Technetium-99m-ECD SPECT Fails to Show Focal Hyperemia of Acute Herpes Encephalitis

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This is a case of herpetic simplex encephalitis (HSE) examined with Tc-ethyl cysteinate dimer (ECD) and 99mTc-hexamethyl propyleneamine oxime (HMPAO) SPECT. Static images obtained with 99mTc-ECD showed a reduced tracer uptake of the temporal lobe but focal hyperactivity using 99mTc-HMPAO. Dynamic images indicated regional increase of cerebral blood perfusion with both tracers. Technetium-99m-ECD had rapid washout from the inflamed tissue, while 99mTc-HMPAO had avid uptake. Hypofection of 99mTc-ECD leads to failure to detect the characteristic finding of temporal lobe hyperemia in acute HSE.

Key Words: herpes simplex encephalitis; technetium-99m-ethyl cysteinate dimer, technetium-99m-hexamethyl propyleneamine oxime; tracer uptake; SPECT


Technetium-99m-ethyl cysteinate dimer (99mTc-ECD) has been proposed as a safe and effective marker of regional cerebral perfusion. In normal controls and patients with chronic neurologic disorders, the distribution of ECD was shown to be linearly related to regional cerebral blood flow as measured by SPECT with 133Xe with only mild undersaturation of flow at the high end of the normal range (1). In comparison to 99mTc-hexamethyl propyleneamine oxime (99mTc-HMPAO), the distribution of both tracers appeared initially to be similar with the advantage that 99mTc-ECD had greater radiochemical stability and more rapid washout from extracerebral tissues (2,3). Subsequently, it is reported that 99mTc-ECD does not show reperfusion hyperemia in the subacute phase of a stroke (4,5). We present a case in which 99mTc-ECD fails to show hyperemia associated with focal cerebral inflammation. Focal hyperactivity of the temporal lobe has been considered a hallmark finding of acute herpes simplex encephalitis (HSE) on static brain SPECT (6-9) using 99mTc-HMPAO.

CASE REPORT

A 73-year-old woman with a headache and subfebrile temperature had become confused over the course of a few days. Neurologic findings consisted of short episodes of aphasia and a mild right hemiparesis. There was a past history of two ischemic strokes, and CT of the head showed leukoaraiosis with old lacunar lesions of the basal ganglia bilaterally. A diagnosis of cerebral vascular disease aggravated by some infectious process was considered. Further deterioration with psychotic symptoms and somnolence prompted...
a lumbar puncture (97 lymphoplasmoid cells; total protein 87 mg/dl) and MRI of the brain that showed a mass lesion in the left mediotemporal lobe (Fig. 1). Brain SPECT images were obtained to evaluate a diagnosis of herpes simplex encephalitis (HSE).

Studies were performed with the Tomomatic 564 (Medimatic, Copenhagen, Denmark) consisting of an array of four rotating banks each containing 16 detectors. Dynamic data acquisition at intervals of 30 sec after bolus injection was performed with a low-resolution collimator yielding five contiguous slices. Static images were obtained as two subsequent sets of three interleaved axial slices with a collimation yielding an in-plane resolution of 7.3 mm and an average slice thickness of 9.76 mm at FWHM.

Static SPECT with $^{99m}$Tc-ECD showed a focal area of hypoactivity corresponding to the temporal lobe lesion shown on MRI (Fig. 2A). Dynamic data collection, however, showed an increased tracer concentration in the left temporal lobe region immediately after injection that suggested hyperperfusion. Another SPECT study with $^{99m}$Tc-HMPAO 1 day later confirmed increased tracer delivery to the left temporal lobe and showed a corresponding area of marked hyperactivity on static images (Fig. 2B). Technetium-99m-ECD SPECT was repeated 2 days later with similar findings to the initial study. Figure 3 compares the course of tracer uptake between the $^{99m}$Tc-ECD and $^{99m}$Tc-HMPAO studies in the inflamed temporal lobe and the corresponding region of interest on the contralateral side. Hyperactivity of the involved side is clearly noted in all three studies 1 min after tracer injection. Thereafter, both $^{99m}$Tc-ECD studies show rapid decrease in tracer activity in the inflamed region with a reduction below the counting rates of the normal tissue. In contrast, $^{99m}$Tc-HMPAO is retained in the involved area without washout.

After $^{99m}$Tc-HMPAO SPECT, the patient was put on acyclovir. Polymerase chain-reaction studies confirmed a herpes simplex virus infection. MRI signal abnormalities in the temporal lobe regressed and the patient made a good recovery except for residual cognitive deficits.

**DISCUSSION**

SPECT has been advocated as a sensitive and rather specific tool for the early diagnosis of HSE (6–9). Using $^{99m}$Tc-HMPAO or $^{123}$I-iodoamphetamine, increased tracer uptake was noted in the acute phase of the disease even before any morphologic abnormalities had become visible or were matching the lesions seen on CT or MRI. Consistent with neuropathologic observations, hyperactivity typically involves the mesiotemporal region and may spread to the adjacent basal ganglia. Based on these data, the regional hypoactivity seen in our

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**FIGURE 1.** Spin-echo T2-weighted brain MRI (TR 2500 msec/TE 90 msec) shows a large area of hyperintensity with a mild mass effect in the left temporal lobe.

**FIGURE 2.** (A) Static $^{99m}$Tc-ECD SPECT shows focal hypoactivity corresponding to MRI lesion. (B) The same region appears markedly hyperactive on $^{99m}$Tc-HMPAO SPECT image 1 day later.

**FIGURE 3.** Time course of tracer activities in the inflamed temporal lobe region compared to the corresponding contralateral side.
The patient on $^{99m}$Tc-ECD SPECT was thought to exclude HSE. The expected hyperactivity of the temporal lobe was seen when the patient was reevaluated with $^{99m}$Tc-HMPAO.

Technetium-$^{99m}$ECD and $^{99m}$Tc-HMPAO are both lipophilic agents that penetrate the normal blood-brain barrier. Both are retained by conversion of the lipophilic molecule into hydrophilic compounds. Technetium-$^{99m}$ECD is hydrolized to polar metabolites by deesterification (10). The decrease of $^{99m}$Tc-ECD activity on dynamic SPECT of our patient indicates the absence or reduction of this enzymatic process in the inflammatory lesion of HSE. The resulting lack of retention causes the pathologic area to appear hypoactive despite the initial presence of hyperperfusion.

Similar observations have been made in the subacute phase of an ischemic stroke where $^{99m}$Tc-ECD was noted to miss reflow hyperemia (4,5). In such a setting, this need not constitute a significant disadvantage as the failure to achieve the enzymatic transformation of $^{99m}$Tc-ECD may be a better indicator of the extent of tissue damage and prognosis than the visualization of hyperemia (5,11). The inability to detect hyperemia with $^{99m}$Tc-ECD in the presence of cellular dysfunction must be viewed differently when considering HSE. Routinely performed dynamic data collection can reduce this problem, but these images have limited resolution and may not be available.

CONCLUSION

Dynamic acquisition following the administration of $^{99m}$Tc-HMPAO, $^{11}$I-IMP or $^{99m}$Tc-ECD demonstrates regional hyperemia of the temporal lobe in HSE. Technetium-$^{99m}$ECD, however, washes out. Consequently, hyperemia characteristic of HSE is not detected in clinical SPECT images acquired 2 min later.

REFERENCES


Reproducibility of the Distribution of Carbon-11-SCH 23390, a Dopamine D$_1$ Receptor Tracer, in Normal Subjects

Grace L.-Y. Chan, James E. Holden, A. Jon Stoessl, Doris J. Doudet, Yue Wang, Teresa Dobko, K. Scott Morrison, Joe M. Huser, Carolyn English, Barbara Legg, Michael Schulzer, Donald B. Calne and Thomas J. Ruth

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The reproducibility of $[^{11}]$C]SCH 23390 in PET was studied in 10 normal human subjects. Methods: The scan-to-scan variation of several measures used in PET data analysis, including the radioactivity ratio, plasma-input Logan total distribution volume (DV), plasma-input Logan DV ratio (DVR), tissue-input Logan B$_{max}$/K$_{D}$ values, was determined. Results: There were significant correlations among the radioactivity ratio, plasma-input DVR and tissue-input B$_{max}$/K$_{D}$. With the cerebellum as the reference region, these three measures also had high reliability (86%–95%), high between-subject s.d. (7.7%–11.3%) and small within-subject s.d. (2.3%–3.6%), indicating that they are comparable and useful measures for the assessment of dopamine D$_1$ receptor binding. Conclusion: The radioactivity ratio and the tissue-input B$_{max}$/K$_{D}$ may be preferred methods for the evaluation of dopamine D$_1$ receptor binding because these two methods do not require arterial blood sampling and metabolite analysis. Our results show that cerebellum is a reliable reference region for SCH 23390. When the Logan plasma-input function method is used in data analysis for SCH 23390, DVRs rather than total DV values should be used because of the poor reliability of the DV values and their lack of correlation with other measures. Carbon-11-SCH 23390 is thus a reliable and reproducible ligand for the study of dopamine D$_1$ receptor binding by PET.

Key Words: carbon-11-SCH 23390; PET imaging


The tracer $[^{11}]$C]SCH 23390 is widely used as a ligand to study dopamine D$_1$ receptor function using PET (1–4). The binding of SCH 23390 to dopamine D$_1$ receptors, as determined by PET, can be assessed by several methods. The simplest method uses the ratio of activity in regions of high specific binding (such as striatum) to those of nonspecific binding (such as cerebellum). Another method measures the distribution volume (DV) of the ligand in specific and nonspecific regions of