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Assessment of Regional Cerebral BloodFlow (rCBF) in Ischemic Stroke Using Tc−99m HMPAO SPECT

−Comparison with CT and MR Findings−

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To assess the regional cerebral blood flow (rCBF) in ischemic stroke, we analyzed the findings of single photon emission computed tomography(SPECT) using technetium−99m hexamethyl propyleneamine oxime (Tc−99m HMPAO).
The SPECT images revealed abnormal areas of decreased perfusion in 29 out of 31 subjects (93.5%), which represented a higher detection rate than those for CT and MR (89.5%, respectively). Also, the areas of decreased perfusion were frequently larger than the lesions on CT and MR. Areas of decreased perfusion remote from the CT/MR lesions were found in 10 patients, including 8 with crossed cerebellar diaschisis (CCD). Thus, studies of rCBF by Tc−99m HMPAO SPECT can be useful in the assessment of ischemic stroke.

Key Words : *Regional cerebral blood flow, Tc−99m HMPAO SPECT, Ischemic stroke, Diaschisis, CT, MR.*

INTRODUCTION

Although computed tomography (CT) represents a useful tool for detecting hemorrhagic stroke, the diagnosis of ischemic stroke by CT is often difficult at the early stage. The recently developed technique of magnetic resonance (MR) imaging has, to some extent, resolved this problem. Positron emission tomography (PET) can graphically demonstrate changes in the regional cerebral physiology in stroke even in patients whose CT studies reveal no abnormality (Phelps et al., 1982). Despite the fact that PET studies permit noninvasive measurements of the regional cerebral blood flow, glucose metabolism, and oxygen utilization in man, their high cost and specialized instrumentation do not permit their use in routine patient management.

On the other hand, single photon emission computed tomography (SPECT) affords an image of the cerebral blood flow free of high technology and cost. Assemssments of the regional blood flow in ischemic stroke may have an impact on the clinical management of patients with stroke. Tc−99m labeled hexamethyl propyleneamine oxime (Tc−99m HMPAO) has recently been introduced as a promising new lipophilic agent with a high first-pass extraction fraction and cerebral uptake propo-

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rtional to the cerebral blow flow (Holmes et al., 1985). We therefore attempted to analyze the changes in regional cerebral blood flow using Tc—99m HMPAO SPECT in patients with ischemic stroke. Comparisons were made with the MR and CT findings in order to confirm the usefulness of SPECT in evaluating ischemic stroke.

MATERIALS AND METHODS

Patients

The series included 31 patients with CT/MR-proven ischemic stroke or clinically diagnosed transient ischemic attack (TIA) (19 males and 12 females), aged 17 to 83 years (mean age 55.6± 18.2 years), who were all examined by Tc—99m HMPAO scan with SPECT. CT and/or MR imagings were performed on all patients, and the time intervals between the SPECT and CT/MR were less than a couple of weeks (mean interval between SPECT and CT=6.4 days ; that between SPECT and MR=8.1 days). All 3 imaging studies were performed on 7 patients.

Imaging procedures

Immediately after labeling the freeze-dried HMPAO with Tc—99m, 15~20 mCi labeled material was injected intravenously into the patient. After positioning the head so that each slice would be parallel to the orbitomeatal line, scanning was performed using a rotating gamma camera (ROTA ZLC 75, Siemens) with a low-energy high-resolution collimator. Sixty projections were obtained at a 6 degree step rotation collecting 3.6 million to 4 million counts in total. This took about 30 minutes. The collected data were processed with a CDA microdelta computer, and 6.27㎜-thick cross-sectional images (64X64 matrix) were reconstructed by the filtered backprojection method using Butterworth filter superimposed on a ramp filter. Each of the reconstructed slices was corrected for tissue absorption employing Chang's method (Chang, 1978). Pixels were regarded as abnormal if their count decreased by more than 10% compared to that of the homologous ones in the contralateral hemisphere (Leonard et al., 1986 ; Nakano et al., 1989 ; Moon et al., 1989).

CT was performed with a GE 8800 or GE 9800 total body scanner. Scans were considered abnormal if they revealed areas of decreased attenuation, mass effect, or abnormal gyral enhancement with contrast media. T1-weighted, T2-weighted, and proton density MR images were obtained using a 2.0 T superconducting type scanner (SPECTRO-20000, Goldstar). Abnormal high signal intensity areas relevant to the clinical findings were defined as lesions on the T2-weighted images.

Comparisons of lesion size

The slice of maximum abnormality within the area of clinical interest was selected for each imaging modality.

In SPECT, the region of interest (ROI) was defined by the collection of pixels whose counts were less than 90% of that of the homologous ones in the contralateral hemisphere. The % area of decreased perfusion was obtained as fllows :

$$\% \text{ area of decreased perfusion} = \frac{\text{number of pixels in ROI}}{\text{number of pixels in slice}} \times 100(\%)$$

In the case of CT and MR imaging, the areas of the lesion were obtained by tracing the boundaries of the lesion using the electronic cursor of a RAS—1000 computer system. Then, dividing by the whole brain area on the slice, the % area of the lesion was calculated. The % area of decreased perfusion on SPECT was compared with the % area of lesion on CT and/or MR in each of the patients. If the difference was greater than 5% of the whole brain area of the slice, it was considered significant.

RESULTS

Areas of decreased perfusion on SPECT were detected in 29 out of the 31 subjects(93.5%) (Table 1). The two patients who showed no abnorma-

Table 1. Frequency of abnormal findings in ischemic stroke

	Normal	Abnormal (detection rate)
SPECT	2*	29 (93.5%)
CT	2**	17 (89.5%)
MR	2***	17 (89.5%)

* Lacune
** Brainstem infarct (1) and diffuse cortical atrophy (1)
*** TIA

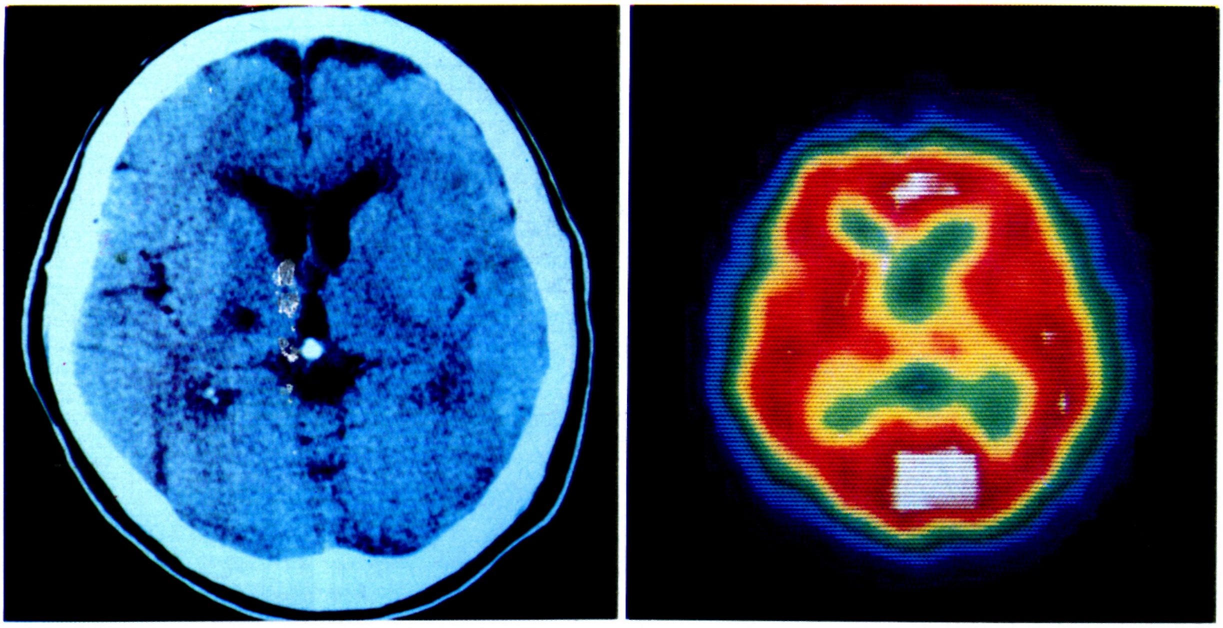

Fig. 1. CT (left) revealed a lacune in the right thalamus, whereas a SPECT image with atteuation correction (right) showed no abnormality.

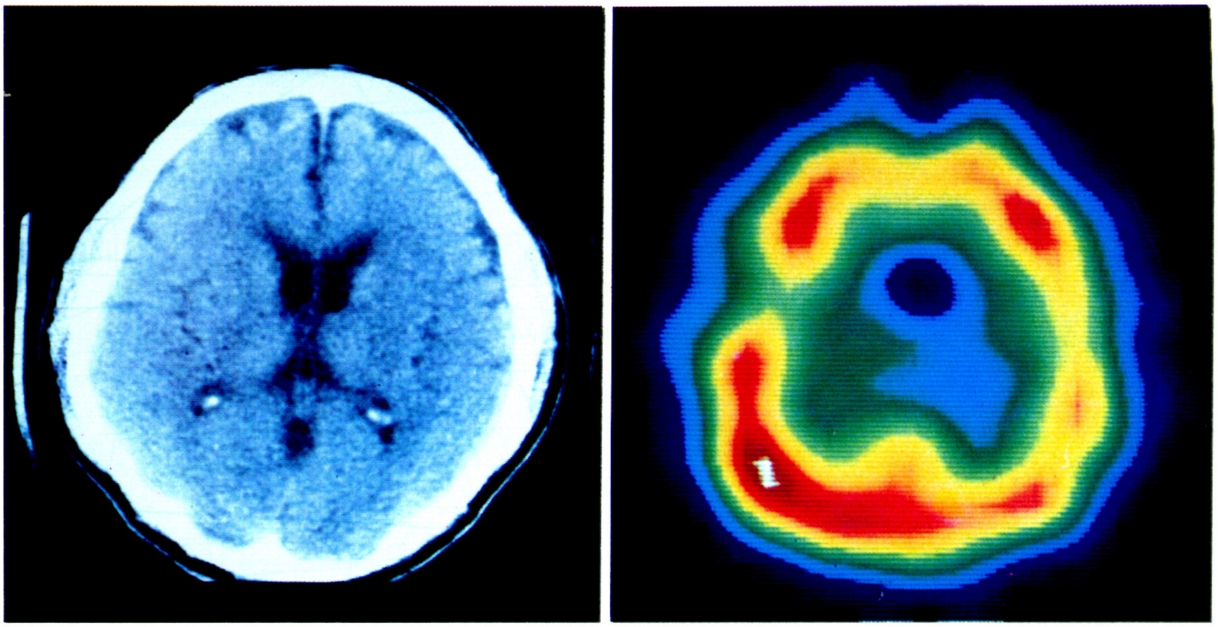

Fig. 2. The patient, with hypertension for 10 years, had right hemisensory deficit and a weak right leg. CT (left) revealed only diffuse cortical atrophy, but bilateral cortical areas of decreased perfusion (worse on the left side) were observed on SPECT (right). His MR image demonstrated multiple small high-signal intensity lesions, while severe atherosclerotic stenosis of both internal carotid arteries was found on cerebral angiography.

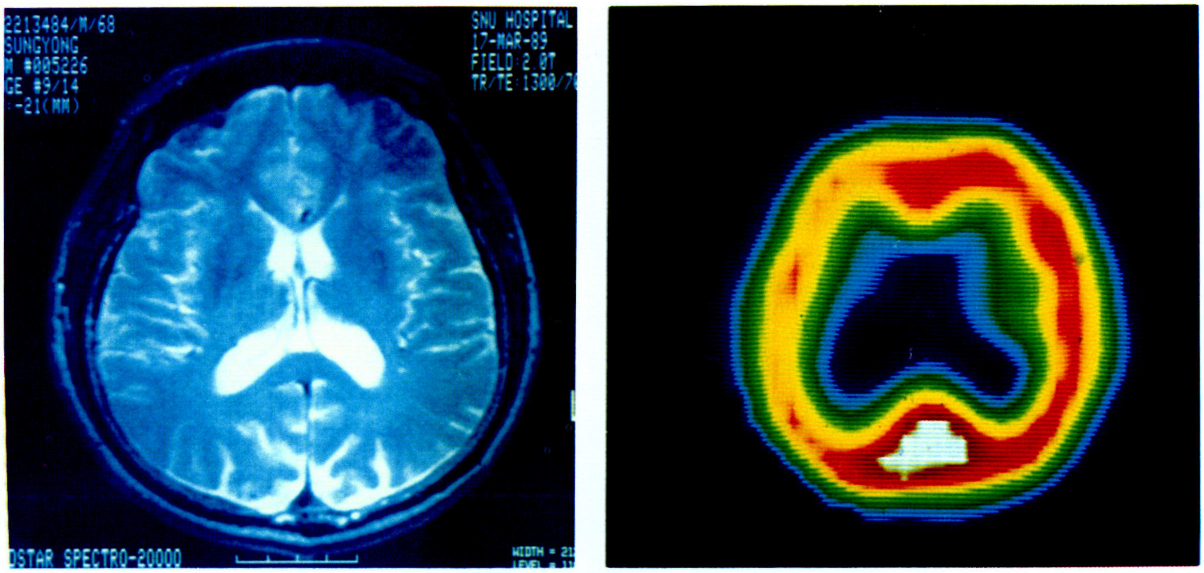

Fig. 3. Patient with TIA. Although his MR (left) showed no abnormality, a SPECT image (right) revealed decreased perfusion in the right frontoparietal cortex.

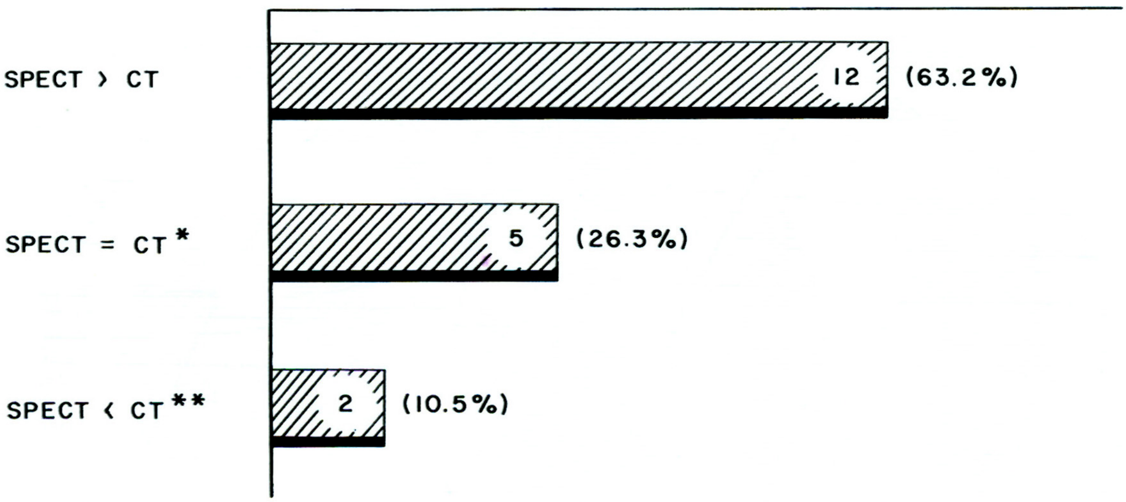

Fig. 4. Comparison of SPECT with CT for size of abnormality in ischemic stroke. The difference in lesion size was less than 5% of the whole brain area of the slice (*). Lacunes were observed on CT (**).

lity in perfusion had lacunes on CT (Fig 1). CT scans revealed abnormal findings in the area of interest in 17 out of 19 patients (89.5%). Of the remaining 2 patients, one showed only diffuse cortical atrophy. The other was presumed to have brainstem infarction, but this was not evident on his CT scan. MR depicted lesions which were consistent with their symptoms, and diffuse atherosclerotic changes were found on cerebral angiography. SPECT showed diffuse, bilateral cortical and subco-

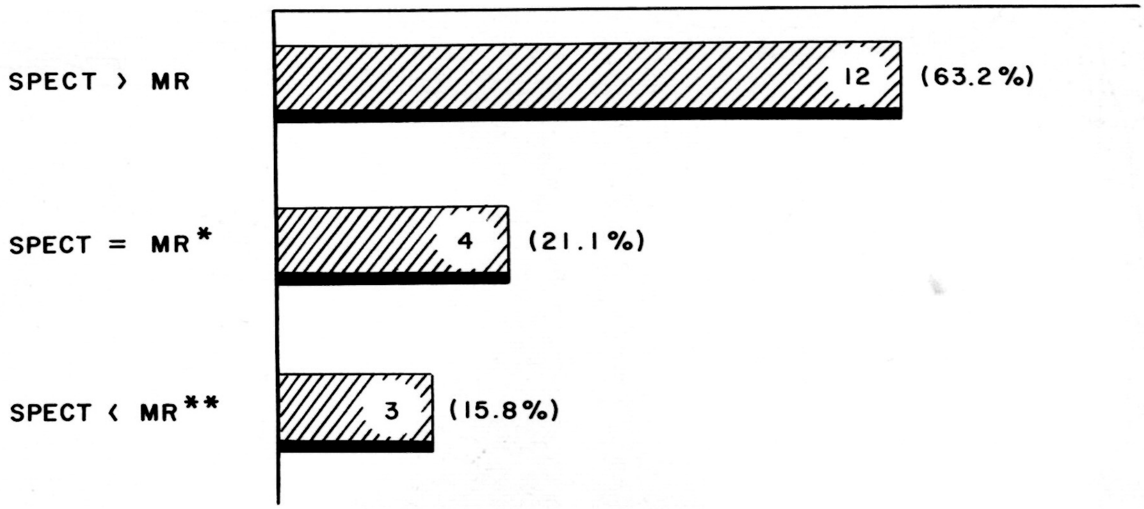

Fig. 5. Comparison of SPECT with MR for size of abnormality in ischemic stroke. The difference in lesion size was less than 5% of the whole brain area of the slice (*). Two lacunes and 1 small cortical infarct were observed on MR (**).

rtical areas of decreased perfusion (Fig. 2). Also, in 17 out of 19 patients (89.5%), the MR images revealed abnormal findings consistent with the clinical manifestations. The 2 patients whose MR findings were normal had TIA, and their SPECT scans disclosed decreased perfusion areas (Fig. 3).

The size of the lesion on CT or MR was compared with that of the decreased perfusion area on SPECT (Fig. 4, 5). Of the 19 patients who underwent both SPECT and CT, 12 (63.2%) showed a larger area of decreased perfusion on SPECT than the CT lesion, and 5 (26.3%) had equal-sized abnormalities in both images. The 2 patients with thalamic lacunes on CT revealed normal SPECT scans. In comparison with MR, SPECT showed a larger abnormal area in 12 out of 19 patients (63.2 %). Four (21.1%) exhibited a SPECT abnormality which was equal in size to the lesion on MR. Smaller perfusion deficit areas than the MR lesion were found in the other 3 patients, with 2 lacunes and 1 small cortical infarct.

Decreased perfusion areas remote from the CT/MR lesions were observed in 10 patients (32.3 %). Of these, 2 disclosed abnormalities in the supratentorial regions, and 8 had crossed cerebellar diaschisis (CCD) (Fig. 6).

DISCUSSION

Assessment of the regional cerebral hemodynamics in cross sections of the head has recently been achieved with the emergence of PET and SPECT (Yamamoto et al., 1977 ; Baron et al., 1981 ; Devous et al., 1986). While PET permits measurement of the brain metabolism as well as the regional cerebral blood flow, its high cost precludes widespread clinical usage. SPECT equipment is currently available, and measurements of the regional cerebral blood flow are feasible without a cyclotron.

Xenon-133, an inert and freely diffusable radioactive gas, was first introduced successfully by Lassen et al.(1981) and has been used for clinical evaluations of the flow to the brain, in particular prior to the development of PET. The merits of Xe-133 SPECT include its absolute quantitation (expressed in ml/min/100g), capability for short-interval repeat studies due to rapid washout over a period of a few minutes, and favorable radiation dosimetry. Nevertheless, it does have some drawbacks. The spatial resolution is poor (spherical volumes of less than 40mℓ are not accurately measured), and adequate measurements are not possible with ordinary imaging devices (Ell et al., 1987).

I-123 labeled amines such as I-123-N,N,N'-trimethyl-N'-(2-hydroxy-3-methyl-5-iodo-benzyl)-1, 3-propane diamine (HIPDM) and I-123-n-isopropyl-p-iodoamphetamine (IMP) have been used for single photon studies for some years to map the regional cerebral blood flow in man (Hill et al., 1982, 1984 ; Holman et al., 1984). These lipid-soluble radiopharmaceuticals are taken up by the brain cells in proportion to the blood flow, reside stationarily in the brain

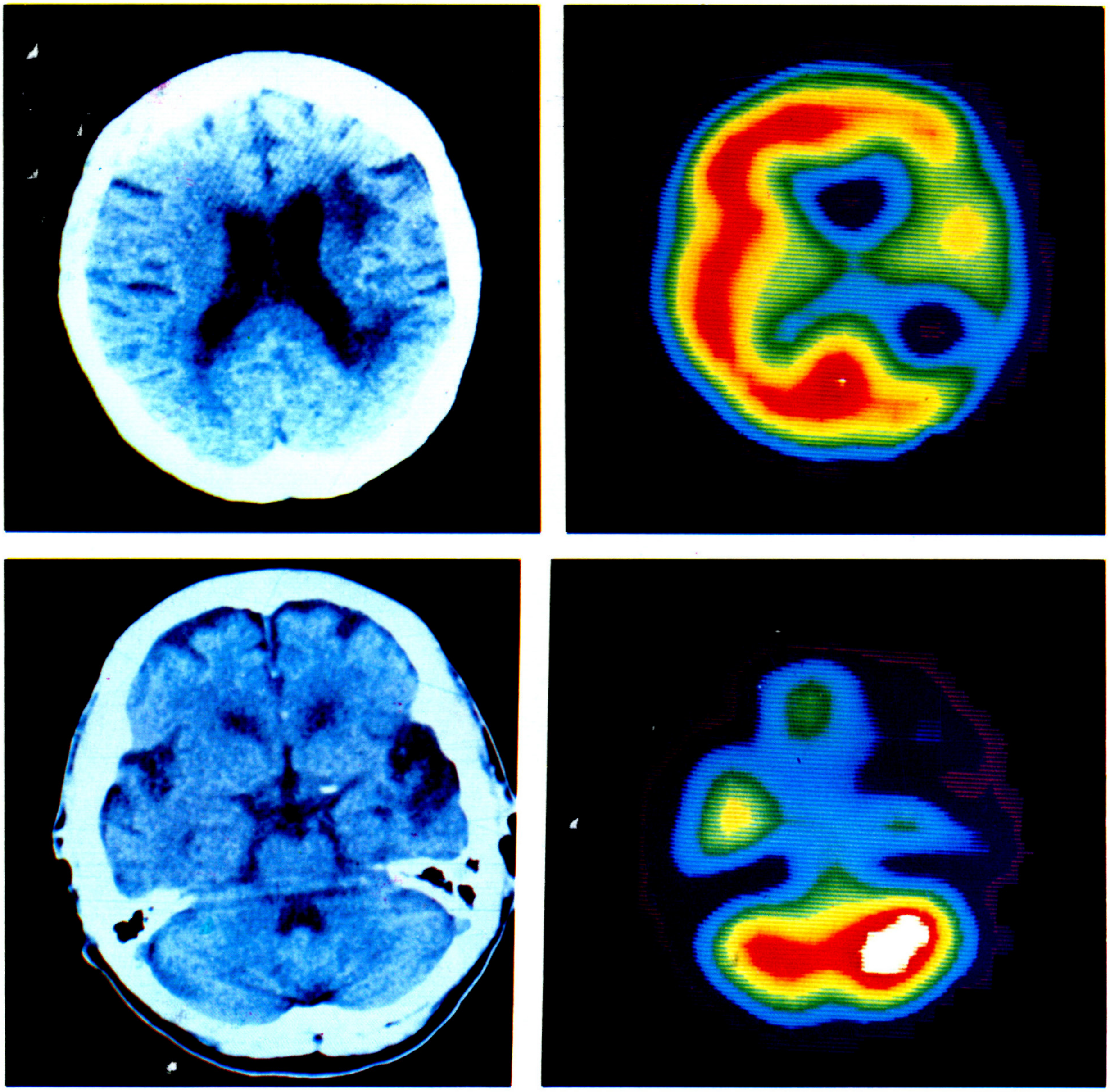

Fig. 6. Crossed cerebellar diaschisis. Cerebral infarction in the left cerebral hemisphere was seen on CT (upper left), while the SPECT image had a larger area of decreased perfusion in the same region (upper right). A decreased uptake in the contralateral cerebellar hemisphere (lower right) was evident despite no cerebellar lesion on CT (lower left).

long enough for acquisition, and permit the use of existing, conventional instrumentation. The major disadvantages of I−123 labeled compounds, however, are thier cost and limited availability with a relatively short half-life (13 hours). Moreover, contamination by I−124 increases the radiation dose to the patient and degrades the image because of the increased scattering of photons, making the counting statistics worse (Polak et al., 1984).

Tc−99m is obtainable from a highly convenient generator, which permits a daily availability throughout the week. Tc−99m HMPAO, which has been developed recently, represents a promising new Tc−99m labeled lipophilic agent with a high first-pass extraction fraction and deposition in the brain proportional to the cerebral blood flow and remains constant throughout a certain period of time (Holmes et al., 1985 ; Leonard et al., 1986 ; Podreka et al., 1987).

A significant improvement in image quality has been achieved by utilizing either a conventional gamma camera or more specialized multidetection instrumentation (Costa et al., 1987). The detection and visualization of metabolic or CBF changes in the brain are among the principal items of interest to neurologists. This is especially true in the case of stroke. CT and MR imaging techniques serve as good tools for detecting areas of the brain with morphoanatomical changes, but the changes in blood flow in certain areas cannot be assessed only by these methods. It is not unusual to find negative CT scans in patients with TIA, who display abnormalities in their cerebral angiography. Neuronal activity and metabolism in the brain are closely related to the status of the regional perfusion (Powers and Raichle, 1985), and the changes in the former reflect the symptoms and signs in the clinical neurology. If assessments of the regional CBF in ischemic stroke are useful for detecting the disease, planning the management, and predicting the prognosis, single photon studies can be considered beneficial for clinical practice.

We therefore examined the changes in regional CBF using Tc−99m HMPAO SPECT and compared the SPECT results with those for CT and MR imaging. Based on the right-to-left ratio in both hemispheres, a depression of pixel activity of more than 10% has been previously considered by us to be abnormal (Moon et al., 1989) as in other reports (Leonard et al., 1986 ; Perani et al., 1988). In the present investigation, abnormal perfusion areas on SPECT were found in 93.5% of the patients with ischemic stroke, which represented a higher detection rate than that for CT or MR. Other authors have reported similar results ranging from 85.9% to 100%, indicating the superiority of SPECT images to CT scans (Lee et al., 1982 ; Hill et al., 1984 ; Brott et al., 1986 ; Bartolini et al., 1988). Seiderer et al. (1989) found that MR imaging (100%) was superior in the detection of pathologic areas to IMP SPECT (91%). However, they did not include patients with TIA. In the present study, 2 TIA patients had normal MR images, despite abnormal perfusion areas on SPECT. In the report of Bartolini et al. (1988), abnormal decreased perfusion areas on HMPAO SPECT were noted in 28% of the TIA patients with normal CT findings. Two of our patients who had lacunes on CT displayed no abnormality on SPECT. Similar results are also described in the report of Hill et al. (1984). We consider these findings to be attributable to the lower resolution of SPECT scans compared to that of CT.

In about two-thirds of the patients, SPECT demonstrated greater sized lesions than CT or MR. Such a situation was also suggested by other researchers (Hill et al., 1984 ; Brott et al., 1986 ; Seiderer et al., 1989). This discrepancy in size may be due to the penumbra supplied by a very limited blood flow which is sufficient to keep the tissue alive but is insufficient to allow normal activity (Astrup et al., 1981). Since SPECT scans are thought to visualize not only the area of ischemia but also the area of decreased function due to ischemia, it is not surprising that the lesion size should be the largest among the various imaging modalities.

The term "diaschisis" (from the Greek meaning "split or shocked throughout") was employed originally by von Monakow (1914) and has been described as the cerebral counterpart of spinal shock. Nowadays this term is employed to represent a decreased functional capacity in one brain region caused by damage to, or disconnection from, a distant but functionally related brain region. With the advent of the PET scan, a matched decrease in CBF and metabolism beyond the infarct boundaries has been reported (Heiss et al., 1983). SPECT images also reveal regions of decreased perfusion outside the infarct area (Brott et al., 1986 ; Johansson et al., 1988 ; Raynaud et al., 1989). Several kinds of diaschisis have been described : transcallosal, crossed cerebellar, intracortical, thalamocortical, and thalamostriatal (Feeney and Baron, 1986). Using SPECT, Brott et al. (1986) and Johansson et al. (1988) found a decreased uptake in areas other than the ischemic region. Crossed cerebellar atrophy has been observed and recently described in 4 autopsied cases (Chung, 1985). Crossed cerebellar hypometabolism contralateral to supratentorial infarction was first reported by Baron et al. (1980) using PET and was interpreted as a functional cerebellar depression caused by interruption of the cortico-ponto-cerebellar pathway at the supratentorial level. Crossed cerebellar diaschisis (CCD), however, does not always exist, and the reasons for this have been proposed to be the difference in location and extent of the primary lesion as well as the time of investigation after the ischemic insult.

In conclusion, SPECT imaging with Tc−99m HMPAO appears to be useful for assessing the brain perfusion in patients with ischemic stroke. It may also be possible to evaluate the effects of medical and surgical therapies in ischemic stroke. Further refinements of SPECT instrumentation should provide more sophisticated maps of the regional blood flow, thereby assisting clinicians in better management of stroke patients.

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