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Assessment of outcome by EC/IC bypass with ^{123}I-iomazenil brain SPECT

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We report two patients with occlusive cerebrovascular disease who were examined by means of benzodiazepine receptor SPECT(BZR-SPECT) with ^{123}I-iomazenil (IMZ) before extracranial-intracranial bypass surgery (EC/IC bypass). Preoperative low perfusion areas detected by cerebral blood flow SPECT (CBF-SPECT) were divided into two parts on BZR-SPECT images. In the low perfusion areas where the BZR were preserved, regional cerebral blood flow (rCBF) increased on postoperative CBF-SPECT, but where the BZR were not preserved, rCBF did not increase on postoperative CBF-SPECT. On visual inspection, the SPECT images of postoperative CBF-SPECT appeared similar to those of preoperative BZR-SPECT. For evaluation of the ischemic brain condition itself, instead of the cerebral metabolism, the distribution and activity of cerebral neurons indicated by BZR-SPECT with IMZ might be utilized.

Key words: ^{123}I-iomazenil, benzodiazepine receptor, SPECT, ischemia, EC/IC bypass

INTRODUCTION

^{123}I-IOMAZENIL (IMZ), which is a single-photon emission computed tomography (SPECT) tracer that selectively binds to central type benzodiazepine receptors (BZR) in the neuron membrane, was developed to facilitate the diagnosis of various cerebral diseases involving BZR dysfunction, by determining its regional distribution pattern in the brain.[1–3] Central type BZR are present mainly in the neurons of the cerebral cortex. Several studies involving positron emission tomography (PET), anatomical studies of the brains of patients and animal experimental studies have revealed changes in central type BZR in various cerebral diseases, including epilepsy, Huntington's chorea, Alzheimer's disease, hepatic encephalopathy and ethanol dependence.[4–6] The distribution of central type BZR has also been reported to provide information other than blood flow information; for example, analysis of the distribution has also been used to detect brain ischemia.[7] A PET study with ^{11}C-flumazenil showed that the distribution of BZR correlated with the cerebral metabolic rate for glucose in the ischemic brain.[8] Hayashida et al. showed that reduced uptake in BZR-SPECT with IMZ reflects oxidative hypometabolism causing neuronal damage in hemodynamically and metabolically impaired areas in patients with cerebrovascular disease.[9] We report on two patients with occlusive cerebrovascular disease who were examined by BZR-SPECT with IMZ before extracranial-intracranial bypass surgery (EC/IC bypass).

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BZR-SPECT METHOD

After intravenous administration of 222 MBq (Case 1) and 167 MBq (Case 2) of IMZ, SPECT data were collected between 170 and 190 min.[10] A three-detector-type gamma camera (Toshiba GCA9300A) and a low-energy super-high-resolution fan beam collimator were used for the SPECT, with a Ramp filter and a Butterworth filter for preprocessing (0.1 cycle/pixel). The slice-thickness was 3.4 mm and the matrix size was 128 × 128 pixels.

CASE REPORT

Case 1: A 55-year-old male. Loss of strength in the left forearm occurred on January 3, 1995. Two days later, loss of strength in the right upper limb and dysarthria also occurred. On January 17, the patient was admitted to our hospital. On admission, left incomplete hemiparesis,

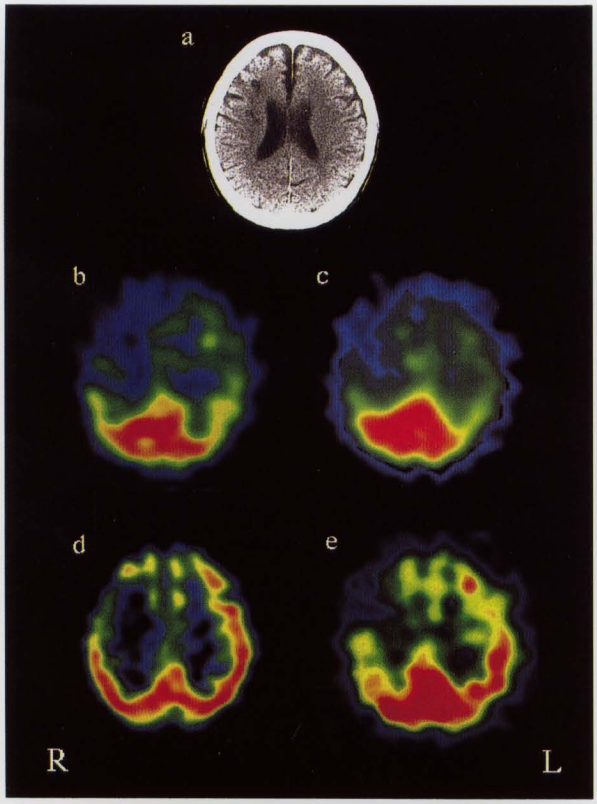

Fig. 1 A 55-year-old male with occlusion of both internal carotid arteries at their origins. (a) Head CT revealed infarction foci in the right frontal lobe subcortex. (b) CBF-SPECT before EC/IC bypass at rest (on day 14 after the onset) revealed extensive low-perfusion areas including both frontal lobes, temporal lobes and parietal lobes. (c) CBF-SPECT following administration of acetazolamide before EC/IC bypass (on day 17 after the onset) revealed a severe perfusion decrease in the frontal lobes and parietal lobes and a moderate perfusion decrease in the temporal lobes. (d) On BZR-SPECT before EC/IC bypass (on day 24 after the onset) BZR-deficient areas were detected in the right frontal lobe and the left anterior-most frontal cortex. (e) Postoperative blood flow images obtained by CBF-SPECT at rest (6 months after the onset) were very similar to those obtained by preoperative BZR-SPECT, revealing low-perfusion areas in the right frontal lobe and the left anterior-most frontal cortex.

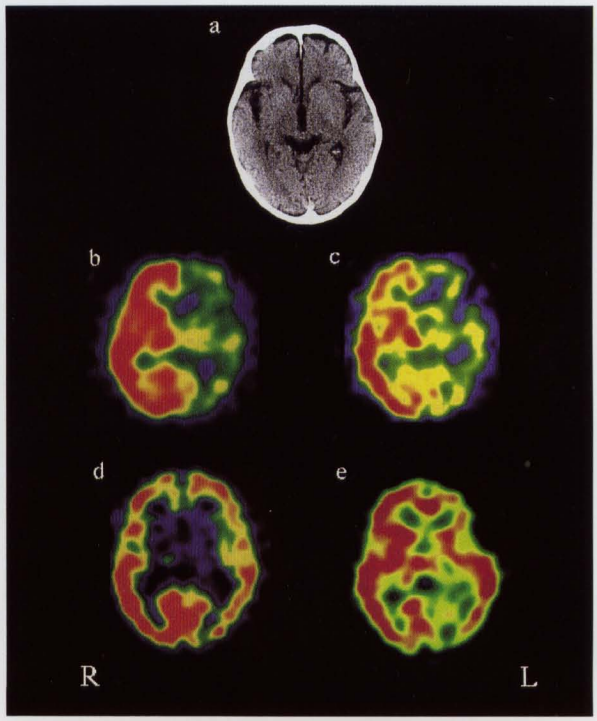

Fig. 2 A 77-year-old male with occlusion of the left internal carotid artery. (a) Head CT showed no low-density area caused by cerebral infarct. (b) CBF-SPECT at rest (on day 7 after the onset) before EC/IC bypass revealed that most of the left cerebral hemisphere had become a low-perfusion area. (c) CBF-SPECT following administration of acetazolamide before EC/IC bypass (on day 11 after the onset) revealed a severe perfusion decrease in the left cerebral hemisphere. (d) BZR-SPECT before EC/IC bypass (on day 18 after the onset) revealed no BZR-deficient area. (e) Postoperative CBF-SPECT (on day 28 after the onset) revealed improvement in rCBF in the left cerebral hemisphere.

dysarthria and difficulty in walking were detected, and the patient was incontinent. Head CT revealed infarction foci in the right frontal lobe subcortex (Fig. 1a). Cerebral angiographic findings showed occlusion of both internal carotid arteries at their origins. Perfusion to the left cerebral hemisphere was supplied from the left vertebral artery via the basilar artery, through the left posterior cerebral artery, left posterior communicating artery and left internal carotid artery. Perfusion to the right cerebral hemisphere was supplied from the anterior communicating artery. Cerebral blood flow SPECT (CBF-SPECT) at rest, with N-isopropyl-4-[^{123}I]-iodoamphetamine (^{123}I-IMP) on day 14 revealed extensive low-perfusion areas including both frontal lobes, temporal lobes and parietal lobes, with a low rCBF of 24 m*l*/100 g/min in the left frontal lobe cortex (Fig. 1b). CBF-SPECT following administration of acetazolamide on day 17 revealed a severe perfusion decrease in the frontal lobes and parietal lobes and a moderate perfusion decrease in the temporal lobes, indicating a decrease in the cerebral vascular reserve (CVR) of the respective regions (Fig. 1c). In BZR-SPECT on day 24, BZR-deficient areas were detected in the right frontal lobe and the left anterior-most frontal cortex (Fig. 1d). On day 46, right STA-MCA anastomosis was performed and on day 86, a radial artery graft was performed to connect the left external carotid artery with the left middle cerebral artery. Six months after onset, blood flow images obtained by CBF-SPECT at rest were very similar to those obtained by preoperative BZR-SPECT, revealing low-perfusion areas in the right frontal

lobe and the left anterior-most frontal cortex (Fig. 1e). The rCBF was increased to 33 ml/100 g/min in the left frontal lobe cortex.

Case 2: A 77-year-old male. The patient developed right hemiplegia and a speech disorder on January 13, 1995 and was admitted to our hospital. Head CT showed no low-density area caused by cerebral infarct (Fig. 2a). Angiography revealed an occlusion at the origin of the left internal carotid artery, and perfusion of the left middle cerebral artery region was supplied from collateral circulation routes via the anterior and posterior communicating arteries. CBF-SPECT at rest with ^{123}I-IMP on day 7 revealed that most of the left cerebral hemisphere had become a low-perfusion area (Fig. 2b). CBF-SPECT following administration of acetazolamide on day 11 revealed a severe perfusion decrease in the left cerebral hemisphere, indicating a severe reduction in CVR (Fig. 2c). rCBF in the left frontal lobe cortex was 26 ml/100 g/min at rest. BZR-SPECT on day 18 revealed no BZR-deficient area (Fig. 2d). On day 24, left superficial temporal artery to middle cerebral artery (STA-MCA) anastomosis was performed. CBF-SPECT on day 28 revealed improvement in rCBF in the left cerebral hemisphere. The rCBF in the left frontal lobe cortex was improved to 33 ml/100 g/min (Fig. 2e).

DISCUSSION

In case 1 in the present study, the reduced rCBF and decreased CVR extended to both frontal lobes, whereas BZR were detected in all parts of the brain except in part of the right frontal lobe and the left anterior-most frontal cortex, which were BZR-deficient. The distribution of rCBF after bilateral vascular reconstruction was very similar to the preoperative BZR distribution. In the parts of the brain in which BZR were detected, the blood flow was thought to have recovered due to the increase in the perfusion pressure resulting from the vascular reconstruction. Regarding the part of the brain in which the BZR density was decreased or no BZR were detected, the brain did not require blood flow despite the increased perfusion pressure, and as a consequence, the blood flow did not increase. In case 2 as well, BZR were maintained and the postoperative rCBF was improved despite the extensive reductions in the blood flow and the CVR in the left cerebral hemisphere.

Preoperative evaluation of the effectiveness of vascular reconstruction for occlusive cerebrovascular disease is currently considered to require not only hemodynamic assessment but also assessment of the state of the brain itself with respect to ischemia, including the cerebral metabolic rate for oxygen ($CMRO_2$), oxygen extraction fraction (OEF) and cerebral blood volume (CBV) determination,[11–13] but $CMRO_2$ and OEF are only feasible with PET. In many medical institutions where only SPECT is available, rCBF and CBV can be determined. In such situations, the CVR was utilized for the estimation, by administering CO_2 or acetazolamide in place of the determination of $CMRO_2$ and OEF.[14,15] In our hospital as well, vascular reconstruction has been indicated for patients with a reduced rCBF and reduced CVR assessed on the basis of acetazolamide administration, but it can hardly be said that vascular reconstruction has been effective in all cases. We consider that in ineffective cases partial neuronal loss had already occurred in ischemic areas[16] or they had developed an irreversible disorder; in such cases the indication of vascular reconstruction had already been lost. Therefore hemodynamic assessment alone is insufficient for assessing the condition of the ischemic brain to determine whether EC/IC bypass is indicated. For evaluation of the ischemic brain condition itself, instead of the cerebral metabolism, the distribution and activity of cerebral neurons with BZR-SPECT by IMZ might be utilized.

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