CONCLUSION

Semiquantitative analysis of FDG-PET scans in childhood epileptic encephalopathies adds clinically useful information to that obtained from visual inspection. Detection of focal abnormalities is improved when visual findings are combined with calculation of asymmetry indices, while semiquantitative analysis using ratios of uptake relative to a common reference may reveal bilateral and global metabolic defects not apparent on visual inspection.

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Hyperventilation Technetium-99m-HMPAO Brain SPECT in Moyamoya Disease to Assess Risk of Natural Childbirth

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We report a pregnant 19-yr-old patient with moyamoya disease who had undergone bilateral superficial temporal artery to middle cerebral artery anastomosis and encephalomyosynangiosis at 8 yr with an uneventful postoperative course and who desired natural delivery after becoming pregnant at 18 yr. We determined her cerebral vascular reserve since natural delivery can result in decreased cerebral blood flow during labor. Technetium-99m-HMPAO brain SPECT, with hyperventilation challenge, was performed to assess cerebral vascular reserve since the stress of hyperventilation was thought likely to rehearse that of labor. The brain SPECT images, obtained using 333 MBq ^{99m}Tc-HMPAO, revealed maintenance of cerebral vascular reserve. In addition, whole-body images including the 27-wk-old fetus were obtained. These images demonstrated accumulation in the fetal liver. Natural delivery was, thus, considered indicated for this patient, who subsequently delivered a healthy baby girl. Technetium-99m-HMPAO brain SPECT with hyperventilation challenge was useful for estimating cerebral vascular reserve and for determining whether natural delivery was indicated for this patient with moyamoya disease.

Key Words: hyperventilation challenge; cerebral vascular reserve; labor stress; technetium-99m-HMPAO; moyamoya disease

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Moyamoya disease is a chronically progressive cerebrovascular occlusive disease affecting the brain. The age distribution of patients includes two characteristic peaks, one in childhood and the other in adulthood (*1*). In the pediatric group, the initial

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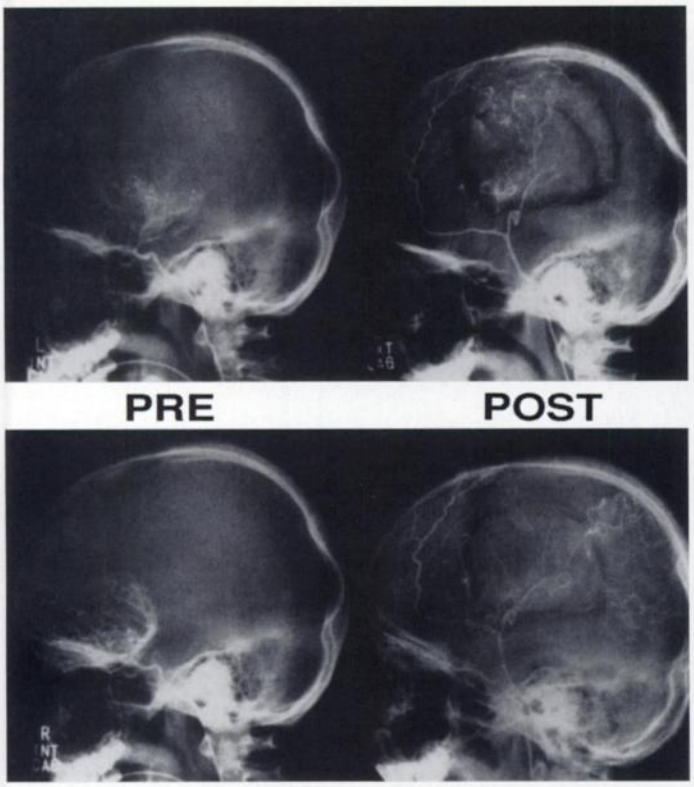

FIGURE 1. (Left) Preoperative carotid artery angiography reveals moyamoya vessels. (Right) Postoperative carotid artery angiography reveals patency of STA-MCA anastomosis.

symptoms are usually those of cerebral ischemia. In recent years, revascularization surgery has been reported to be useful for patients with moyamoya disease (*2,3*), but long-term follow-up of results of this surgery has been insufficient (*4*). When the possibility exists that patients with moyamoya disease are pregnant, it is important to assess cerebral vascular reserve since stress during labor can result in decreased cerebral blood flow.

We report a patient with moyamoya disease who underwent bilateral superficial temporal artery to middle cerebral artery anastomosis (STA-MCA) and encephalomyosynangiosis (EMS) at 8 yr. Her postoperative course was uneventful, and at 18 yr she became pregnant and desired natural delivery of the baby. Since natural delivery can result in decreased cerebral blood flow, it was necessary to assess her vascular reserve. Technetium-99m-HMPAO brain SPECT with hyperventilation challenge, which revealed maintenance of cerebral vascular reserve, was useful in showing that natural delivery was indicated for this patient.

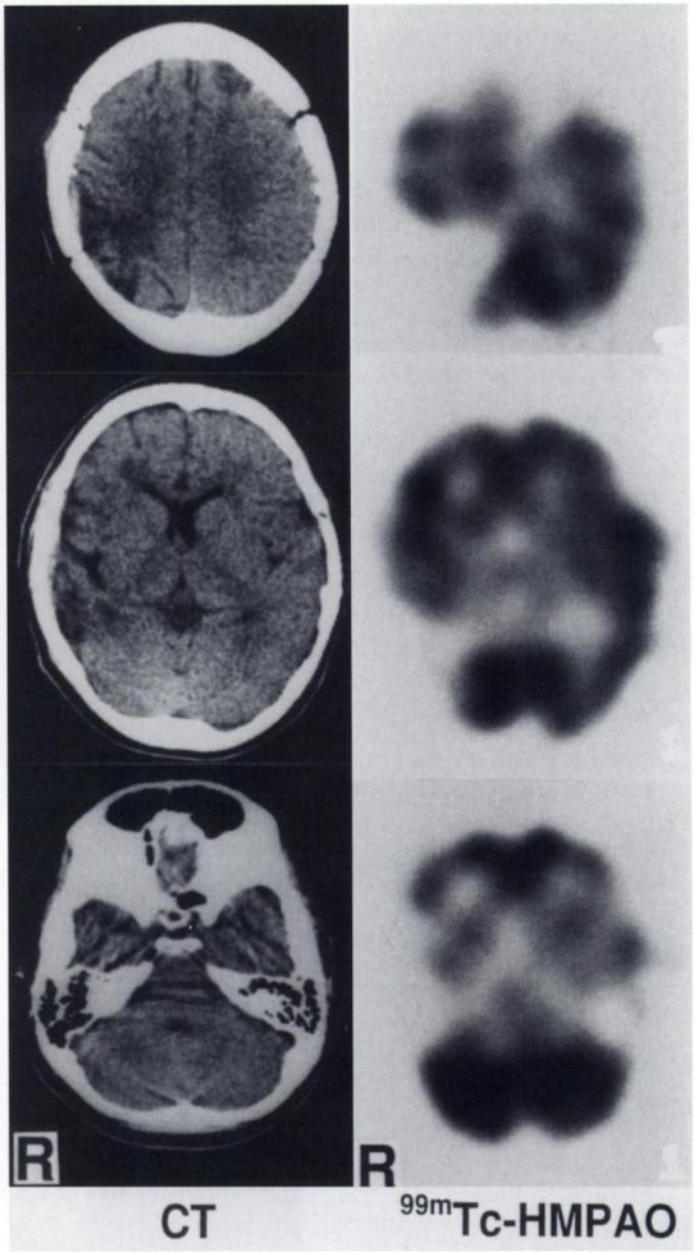

FIGURE 2. Technetium-99m-HMPAO brain SPECT images reveal no abnormality in cerebral blood flow, except in regions imaged as low density areas on brain CT (right). Radiograph CT scans demonstrate low density areas in theright temporal, parietal and left frontal areas (left).

CASE REPORT

This 19-yr-old pregnant female first experienced transient ischemic attack (TIA) with fainting on standing at 2 yr. She subsequently experienced episodes of cataplexy about five or six times per month. She was diagnosed with moyamoya disease by angiography, which revealed moyamoya vessels bilaterally. She had also experienced amaurosis fugax from 6 yr, and right scintillating scotoma and right hemiplegia from 8 yr. She had difficulty with schoolwork in elementary school. Since her signs and symptoms and her EEG findings had worsened, bypass surgery was indicated. She underwent left STA-MCA and EMS at 8.5 yr. The TIAs with right hemiparesis completely disappeared after this surgery. Four months after the first surgery, she underwent STA-MCA and EMS in the right hemisphere. Postoperative angiography revealed a patent STA-MCA anastomosis and reduction of moyamoya vessels (Fig. 1). Her postoperative course was uneventful, and she did not experience TIAs postsurgically.

Since the start of the patient's pregnancy, she and her fetus were carefully followed. She was admitted to our institute for evaluation of risk of labor at 27 wk gestation. After informed consent was obtained from her and her parents, we performed ^{99m}Tc-HMPAO brain SPECT with hyperventilation challenge, instead of acetazolamide administration, for examination of cerebral blood flow and vascular reserve. At examination, she lay supine and continued to hyperventilate for 5 min, and was injected with 333 MBq ^{99m}Tc-HMPAO. Ten minutes after the

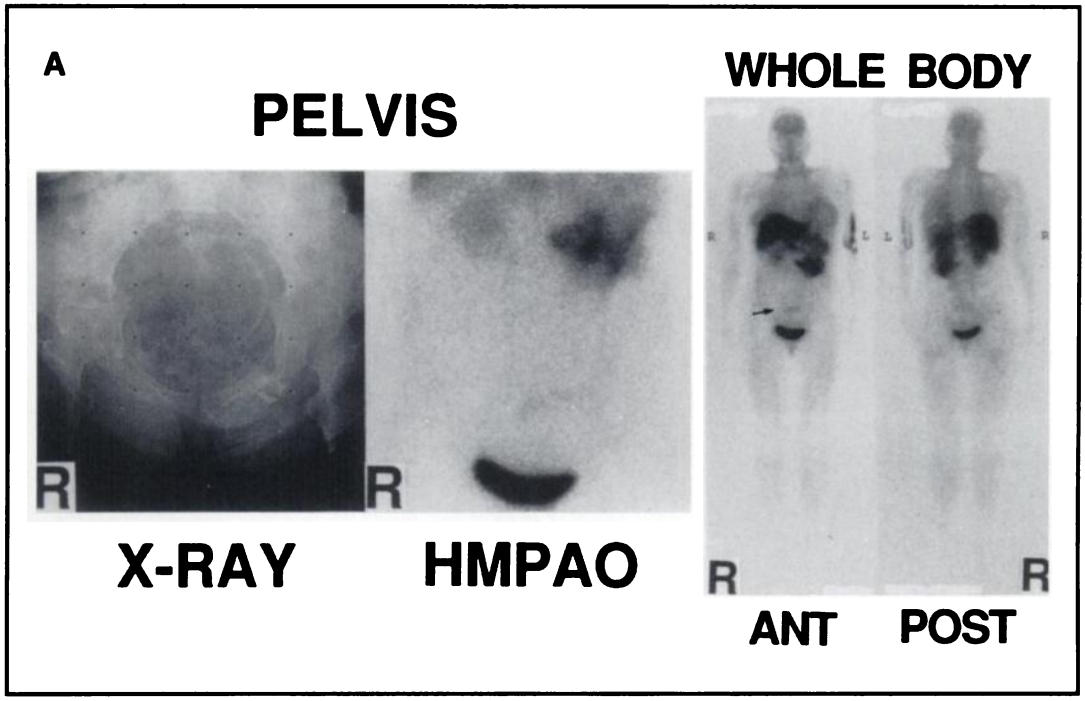

FIGURE 3. (Right) Whole-body ^{99m}Tc-HMPAO images reveal focal uptake in the pelvis. (Left) Pelvic radiography was the only source of irradiation other than brain SPECT to which the patient was exposed during her pregnancy. Anterior abdominal ^{99m}Tc-HMPAO image reveals uptake in the fetal liver (↑).

injection, ^{99m}Tc-HMPAO brain SPECT was performed using a ring-type gamma camera (Headtome SET 070, Shimadzu Co.; Kyoto, Japan) with an 8-mm FWHM. Image data from a 20-min acquisition for SPECT studies were collected into a 128 × 128 matrix using a general, all-purpose collimator. Technetium-99m-HMPAO brain SPECT revealed no abnormality in cerebral blood flow and maintenance of vascular reserve except in regions found to exhibit low density on brain CT (Fig. 2). In addition, images of the whole body and of the pelvis including the 27-wk-old fetus were obtained. The images demonstrated focal fetal accumulation, probably in the liver (Fig. 3). The patient delivered a healthy, 2542-g baby girl at 38 wk gestation, with Apgar scores of 8 (1 min), 9 (5 min) and 9 (10 min).

DISCUSSION

Moyamoya disease is characterized by progressive stenoocclusive change in the anterior circulation of the circle of Willis and the abnormal development of moyamoya vessels. Revascularization surgery, such as STA-MCA with EMS, is thought to be effective in preventing cerebral ischemia by reducing hemodynamic stress in the collateral circulation, including moyamoya vessels (*2*). Since labor with natural delivery by a patient with moyamoya disease might worsen neurological deficits as a result of decreased cerebral blood flow, it is important to assess this type of patient's cerebral vascular reserve prior to delivery.

The usefulness of the acetazolamide challenge in assessing cerebral vascular reserve by determination of the capacity for dilatation of cerebral vessels in moyamoya disease has been reported (*5*). However, acetazolamide can induce fetal malformations if it is given during pregnancy (*6*). Hyperventilation challenge has also been used for evaluating cerebral vascular reserve (*7*) since hyperventilation induces hypocarbia, which can induce cerebral ischemia (*8*). Hyperventilation challenge is dangerous for patients with moyamoya disease, but in the present case was considered necessary for evaluation of cerebral vascular reserve.

The dose of ^{99m}Tc-HMPAO used was 333 MBq, which is half the dose we routinely use. In terms of radiation risk to the fetus, the dose absorbed by the red bone marrow, bone and ovaries, in which ^{99m}Tc-HMPAO did not accumulate, was similar to that for the whole body (*9*). The estimated dose absorbed by the ovaries was 1.39 mSv per 333 MBq in a previous study (*9*). Anterior and lateral pelvic radiographs were the only sources of medical irradiation delivered to the patient during her pregnancy other than the brain SPECT, and the estimated dose of radiation to the pelvis per anterior pelvic radiograph was only 0.25 mSv (*10*). The total radiation dose was 2.39 mSv (the estimated radiation dose per lateral pelvic radiograph was about three times that of an anterior pelvic radiograph, 0.75 mSv), which was estimated to be the same as that of natural background radiation during one year (2.4 mSv) (*10*).

The normal biodistribution of ^{99m}Tc-HMPAO includes significant uptake in the brain, liver and kidneys. In the fetus after transplacental delivery, ^{99m}Tc-HMPAO is distributed in the liver, but not in the brain, due to the prolonged circulation time from injection to fetal organs resulting from impeded transit of tracer through the placental blood pool and the immaturity of glutathione metabolism in the fetus (*11*). The focal accumulation detected in the patient's pelvis was thought to correspond to the fetal liver.

CONCLUSION

We considered natural delivery indicated for this patient with moyamoya disease, who had previously undergone STA-MCA, given the maintenance in cerebral vascular reserve as revealed by hyperventilation studied with ^{99m}Tc-HMPAO brain SPECT using small doses of radiation considered to constitute a negligible radiation risk for the fetus.

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Technetium-99m-HMPAO, Technetium-99m-ECD and Iodine-123-IMP Cerebral Blood Flow Measurements with Pharmacological Interventions in Primates

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Technetium-99m-bicisate ethyl cysteinate dimer (ECD) presents a different pattern from cerebral blood flow (CBF) in the subacute phase of cerebral infarction, as measured by PET, perhaps due to lack of oxygen and enzyme activity; this pattern is contrary to that of hexamethyl-propyleneamine oxime (HMPAO) but similar to that of N-isopropyl-[^{123}I]β-iodoamphetamine ([^{123}I]IMP). This study explores possible CBF differences among HMPAO, ECD and IMP, with various relevant drug interventions. **Methods:** Anesthetized adult baboons were used in these SPECT studies. Four studies (n = 6 baboons for each study), one control study and three intervention studies involving intravenous acetazolamide, nimodipine infusion and intramuscular sumatriptan, were followed with ^{99m}Tc-HMPAO, ^{99m}Tc-ECD and [^{123}I]IMP. The split-dose method was used as follows. For each tracer, intervention data from the second SPECT (SPECT-2) after the second tracer injection (444 MBq) reflected a change in CBF with respect to the baseline SPECT (SPECT-1) data from the initial injection (222 MBq). These changes as a ratio, R (R = SPECT-2/SPECT-1), for each study, and the R values for each tracer were compared to R values from the corresponding control studies, yielding a quantitative estimate of drug effects. **Results:** There were no significant differences ($p > 0.05$) between HMPAO and ECD for the control, acetazolamide and sumatriptan studies, but there was indeed a difference between the two for the nimodipine study, indicating a nimodipine-dependent underestimation of CBF with ECD (and also with IMP), with respect to HMPAO. A further significant difference was that larger CBF increases were observed with acetazolamide, as measured with [^{123}I]IMP. **Conclusion:** This is a crucial observation for the clinical interpretation of CBF SPECT data and should direct the choice of tracer for a specific examination.

Key Words: drug–tracer interaction; CBF SPECT; baboon model
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There is considerable interest in the development of tracers to measure cerebral blood flow (CBF) with SPECT. Such tracers should be trapped in the brain long enough so that their distribution can be quantitated and should demonstrate good spatial resolution.

Among the tracers that have been found useful are the iodine-labeled amines, e.g., N-isopropyl-[^{123}I]β-iodoamphetamine ([^{123}I]IMP) (*1*). Its uptake linearly corresponds to a wide range of flow, as assessed by microspheres (*2*). The brain retention of IMP will be a balance of washin and washout, which in turn will be influenced by blood flow, a retention mechanism that is stereoselective, and by metabolism of the tracer (*3*). Despite its widespread use as a cerebral blood perfusion agent, IMP appears to redistribute in the brain with time (*4*). Of several ^{99m}Tc-labeled compounds synthesized as cerebral perfusion agents, ^{99m}Tc-hexamethyl-propyleneamine oxime (^{99m}Tc-HMPAO) has been used extensively, in spite of its unfavorable stability after preparation. Its retention in the brain is limited to the enzymatic reactions with glutathione, of which there is a high prevalence (*5,6*). The CBF agent N,N′−1,2-ethylene-di-yl-bis-L-cysteinate diethyl ester, labeled with ^{99m}Tc-bicisate ethyl cysteinate dimer (ECD), has a high initial brain extraction with a slow clearance (*7*). The retention in the brain is associated with stereospecific deesterfication to hydrophilic acid derivatives (*8,9*). As a CBF agent in healthy subjects, it corresponds well with ^{133}Xe (*10*), although ECD underestimates higher flow rates, as HMPAO is also known to do. However, in cases of subacute stroke, ECD failed to show reflow hyperemia in the infarct area, contrary to the action of HMPAO (*11,12*) but similar to the known action (albeit to a lesser extent) of [^{123}I]IMP (*13*).

It is important to know and understand quantitative and qualitative differences that are related to CBF, as measured by the various CBF agents. Such differences between the tracers may occur during various pathological conditions, as well as after relevant pharmacological interventions. Changes in the metabolic states of the brain appear to influence the kinetics and net accumulation of ^{99m}Tc-HMPAO at the cellular level by modifying the uptake, the backdiffusion or both (*14*). Studies comparing these tracers under pharmacological intervention conditions have not yet been reported, and these comparisons were the aim of this study.

The drugs used for this purpose were chosen from previous studies reported in the literature. Acetazolamide has been used frequently in neuro-SPECT studies to evaluate cerebrovascular reserve. The recently developed lipophilic dihydropyridine calcium channel blocker, nimodipine, demonstrates superiority in its influence on CBF compared to other calcium channel blockers and has been used for migraine and dementia (*15*). The recent introduction of the 5-HT_{1D}-agonist, sumatriptan, for the treatment of migraine has been a therapeutic breakthrough, with its undoubtable influence on abnormal CBF.

Drug intervention on CBF can ideally be investigated by the

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