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# Sequential MR imaging and SPECT studies in herpes simplex encephalitis with crossed cerebellar hyperperfusion

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We report a case of herpes simplex encephalitis in which sequential MR imaging and SPECT studies showed interesting findings. SPECT in the acute stage showed wide increased uptake in the left cerebral hemisphere, as well as increased uptake in the contralateral right cerebellar hemisphere. T1-weighted images in the subacute stage showed hyperintense signals along the cerebral cortices, but T2*-weighted gradient-echo images did not show any signal decrease caused by the magnetic susceptibility effect of hemoglobin degradation. Sequential SPECT studies in addition to MR imaging facilitate precise understanding of the pathophysiology of herpes simplex encephalitis.

**Key words:** MR imaging, SPECT, herpes simplex encephalitis

## INTRODUCTION

HERPES SIMPLEX ENCEPHALITIS (HSE) in adults is caused by the herpes simplex virus (HSV) type 1. Several reports have described the usefulness of MR imaging and single photon emission computed tomography (SPECT) in HSE.[1–3] The characteristic findings of MR imaging in HSE are the prolongation of the T1 and T2 relaxation times in the affected areas, which are usually the medial temporal lobes, inferior frontal lobes, and occasionally the insular cortices and cingulate gyri. Furthermore, increased uptake by the affected areas in SPECT images using $^{99m}$Tc-hexamethyl propyleneamine oxime ($^{99m}$Tc-HMPAO) in the acute stage is valuable for early diagnosis. However, few reports have compared sequential MR imaging and SPECT analyses in HSE.[3,4] We performed MR imaging and SPECT sequentially in our patient with unique results, namely, crossed cerebellar hyperperfusion in acute SPECT and cortical necrosis in subacute MR imaging.

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## CASE REPORT

A 69-year-old woman was admitted to our hospital with progressive conscious disturbance which had begun 6 days earlier. Before admission, she was generally healthy, although she had been undergoing treatment for Parkinson's disease for 5 years. On admission (acute stage), a plain computed tomography (CT) showed low attenuation adjacent to the left cingulate gyrus. Electroencephalography showed periodic lateralized epileptiform discharges over the left hemisphere. However, no seizure was observed clinically. At 7 days after onset, $^{99m}$Tc-HMPAO-SPECT showed wide increased uptake in the left frontal lobe, left temporal lobe, as well as increased uptake in the contralateral right cerebellar hemisphere (Fig. 1a–c). MR imaging was performed at 8 days after onset. On T2-weighted and fluid-attenuated inversion recovery (FLAIR) images, hyperintense signal lesions were observed in the bilateral cingulate gyri, insular cortices and left medial temporal lobe, while hypointense signal lesions were observed on T1-weighted images in the same areas. HSE was suspected, and systemic administration of acyclovir was started. The diagnosis of HSE was proved by intrathecal production of antibodies against HSV 17 days after onset. Acyclovir was effective, and her consciousness improved gradually, but short-term memory disturbance persisted to three months after onset.

At 21 days after onset (subacute stage), T1-weighted

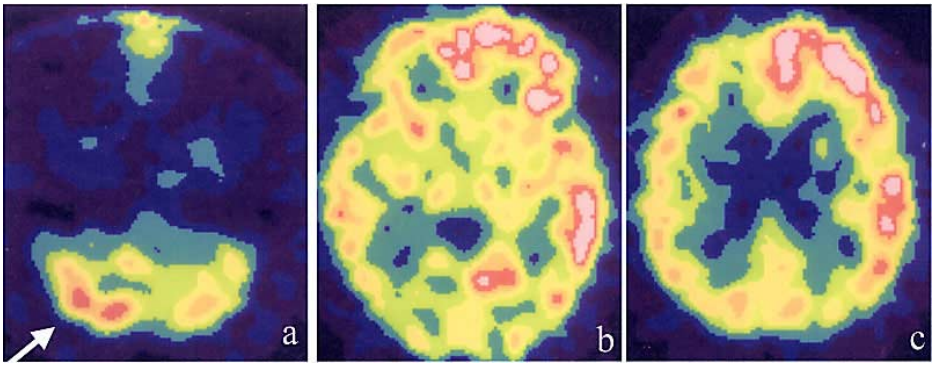


**Fig. 1** (a–c) SPECT images at 7 days after onset showed wide increased uptake in the mainly left frontal lobe, left insula and the right cerebellar hemisphere (*arrow*).

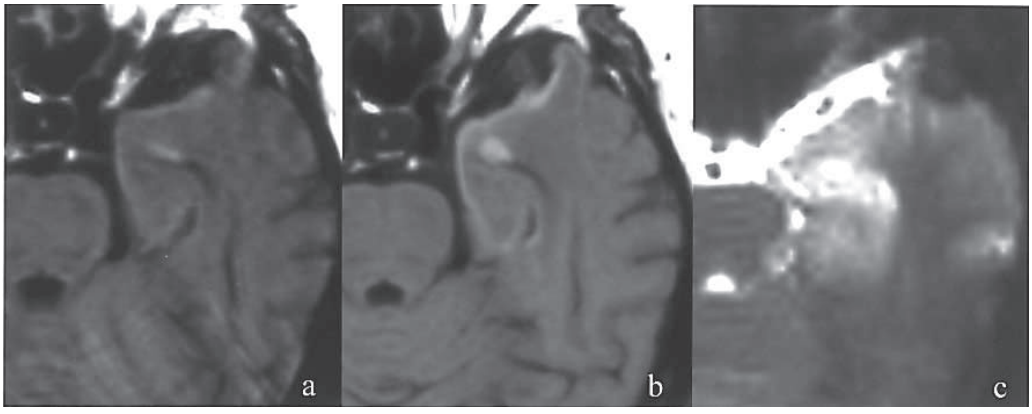


**Fig. 2** (a) Enhanced T1-weighted image at 21 days showed curvilinear enhancement along the cortices of left medial temporal lobe. (b) The enhancing areas on the enhanced T1-weighted images at 21 days well corresponded to the areas of the curvilinear hyperintense signals along the left medial temporal cortices observed on unenhanced T1-weighted images at 35 days. (c) T2*-weighted gradient-echo image demonstrated no signal decrease around the areas of curvilinear hyperintense signals along the cerebral cortices observed on unenhanced T1-weighted image.

images with gadolinium-diethylenetriamine-penta-acetic acid (Gd-DTPA) showed curvilinear enhancement along the cortices of the bilateral cingulate gyri, insula, and left medial temporal lobe (Fig. 2a). Hyperintense signals had not been observed on T1-weighted images by this stage. At 35 days after onset, FLAIR images clearly demonstrated the involvement of bilateral cingulate gyri, insular cortices, and left medial temporal lobe, and their underlying white matter (Fig. 3a–c). Unenhanced T1-weighted images showed curvilinear hyperintense signals along the cerebral cortices of the bilateral cingulate gyri, insula, and left medial temporal lobe (Fig. 2b). T2*-weighted images by echo-planar gradient-echo imaging were obtained at the same time in order to determine whether the hyperintense signals were the result of hemorrhage. T2*-weighted gradient-echo images showed no signal decrease caused by the magnetic susceptibility effect of hemoglobin degradation product (Fig. 2c). The areas of the curvilinear hyperintese signals along the cerebral cortices observed on unenhanced T1-weighted images well corresponded to the enhancing areas on enhanced T1-weighted images at 21 days after the onset (Fig. 2b). $^{99m}$Tc-HMPAO-SPECT at 36 days after onset showed markedly increased uptake in the left medial temporal lobe, bilateral cingulate gyri and bilateral insular cortices, which was in good agreement with the areas of abnormal intensity on MR imaging (Fig. 4d–f). Wide increased uptake in the left frontal lobe in acute SPECT had almost normalized by this time except for the cingulate gyrus.

Three months after onset (chronic stage), $^{99m}$Tc-HMPAO-SPECT showed decreased uptake in the same areas where the last SPECT had shown increased uptake (Fig. 5g–i). The hyperintense signals along the cortex on T1-weighted images remained unchanged even three months after onset. The hyperintense signals on FLAIR images spread over deep white matter, and mild atrophy of the cerebrum was observed.

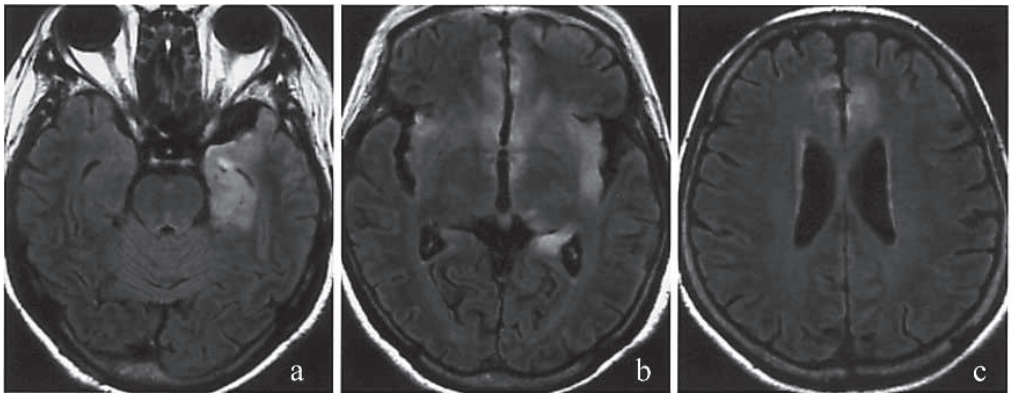


**Fig. 3** (a–c) FLAIR images at 35 days after onset showed hyperintense signals in bilateral cingulate gyri, insular cortices and left medial temporal lobe.

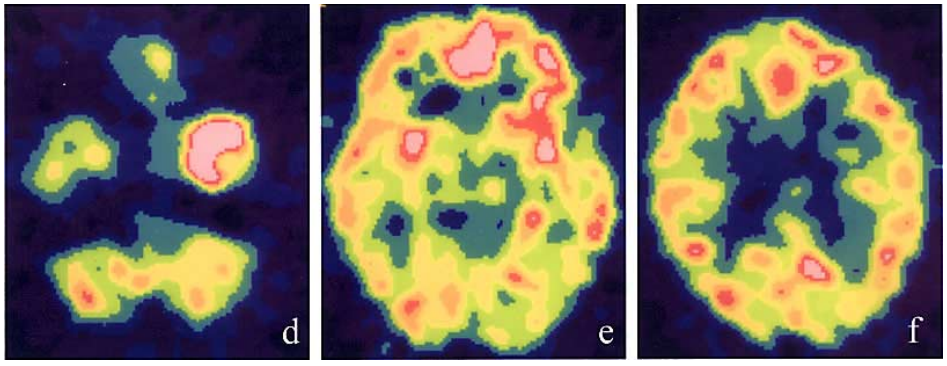


**Fig. 4** (d–f) SPECT images at 36 days after onset showed localized increased uptake in the left medial temporal lobe, left insular cortices, and cingulate gyri.

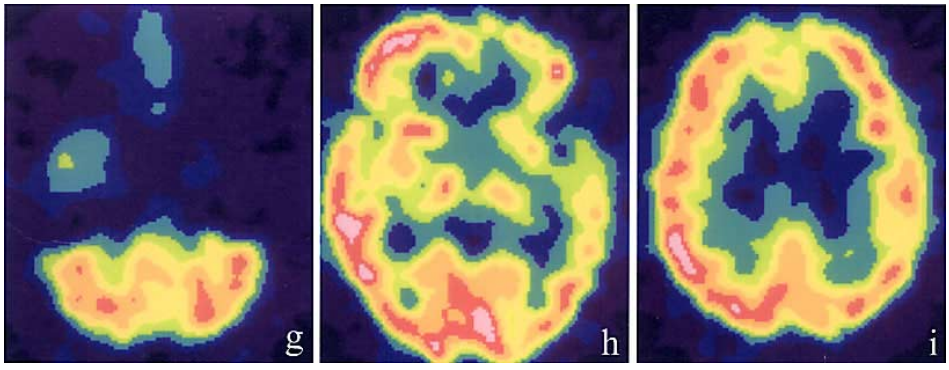


**Fig. 5** (g–i) SPECT images at three months after onset showed decreased uptake in the same areas where the second SPECT had shown increased uptake (Fig. 4).

## DISCUSSION

The neuropathological findings of HSE are hemorrhagic necrosis with loss of all neural elements, and lymphocytic infiltration of the brain and leptomeninges, and are generally localized to the temporal lobes, insular cortex, subfrontal area, and cingulate gyri.[5] The characteristic MR imaging appearance of HSE has been well documented.[1–3] However, few reports have compared sequential MR imaging and SPECT, and to our knowledge, there is only one report of curvilinear hyperintense signals along the cortex on unenhanced-T1-weighted images in HSE.[6] On SPECT, the mechanisms of increased uptake in the affected areas in HSE are unclear. Increased regional blood flow, activation of cellular redox systems, and firing of neurons in the early phase of inflammation in the

affected areas are believed to be responsible.[7]

In the acute stage, we found discrepant findings between MR imaging and SPECT, as well as between acute and subacute SPECT. MR imaging showed localized abnormal signals in the bilateral cingulate gyri, insular cortices and left medial temporal lobe. Acute SPECT showed wide increased uptake in the left cerebral hemisphere. Subacute SPECT showed localized increased uptake of the same lesions where MRI showed abnormal signals. We believe that the key finding to explain this phenomenon is increased uptake of the contralateral right cerebellar hemisphere. This phenomenon is called crossed cerebellar hyperperfusion, and has been reported in symptomatic epilepsy patients.[8–10] Crossed cerebellar hyperperfusion is thought to be the reverse of crossed cerebellar diaschisis, which is a consequence of functional disconnection between the cerebrum and contralateral cerebellar hemisphere through the cortico-ponto-cerebellar pathways. Although no ictal seizure was observed clinically, the normalized uptake in the left frontal lobe in the subacute stage could explain how the increased uptake in the left frontal lobe in the acute stage was caused by ictal seizure in addition to the acute inflammation by HSE. The regions of the decreased uptake in the chronic stage contained regions of both increased uptake in the acute stage and subacute stage. We thought that the reason for these decreased uptakes in the chronic stage was mainly brain damage due to HSE.

In the subacute stage, unenhanced T1-weighted images showed curvilinear hyperintense signals along the cerebral cortices of the bilateral cingulate gyri, insula, and left medial temporal lobe. The hyperintense signals associated with HSE on unenhanced T1-weighted images are usually thought to represent hemorrhage. However, these signals along the cortex were not evidence of hemorrhage as no signal decrease was observed on T2*-weighted gradient-echo images and the hyperintense signals remained unchanged to the chronic stage. Kinoshita et al. reported that a signal decrease on T2*-weighted gradient-echo images clearly represents the existence of a small hemorrhage.[11] Furthermore, hyperintense signals representative of hemorrhage should change in the chronic stage. The areas of hyperintense signals on T2-weighted and FLAIR images were in good agreement with the enhanced areas on enhanced T1-weighted images, which were performed two weeks prior to the appearance of the hyperintense signals. These findings are similar to those of cortical necrosis, which occurs as a consequence of oxygen or glucose depletion.[12,13] Cortical necrosis has also been reported in MELAS.[14] The reason for T1 shortening in cortical necrosis remains unclear. In our case, hemorrhage was not observed, and alternative explanations include calcification, deposition of lipid-containing macrophages, protein degradation, or the presence of free radical or cellular components from necrotic tissue.[15]

## CONCLUSION

Crossed cerebellar hyperperfusion was observed in acute SPECT, which is an important finding for increased understanding of acute HSE. Cortical necrosis was observed in subacute MR imaging, and thus cortical necrosis is present not only in conditions of energy depletion but also in infectious conditions such as HSE.

Sequential SPECT studies in addition to the MR imaging are very useful to understand the pathophysiology of HSE.

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