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Correlation of Magnetic Resonance Imaging Findings with Hexamethylpropyleneamine Oxime Brain Single Photon Emission Computed Tomography in Ischemic Stroke Patients in the Subacute Stage

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Purpose: To evaluate the correlation between magnetic resonance imaging (MRI) findings and ^{99m}Tc-hexamethylpropyleneamine oxime (HMPAO) brain single photon emission computed tomography (SPECT) during the subacute stage in ischemic stroke patients.

Material and Methods: The T1 and T2-weighted images and brain SPECT findings of 84 patients (mean age 60.69 ± 12.47 years) with subacute cerebral ischemia during the period 1998–2004 were reviewed. All HMPAO SPECT and MRI studies were performed between 3 and 7 days (mean time delay 4.76 ± 1.29 days) after the onset of stroke symptoms.

Results: An ischemic lesion was seen both in T1 and T2-weighted images with perfusion defects above 60% (severe defect) according to count/pixel data of the lesion in HMPAO SPECT studies in 30 (90.9%) of 33 patients. Otherwise, the ischemic lesion was seen only on T2-weighted images with perfusion defects between 30% and 60% (moderate defect) in HMPAO SPECT studies in 25 (89.3%) of 28 patients. In 20 (87%) of 23 patients who had perfusion defects below 30% (mild defect) on HMPAO SPECT, only non-specific findings such as cerebral atrophy and/or periventricular ischemic-gliotic lesions could be seen in MRI. The difference between these ratios was statistically significant ($P < 0.01$).

Conclusion: Brain ^{99m}Tc-HMPAO SPECT findings indicate good correlation with MRI findings. When the ischemic lesions could be seen in both T1 and T2-weighted images, the patients frequently had severe perfusion defects. When only seen in T2-weighted images, the perfusion defect was moderate. When only non-specific findings were revealed by MRI, only mild perfusion defects were found by SPECT.

Key words: Brain SPECT; cerebral ischemia; MRI; stroke

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Stroke is one of the main causes of mortality in the world and the leading cause of severe deficits in most survivers (6). The clinical diagnosis of acute stroke may be difficult and so the role of neuroimaging continues to increase and gain importance in this setting. In recent years, cerebral blood flow and functional imaging methods have often been used in ischemic stroke patients because changes in regional cerebral blood flow can be observed earlier than structural changes seen on computed tomography (CT) and magnetic resonance imaging (MRI) (10, 11). Among these are xenon (Xe) CT, brain perfusion single photon emission computed tomography (SPECT), positron emission tomography (PET), diffusion and perfusion MRI methods. Of these, PET provides useful information about the cerebral metabolism, but is not yet commonly used because of high cost. Diffusion and perfusion MRI are new introductions to clinical use. Some side effects of Xe CT have been reported, although brain

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perfusion SPECT and MRI are non-invasive and can be used in most hospitals (1, 4, 5, 8, 9, 12, 17, 18, 19).

The difference in lesion size between the images of SPECT and CT/MRI due to ischemic penumbra during the acute stage disappears at the late stage (usually after 72 h). Reports have been written about the prognosis of acute stroke with SPECT (1, 2, 5, 13, 14) depending on this difference. There have been very few reports on the role of brain SPECT in determining the prognosis in the late period (3, 15). There is no difference in the size of the lesions after 3 days between CT/MRI and brain perfusion SPECT images, but SPECT can additionally show the severity of the lesions by evaluating the degree of hypoperfusion (1, 5, 6). The aim of this study was therefore to disclose whether findings by MRI bore any relationship to the degree of loss of hypoperfusion evaluated by ^{99m}Tc-hexamethylpropyleneamine oxime (HMPAO) SPECT following the acute period.

Material and Methods

Ninety-three patients suffering from ischemic stroke admitted to the Department of Neurosurgery and Neurology between 1998 and 2004 were evaluated with ^{99m}Tc-HMPAO SPECT and standard MRI. CT was performed in all patients within 24 h. Patients who had stroke symptoms but no ischemic lesions on the CT study due to a previous cerebrovascular accident were included, while patients who had hemorrhagic lesions were excluded. Because FLAIR imaging had been used only since 2003 at our MR unit, FLAIR images were not evaluated. Nine patients were excluded because the radiological studies had poor image quality either for technical reasons or lack of patient cooperation. The study population therefore consisted of 84 patients (49 M, 35 F) with a mean age of 60.69 ± 12.47 years (age range 34 to 81 years); 45 had right and 39 had left hemiparesia or hemiplegia. The study was performed 3 to 7 days (mean time delay 4.76 ± 1.29 days) after the onset of stroke symptoms. None of the patients was given any thrombolytic agent. All patients with neurological deficits were included in a rehabilitation program. Approval of the ethics committee was not considered necessary, as all examinations were part of our routine examination program. No interventions were made on any patient.

HMPAO SPECT protocol

Sufficient ^{99m}Tc pertechnetate in 3–5 ml serum physiological solution was injected into the Ceretec (Medi-Physics, Amersham Healthcare, Arlington Heights, Ill., USA) vial kit. The mixture was shaken vigoriously for about 30 s. Approximately 20 mCurie ^{99m}Tc-HMPAO was administered intravenously to all patients after 5 min. Within 60 min, high-resolution SPECT images were acquired using one head gamma camera (Picker PRISM 1500; Picker International, Cleveland Heights, Oh., USA) with a low-energy, high-resolution, parallel-hole collimator. A full 360-degree rotation was acquired (60 views, each for 30 s) with a matrix of 128×128. Transverse sections tilted along the orbitomeatal line were reconstructed using the routine filtered back-projection algorithm with an attenuation correction. Subsequently, approximately 20–25 transverse sections obtaining the whole-brain were reconstructed using the ramp filter. All transverse, sagittal and coronal sections were taken at 6.5 mm thickness.

HMPAO SPECT studies were evaluated visually and semi-quantitatively with a color scale according to uptake ratios (Odyssey Fx 380 brain reconstruction software). In cerebral SPECT images, count/pixel intensity from zero to 100, in slices of 10%, were quantitatively graded in different colors according to the color scale bend. More than 60% hypoperfusion was stated as severe perfusion loss, between 30% and 60% as moderate hypoperfusion, and hypoperfusion below 30% as mild. Whole areas of perfusion defects were averaged.

MRI Protocol

Cranial MR imaging was performed on a 1.5T scanner (Picker EDGE; Picker International). The MRI protocol included sagittal T1 (TR=416 ms, TE=16 ms, NEX=1, FOV=23 cm, matrix size=160×256), axial T1 (TR=580 ms, TE=10 ms, NEX=1, FOV=22 cm, matrix size=160×256), and axial T2 fast spin echo (FSE) (TR=5200 ms, TE=96 ms, NEX=1, FOV=22 cm, matrix size=256×144).

Patients in whom cerebral ischemia was found were divided into three groups, i.e. lesions found on both T1 and T2-weighted images, lesions seen only on T2-weighted images, and finally periventricular non-specific ischemic-gliotic lesions. The images were analysed by a specialist in neuroradiology.

Reliability between perfusion defects and findings by MRI was evaluated using the kappa test, and $P < 0.01$ was considered to be statistically significant.

Results

Thirty-three patients had severe perfusion defects according to count/pixel data of the lesions in HMPAO SPECT studies. In 30 of these patients (90.9%), an ischemic lesion was clearly seen on both T1 and T2-weighted images. Twenty-eight patients had moderate perfusion defects in HMPAO SPECT studies, and in 25 (89.3%) of them the ischemic lesion was seen only on T2-weighted images (Figs. 1 and 2). In 23 patients with mild perfusion defects only on HMPAO SPECT studies, only non-specific findings such as cerebral atrophy and/or periventricular ischemic-gliotic lesions were found in 20 (87%) (Table 1). These differences were statistically significant ($P<0.01$).

Discussion

Stroke is a heterogeneous syndrome caused by multiple mechanisms, but all result in some disruption of cerebral blood flow (CBF) and subsequent tissue damage. Despite well-developed collateral circulation, there are regions of the brain that are more vulnerable to abnormal perfusion pressures (22). The earliest changes in neurons occur as soon as just 20 min after complete ischemia, resulting in swollen, disorganized mitochondria and increased intracellular water. All of these mechanisms result in a cytotoxic edema that can be clearly seen on diffusion-weighted imaging (DWI). Macroscopically, visible infarcts are seen as areas of brain "softening" with loss of border between white and gray matter and focal swelling with effacement of the gyri. This swelling, due to intracellular cytotoxic edema, usually reaches a maximum at between 24 and 48 h. The reparative and resorptive mechanisms start at 24–48 h, beginning at the periphery of the infarct and proceeding by gliosis, encephalomalacic cycts, shrunken gyri, enlarged sulci and adjacent dilatation of CSF-containing spaces. This final pathologic state of infarctions is reached by 2–4 weeks (21).

The earliest MR findings are vascular flow-related abnormalities that can be detected within minutes of symptom onset. Other early MR findings include morphologic changes (particularly brain swelling on T1-weighted images). These anatomic changes may precede the development of increased signal on T2-weighted sequences (24). Parenchymal contrast enhancement and edema that appear hypointense to cortex on T1-weighted and hyperintense on T2-weighted images begin to diminish within 1 to 3 days after stroke (7). This is why SPECT and MRI were performed between 3 and 7 days after the onset of stroke symptoms. Signal change due to vasogenic edema or gliosis is often better seen on T2-weighted images. Signal change on T1-weighted images is less apparent because of the limited signal contrast between the ischemic tissue and the surrounding normal tissue (20).

A large ischemic penumbra obtained with the combination of brain perfusion SPECT and diffusion MRI performed in the first 24 h is a messenger of infarct development in the first week and is correlated with the change in the neurologic status of the patients (12). These differences between anatomic and functional images in the early state, due to ischemic penumbra, generally disappear after 72 h (2, 5, 16). Also the perfusion level (obtained by proportioning of count/pixel ratio in the lesion area to the non-lesion area) in HMPAO SPECT studies shows significant correlation with clinical status after 1 month in that 62% of patients with a lack of perfusion on HMPAO SPECT images in the first or second week showed a poor prognosis (1). HARTMANN (9) showed a close correlation between the severity of the clinical findings and the decrease in rCBF. Although the correlation of diffusion and/or perfusion MRI with HMPAO SPECT has been studied previously, so far no study has been done to estimate correlation between standard MRI and HMPAO SPECT findings at the subacute stage.

HMPAO SPECT is of no more value in the diagnosis of cerebral ischemia than radiological examinations, because the sensitivity of HMPAO SPECT decreases markedly in lacunar or small subcortical infarcts or when spontaneous recanalization develops (23). Radiological and radionuclide imaging methods should therefore be performed together in the diagnosis of cerebral ischemia. In our study, we found that MRI showed a good correlation with the perfusion defects disclosed by HMPAO SPECT. Lesions with severe perfusion defects were seen on both T1 and T2-weighted images in 90.9% of the patients, while lesions with moderate perfusion defects was seen on T2-weighted images in only 89.3%.

Our study has several limitations. It is time-consuming to perform MRI and SPECT, especially if the patient is a candidate for thrombolysis. However, in our study the severity of ischemia was assessed with conventional MRI in the subacute and not in the acute stage. Another limitation is that the MRI examinations may be of poor quality due to motion artifacts resulting from the long examination time and lack of patient cooperation. This was observed in nine patients in our study. MRI may

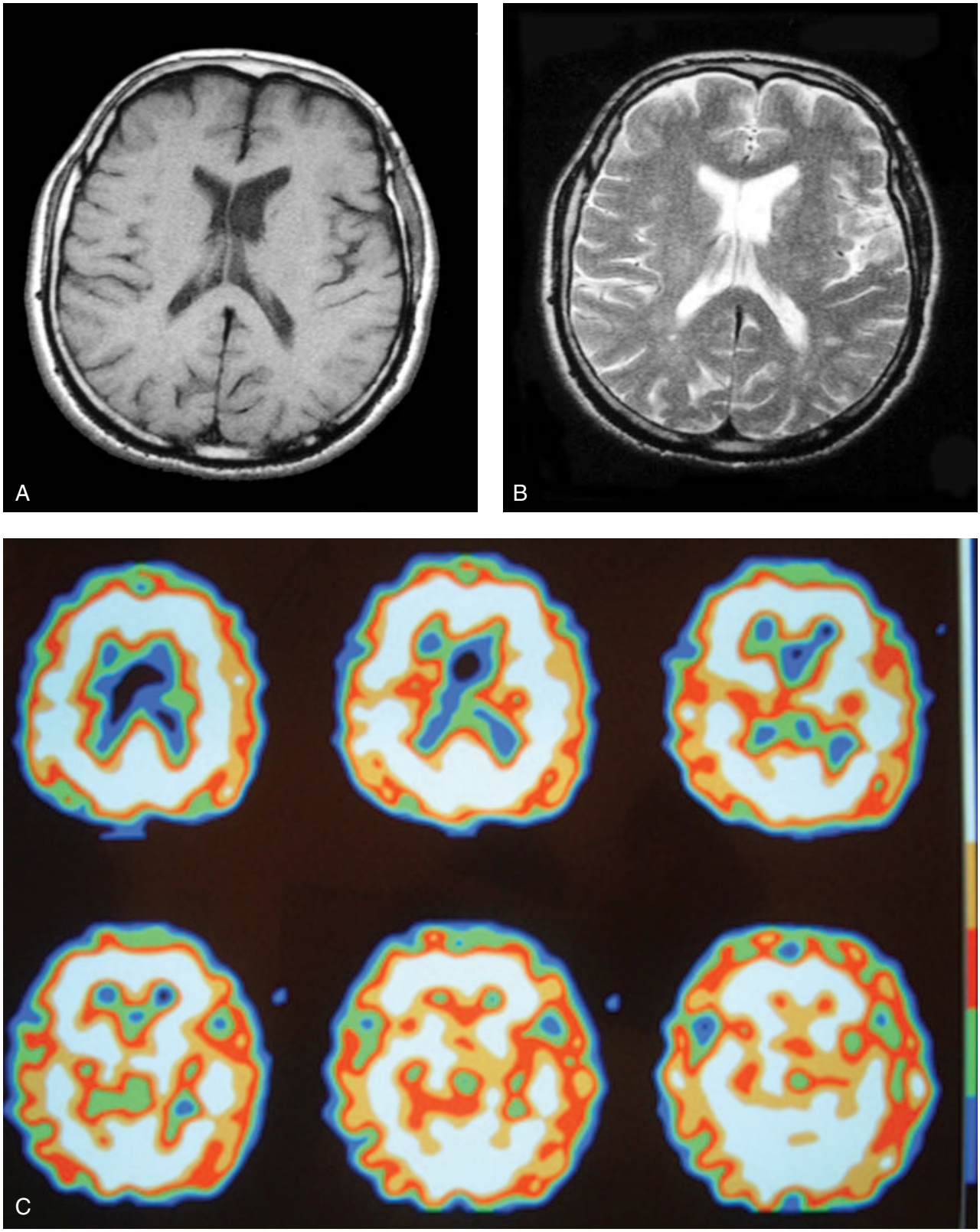

Fig. 1. Moderate perfusion defect. A. No signal abnormalities can be seen on the T1-weighted MR image. B. On the T2-weighted image, a hyperintense lesion can be seen clearly in the insular region. C. Axial HMPAO brain SPECT images show moderate hypoperfusion in the insular region of the left hemisphere.

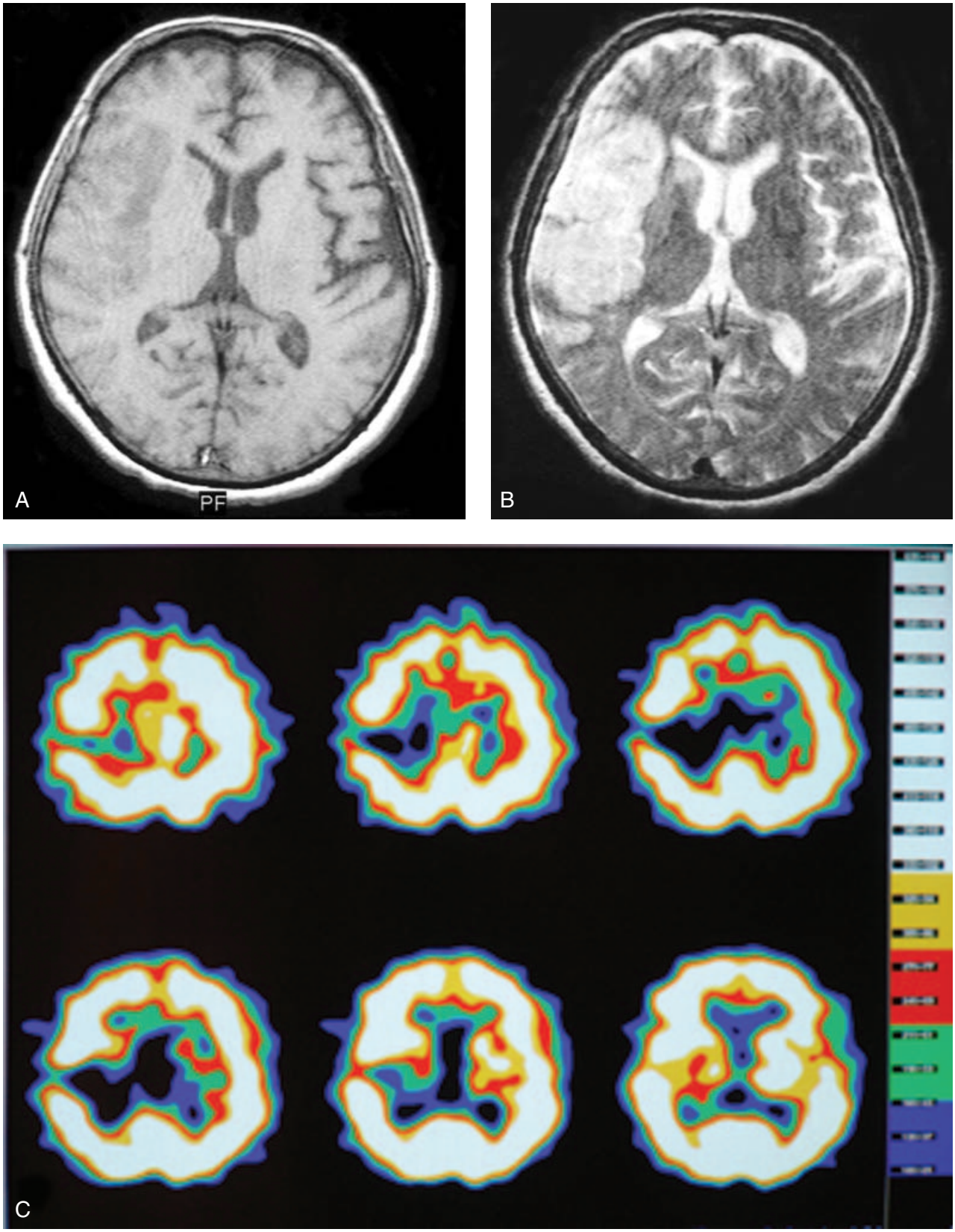

Fig. 2. Severe perfusion defect. Axial T1-weighted (A) and T2-weighted (B) MR scans show the typical wedge-shaped infarct. Lesions can be seen clearly in both the T1 and T2-weighted images. C. Axial HMPAO brain SPECT images show a severe hypoperfusion in the parietal region of the right hemisphere.

Table 1. Relation between the level of perfusion defect and radiologic correspondence.

		Lesions		
In SPECT, perfusion defect	No. of patients	In T1 and T2-weighted images	In only T2-weighted images	In T2-weighted images, periventricular non-specific lesions
Severe (above 60%)	33	30 (90.9%)	3	–
Moderate (between 30% and 60%)	28	–	25 (89.3%)	3
Mild (below 30%)	23	–	3	20 (87.0%)
Total	84			

have a future role in estimating the reversibility of ischemic lesions, but that will definitely not be based on conventional T1 and T2-weighted sequences, but merely on diffusion and perfusion studies.

In conclusion, there is a close correlation between the severity of perfusion defects seen by HMPAO SPECT and MRI findings, because 91% of severe ischemic lesions can be seen on both T1 and T2-weighted images, and 89% of the moderate perfusion defects can be seen on T2-weighted images. If the perfusion defects are mild, only non-specific findings are disclosed by standard MRI sequences. Therefore, standard MRI may have a role in evaluating the severity of perfusion defects in the subacute stage of stroke if modalities such as SPECT, diffusion and perfusion MRI are not available.

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