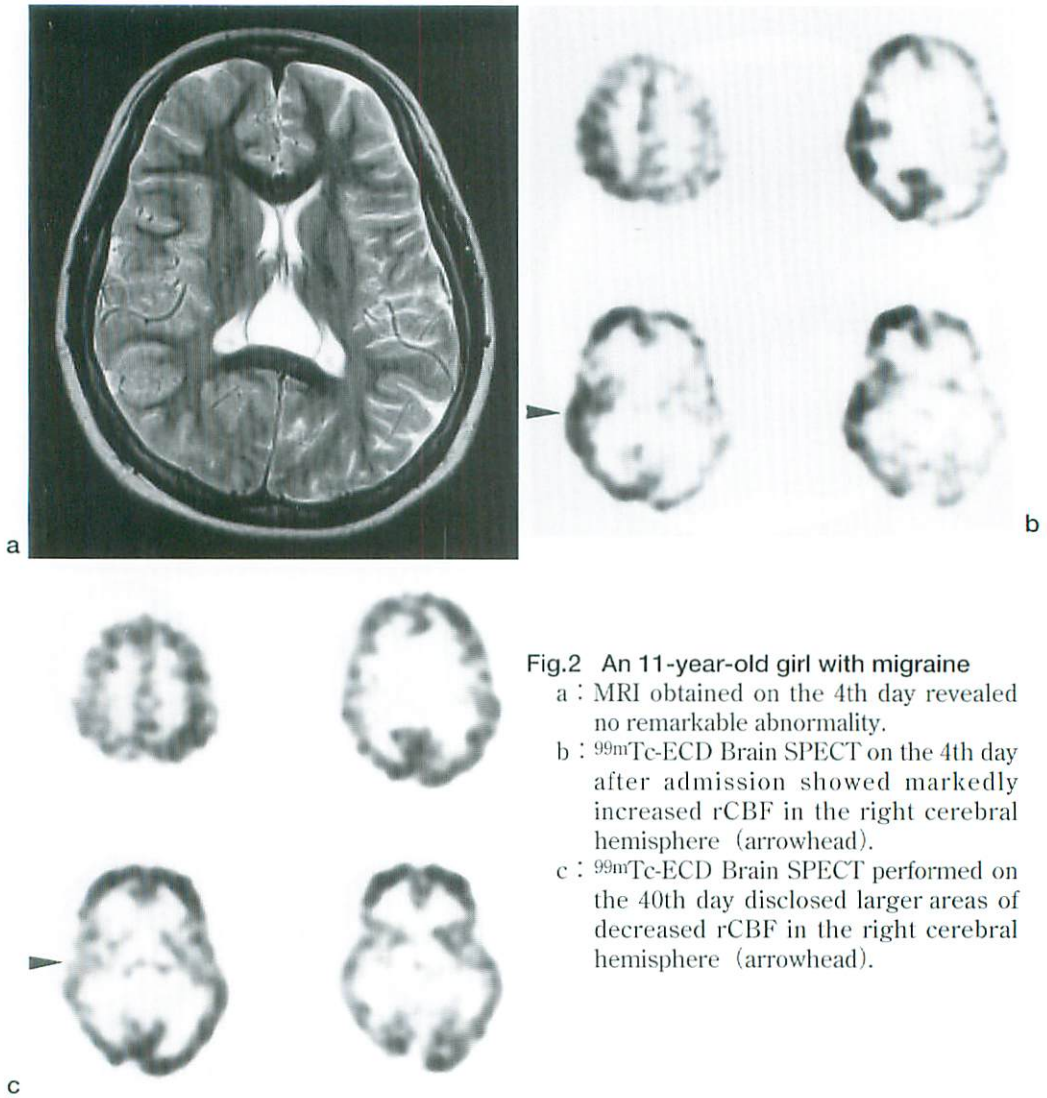


Fig.2 An 11-year-old girl with migraine

- a : MRI obtained on the 4th day revealed no remarkable abnormality.
- b : ^{99m}Tc -ECD Brain SPECT on the 4th day after admission showed markedly increased rCBF in the right cerebral hemisphere (arrowhead).
- c : ^{99m}Tc -ECD Brain SPECT performed on the 40th day disclosed larger areas of decreased rCBF in the right cerebral hemisphere (arrowhead).

results in serious neurologic sequelae and an explanation of its pathophysiological mechanism would be highly desirable. AHS which is estimated by ^{99m}Tc -ECD brain SPECT has rarely been described previously³⁾.

For the cerebral perfusion imaging agents, ^{123}I -IMP, ^{99m}Tc -HMPAO and ^{99m}Tc -ECD are clinically available. ^{123}I -IMP is useful for the detection of cerebral ischemia, because of its sensitivity, non-invasiveness and accurate reflection of the cerebral blood flow distribution⁴⁾. ^{99m}Tc -HMPAO has been shown to improve the sensitivity and accuracy of cerebral imaging in cases of epilepsy,

dementia and stroke⁵⁻⁷⁾. Using ^{123}I -IMP and ^{99m}Tc -HMPAO several cases of viral encephalitis have been reported previously⁸⁻¹¹⁾. But studies of viral encephalitis estimated by ^{99m}Tc -ECD have rarely been reported. Hirayama et al reported¹²⁾ one case of respiratory syncytial virus encephalitis. Nagamachi et al reported³⁾ 6 cases of viral encephalitis estimated by ^{99m}Tc -ECD.

The use of SPECT in viral encephalitis has been controversial. Nagamachi et al reported³⁾ a case of HHV-6 encephalitis which showed hyperperfusion in the affected area (bilateral

frontal and left fronto-temporal lobes) on ^{99m}Tc -HMPAO SPECT examined 23 days after onset. The hyperperfusion phenomenon of increased rCBF which is revealed on the radionuclide brain SPECT is recognized in cases of viral encephalitis, especially in HSV encephalitis. Increased rCBF has been described in the ictal phase of focal epilepsy¹³⁾ and in the luxury perfusion phase of stroke¹⁴⁾, but in the report of Launes et al¹⁵⁾, the magnitude and duration of increased rCBF in these two conditions were considerably less than those seen in HSV encephalitis. Nara et al reported⁹⁾ a case of acute encephalitis which exhibited hyperperfusion. The neurologic outcome of that case was poor. According to Lee et al¹⁶⁾, in stroke or HSV encephalitis, hyperperfusion is believed to be induced by tissue acidosis from the end product of impaired cellular metabolism. Therefore, the demonstration of hyperperfusion indicates necrosis of brain tissue.

In contrast, Kao et al reported¹⁷⁾ that ^{99m}Tc -HMPAO brain SPECT in the acute phase in 17 of their 18 cases, including HSV, Epstein-Barr virus and Japanese B virus encephalitis, had increased rCBF in the initial brain SPECT scans. Follow-up brain SPECT showed that 12 of 17 cases had normal second brain SPECT and 5 cases had decreased rCBF. The group of patients with normal rCBF on the follow-up brain SPECT had a better clinical outcome (no neurologic defect) than those with decreased rCBF (learning disability or decreased intelligence). They concluded that ^{99m}Tc -HMPAO brain SPECT has a high diagnostic accuracy as well as good localization in children with viral encephalitis, and serial ^{99m}Tc -HMPAO brain SPECT should serve as a good guide for predicting the outcome in children with viral encephalitis. The decreased rCBF may suggest more severe damage to the brain secondary to viral encephalitis. This could explain the observation that patients with decreased rCBF had poor clinical outcomes.

Jarjour reported¹⁸⁾ that it is important to

emphasize that SPECT studies cannot quantify absolute values of brain perfusion. Only marked regional asymmetric findings will be seen. Global changes most likely will be missed.

In some of our cases initial brain SPECT could not detect increased rCBF but showed already decreased rCBF. Three reasons for these results are considered.

First, when SPECT study is done, the timing of the examination seems very important. If the SPECT was done in the acute phase of illness, it might have shown hyperperfusion in the affected area. Nagamachi et al reported³⁾ 1 case of influenzal virus encephalitis estimated by ^{99m}Tc -ECD brain SPECT. ^{99m}Tc -ECD brain SPECT obtained 3 days after onset revealed increased rCBF. Follow-up ^{99m}Tc -ECD brain SPECT showed decreased rCBF in the same area.

Second is what radio pharmaceutical is used. ^{99m}Tc -ECD does not show reperfusion hyperemia in the subacute phase of a stroke^{19, 20)}. Fazekas et al reported²¹⁾ that hypofixation of ^{99m}Tc -ECD leads to failure to detect the characteristic findings of temporal lobe hyperemia in acute herpes simplex encephalitis. ^{99m}Tc -ECD is hydrolyzed to polar metabolites by deesterification²²⁾. The decrease of ^{99m}Tc -ECD activity indicates the absence or reduction of this enzymatic process in the inflammatory lesion of encephalitis. ^{99m}Tc -ECD may be a better indicator of the extent of tissue damage and prognosis than the visualization of hyperemia^{20, 23)}.

Third, the toxicity of the relevant viruses is considered. Nagamachi et al reported³⁾ that MRI showed no remarkable abnormality in 51.4% of hypoperfused SPECT lesions of viral encephalitis. About 30% of hypoperfused areas returned to normal on follow-up SPECT. Maeda et al reported²⁴⁾ a case of influenza B virus encephalitis. Although MRI showed no remarkable abnormality, ^{99m}Tc -ECD SPECT revealed decreased rCBF. Follow-up ^{99m}Tc -ECD SPECT showed no focal decreased rCBF. The decreased rCBF revealed on the previous

SPECT disappeared and returned to normal. Fujii et al reported²⁵⁾ a case of influenzal encephalitis which revealed larger areas of decreased uptake on ¹²³I-IMP SPECT, although the patient has no apparent neurologic sequelae. They discussed that decreased uptake on brain SPECT indicates that neuronal function has been impaired and/or that the peripheral circulation is disturbed but not suggestive of widespread infarction or necrosis.

It is important to know the normal distribution of the cerebral perfusion tracers in the infants and younger children. Tokumaru et al reported²⁶⁾ that by age 3 months, the activity appeared in the frontal and temporal cortices but was still lower than that in the parietal and occipital cortices. At 8 months of age, the activity in the frontal and temporal cortices and basal ganglia was lower still, and by 2 years of age, the pattern of ¹²³I-IMP SPECT uptake resembled that of adults. Thus the time course of the changes in ¹²³I-IMP uptake in the developing brain as detected by SPECT is similar to that of myelination and most likely reflects an overall topologic maturational pattern of the brain. Therefore in some of our cases initial brain SPECT might show relatively hyperperfused rCBF in the bilateral frontal and temporal lobes in comparison to the normal infantile distribution of cerebral perfusion tracers.

CONCLUSION

^{99m}Tc-ECD brain SPECT is a useful examination for the diagnosis and follow up management in patients with the acute onset type of pediatric CNS diseases.

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