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CASE REPORT

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Dissociation of ^{99m}Tc-ECD and ^{99m}Tc-HMPAO distributions in herpes simplex encephalitis

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Abstract In herpes simplex encephalitis (HSE), the authors noted an evident dissociation between the ^{99m}Tc-ethyl cysteinate dimer (ECD) and ^{99m}Tc-d,l-hexamethyl-propyleneamine oxime (HMPAO) single photon emission computed tomographies (SPECTs). The patient was a 5-year-old boy with diffuse type of pontine glioma, which was treated with hyperfractionated radiotherapy. Two weeks after the completion of radiation therapy, a lesion suggesting that of HSE was noted in the right frontotemporal region on magnetic resonance images. ^{99m}Tc-HMPAO SPECT showed an increased accumulation of the tracer in this lesion. On the ^{99m}Tc-ECD dynamic SPECT, an exaggerated accumulation of the tracer was noted within 80 s of administration, followed by a rapid drop in the accumulation, resulting in a low accumulation in 10 min. It was assumed that this dissociation was due to the different mechanisms to trap HMPAO and ECD in the brain tissue.

Key words Herpes simplex encephalitis · Single photon emission computed tomography · ^{99m}Tc-ethyl cysteinate dimer · ^{99m}Tc-*d,l*-hexamethyl-propyleneamine oxime

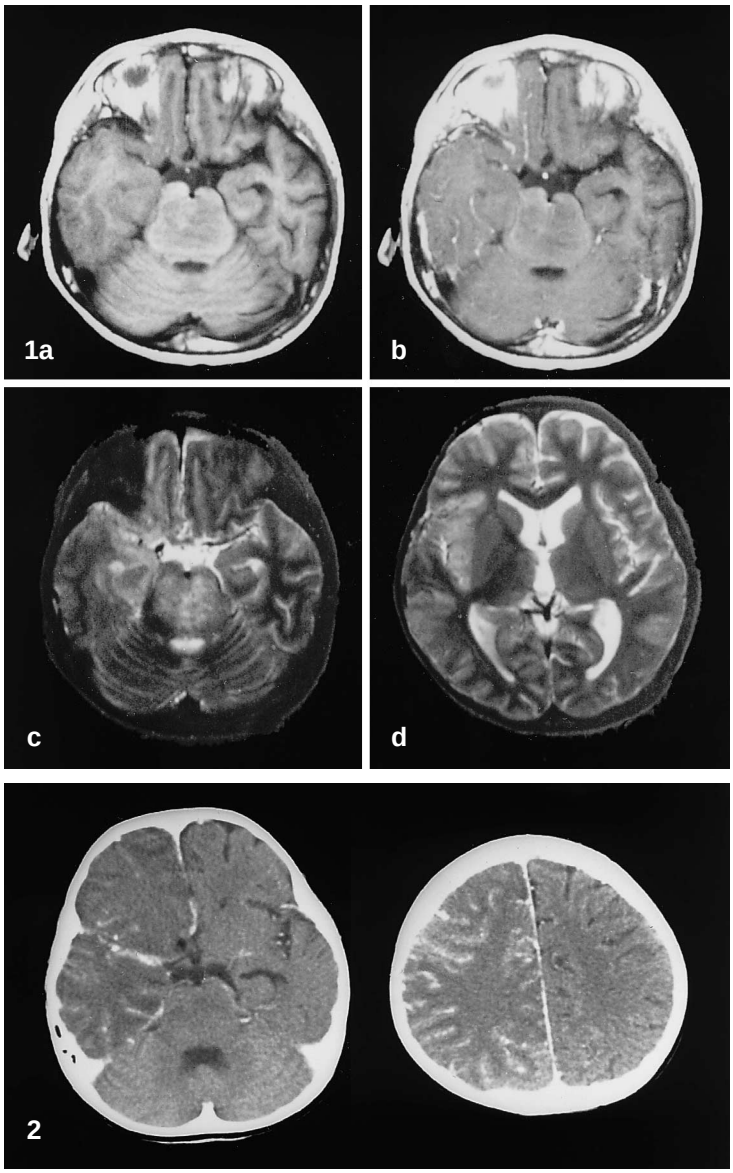
Introduction

With the recent progress in neuroimaging techniques and chemotherapy, early diagnosis and appropriate treatment have become possible for herpes simplex encephalitis (HSE), which have reduced the severity of the life-threatening sequelae [9, 16]. However, the clinical symptoms of this disease vary, and are often serious. The pathological features are mainly composed of hemorrhagic necrosis caused by type 1 herpes simplex virus. The disease is also called acute necrotic encephalitis and presents various pathological changes, such as diffuse edema, hemorrhage, cellular infiltration, and necrosis [2].

In the present case of HSE, which developed following radiotherapy of a pontine glioma, ^{99m}Tc-ethyl cysteinate dimer (ECD) dynamic single photon emission computed tomography (SPECT) and ^{99m}Tc-*d,l*-hexamethyl-propyleneamine oxime (HMPAO) SPECT were conducted. We recognized dissociation in the distributions of the tracers. The use of SPECT in HSE has been reported [1, 3, 5, 7, 8, 10, 11], but there have been no reports on the dissociation of intracerebral distributions of ^{99m}Tc-ECD and ^{99m}Tc-HMPAO in HSE.

Case report

A 5-year-old boy presented with a 2-month history of bilateral ocular abduction and unsteady gait. The patient was admitted to our hospital on 20 May 1994. A diagnosis of pontine glioma was made, based on the clinical course and the neuroradiological examinations. The treatment consisted of 40 mg of nimustine hydrochloride (given intravenously) and focal radiotherapy with 64 Gy in accelerated hyperfractionation. The patient developed fever on 11 July 1994, approximately 2 weeks after the completion of radiotherapy, with associated symptoms of a somnolescent tendency and partial seizures in the left face, neck and arm. Magnetic resonance imaging (MRI) showed swelling of the right temporal lobe and insular gyrus on



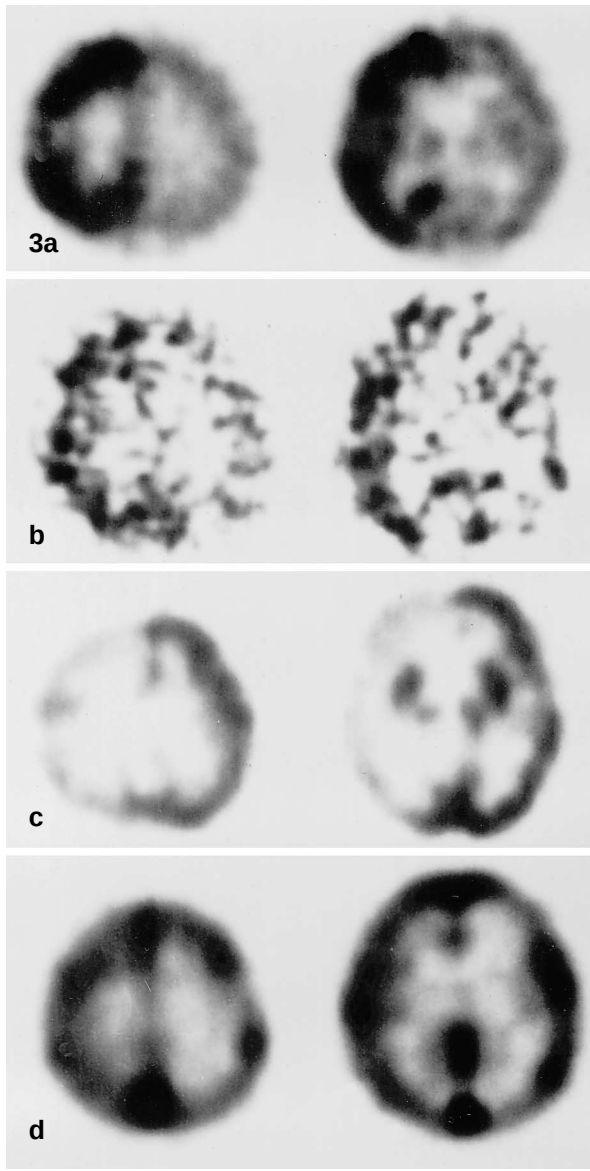


Fig. 1 **a** T1-weighted magnetic resonance imaging (MRI) at 4 days after the onset of symptoms shows swelling of the right temporal lobe. **b** Gadolinium diethylene triamine pentaacetic acid (Gd-DTPA) markedly intensifies the vasculature of the right hemisphere on T1-weighted MRI. **c,d** T2-weighted MRI shows high-signal areas in the right temporal lobe and insular gyrus

Fig. 2 Enhanced computed tomography (CT) at 10 days after the onset of encephalitis shows vascular enhancement and cerebral edema in the right hemisphere

Fig. 3 **a** Single photon emission computed tomography (SPECT) images of ^{99m}Tc-*d,l*-hexamethyl-propyleneamine oxime (HMPAO) at 2 weeks after the onset of herpes simplex encephalitis (HSE) exhibit an increased accumulation in the right frontal and temporal lobes. **b** Early SPECT images of ^{99m}Tc-ethyl cysteinate dimer (ECD) show an exaggerated accumulation of the tracer in the right cortex. **c** SPECT images 10 min after injection of ECD exhibit a reduction in accumulation in the right cortex. **d** SPECT images of ^{99m}Tc-labeled red blood cells show a slightly increased accumulation of the tracer over the entire right hemisphere

T1-weighted images (Fig. 1a), and high-signal areas of the cortex on T2-weighted images (Fig. 1c,d). Gadolinium diethylene triamine pentaacetic acid (Gd-DTPA) markedly intensified the vasculature of the right hemisphere on T1-weighted images (Fig. 1b). Electroencephalography exhibited periodic high-amplitude sharp waves in the right parietal region. HSE was suspected, and systemic administration of acyclovir was started. Vascular enhancement and cerebral edema affecting the entire right hemisphere were noted on the computed tomographic (CT) scan (Fig. 2). The ^{99m}Tc-HMPAO SPECT examined 2 weeks after onset of HSE exhibited an increased accumulation in the right frontal and temporal lobes (Fig. 3a). The ^{99m}Tc-ECD dynamic SPECT showed an exaggerated accumulation of the tracer in the lesion for 80 s following ^{99m}Tc-ECD administration (Fig. 3b), followed by a rapid reduction in accumulation, and resulted in a low accumulation after 10 min (Fig. 3c). The ^{99m}Tc-labeled red blood cell (RBC) SPECT showed a slightly increased accumulation of the tracer over the entire right hemisphere(Fig. 3d). The patient's consciousness level gradually improved, but motor aphasia and slight hemiparesis on the left side persisted. The serum anti-herpes simplex antibody titer increased to 512 times and the cere-

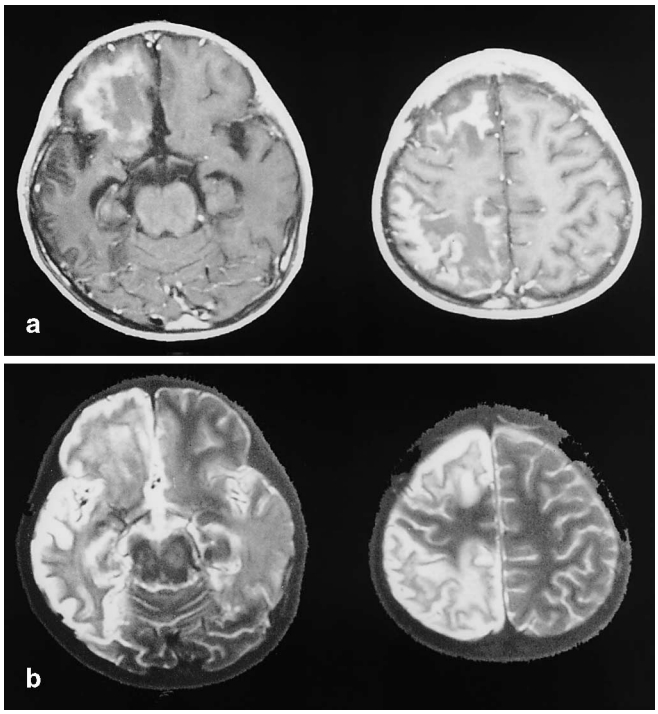


Fig. 4 **a** Gd-DTPA enhanced T1-weighted MRI at 1 month after the onset of HSE shows the enhanced areas in the right frontal and parietal lobes. **b** T2-weighted MRI shows high-signal areas in the right hemisphere and extension of the lesion to the left temporal lobe

brospinal fluid titer to 32 times normal, confirming the diagnosis of HSE. The second MRI 1 month after the onset of HSE revealed high signal intensity in the right frontal and parietal lobes and extension of the lesion to the left temporal lobe on T2-weighted images (Fig. 4). The patient was discharged on 14 September, while still suffering from motor aphasia and mild left hemiparesis.

Discussion

HSE is known for its varied and severe clinical symptoms and poor prognosis. The most appropriate chemotherapy for HSE made it possible to reduce mortality and morbidity because of the early diagnosis [16]. Furthermore, recent progress in neuroimaging techniques has provided new findings in HSE that cannot be detected by CT scan alone [9, 12]. SPECT can reveal an abnormal finding, such as increased blood flow in the foci, before the appearance of abnormality in the CT scan [5, 7, 8].

It has been said that in the acute stage of HSE, angiitis causes vascular dilatation, resulting in an increase in blood flow. An increase in blood flow is seen as an accumulation of ^{99m}Tc-HMPAO in the SPECT study, and an increase in cerebral blood volume is reflected in the ^{99m}Tc-RBC SPECT study. It has been reported that the increased blood flow detected by SPECT is maintained for 4–8 weeks following the onset of HSE [1, 3, 5, 7, 8, 10, 11]. Our ^{99m}Tc-HMPAO data in the present study showed good agreement with previous observations. However, ^{99m}Tc-ECD SPECT showed a high degree of accumulation in the foci immediately after tracer administration, which was rapidly reduced in 10 min, showing a pattern that differed from that of ^{99m}Tc-HMPAO. ECD readily passes the blood–brain barrier owing to its lipid solubility. It is postulated that the ester group of this tracer is hydrolyzed by the action of an intracerebral esterase, acquires a polarity, and is retained by the brain tissue [4, 14, 15]. The result of the present study indicates that the ECD enters the brain tissue initially but is washed out owing to the failure of the mechanism to trap this compound. Though it has been speculated that radiotherapy might have affected the results of SPECT studies, the area where SPECT showed abnormal findings was outside the area irradiated during radiotherapy, so that no effect of the radiotherapy on SPECT studies can be assumed.

It has been reported that ischemic brain tissue that was found to be necrotized showed a low accumulation of ^{99m}Tc-ECD in spite of a high accumulation of ^{99m}Tc-HMPAO after reperfusion [6, 13]. This phenomenon is thought to be due to a reduced viability of the cerebral tissue. On the assumption that the patient in the present case had undergone a similar process, his cerebral tissue must already have been affected by irreversible changes when ^{99m}Tc-ECD SPECT was conducted. We believe that ^{99m}Tc-ECD dynamic SPECT is not only effective in the early diagnosis but can also be useful in predicting the prognosis of HSE.

We believe that the observed difference in the pattern of the accumulation of ^{99m}Tc-HMPAO and ^{99m}Tc-ECD in herpes encephalitis indicates the difference in the mechanism by which the cerebral tissue traps these two tracers. The SPECT study accurately showed the state of vascular dilatation due to angiitis and the resultant exaggerated blood flow in the acute stage of HSE. It also seems that ^{99m}Tc-ECD SPECT could provide an accurate indication as to whether the tissue involvement in the acute stage of HSE is reversible.

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