Chronological Changes in Brain Blood Flow and Central Benzodiazepine Receptor Binding Potential in a Patient with Symptomatic Epilepsy after Surgery for Aneurysmal Subarachnoid Hemorrhage: $^{123}$I-Iomazenil Single-Photon Emission Computed Tomography Studies

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Abstract
Early $^{123}$I-iomazenil single-photon emission computed tomography (SPECT) images are correlated with blood flow in the brain, and late images are correlated with cortical benzodiazepine receptor binding potential. Reduced metabolism in the contralateral cerebral hemisphere is indicated by crossed cerebellar hypoperfusion (CCH). We present the case of a 63-year-old man who developed symptomatic epilepsy 13 days after surgery for an aneurysmal subarachnoid hemorrhage. Early images on $^{123}$I-iomazenil SPECT 2 days after seizure onset revealed CCH and hyperperfusion in the affected cerebral hemisphere where benzodiazepine
receptor binding potential was reduced in late images on $^{123}$I-iomazenil SPECT. These abnormal findings resolved on repeated $^{123}$I-iomazenil SPECT 1 month after seizure onset. The case we present here is consistent with the idea that the central benzodiazepine receptor system in the human brain undergoes changes that are related to seizures due to epilepsy.

Introduction

The distribution of central benzodiazepine receptors in the cortex of the human brain has been widely studied with single-photon emission computed tomography (SPECT) using $^{123}$I-iomazenil [1–5]. Images showing benzodiazepine receptor binding potential (BRBP) on $^{123}$I-iomazenil SPECT are obtained by initiating a scan approximately 3 h after administration of $^{123}$I-iomazenil (late images). These images are reportedly associated with neural density in the cerebral cortex, and a reduction in cortical BRBP indicates irreversible cortical neural damage or loss [1, 3–5]. In contrast, SPECT images obtained within 23 min after administration of $^{123}$I-iomazenil (early images) correlate with brain perfusion images [6, 7].

A reduction in blood flow in the cerebellar hemisphere contralateral to a supratentorial lesion is known as crossed cerebellar hypoperfusion (CCH) [8]. CCH can be observed with positron emission tomography or brain perfusion images obtained with SPECT [8–10]. CCH occurs due to damage to the corticopontocerebellar pathway, leading to functional deafferentation and a transneuronal decrease in metabolism in the contralateral cerebellar hemisphere [9, 10]. Patients with unilateral carotid artery occlusive disease show asymmetry in blood flow on the contralateral compared to the affected cerebellar hemisphere that is indicative of the metabolic rate of oxygen in the affected cerebral hemisphere compared to the rate in the opposite side [11].

We describe the case of a patient with symptomatic epilepsy that developed after surgery for an aneurysmal subarachnoid hemorrhage. $^{123}$I-iomazenil SPECT imaging 2 days after seizure onset demonstrated hyperperfusion and reduced BRBP in the affected cerebral hemisphere with CCH. These findings resolved on repeated $^{123}$I-iomazenil SPECT imaging 1 month after the seizure.

Case Report

A 63-year-old man with a subarachnoid hemorrhage due to a ruptured left middle cerebral artery aneurysm underwent neck clipping of the aneurysm via a craniotomy under general anesthesia on the day after the onset. The postoperative course was uneventful until the 13th postoperative day when disorientation with slight left hemiparesis and motor aphasia developed. Magnetic resonance imaging showed no new ischemic lesions and no findings of vasospasm. The symptoms continued, and 5 days later, the patient developed generalized tonic-clonic seizures. After oral administration of an anticonvulsant, additional seizures did not occur, and the neurological deficits gradually improved. $^{123}$I-iomazenil SPECT was performed 2 days after the seizure onset. Scanning was started immediately (early images) and at 180 min (late images) after intravenous injection of 167 MBq $^{123}$I-iomazenil; the duration of each scan was 20 min. On early images, tracer uptake was increased in the left cerebral hemisphere and decreased in the right cerebellar hemisphere compared with the contralateral cerebral and cerebellar hemispheres, respec-
tively (Fig. 1). On late images, tracer uptake was relatively decreased in the left cerebral hemisphere, and no difference in tracer uptake between the 2 cerebellar hemispheres was observed (Fig. 1).

The neurological deficits completely resolved 1 month after onset. Magnetic resonance imaging revealed no new ischemic lesions and no abnormal findings in the cerebral arteries. Repeated 123I-iomazenil SPECT showed resolution of the relative increases and decreases in tracer uptake in the left cerebral hemisphere on early and late images, respectively, that were observed in the first study (Fig. 2). No difference in tracer uptake between the 2 cerebellar hemispheres was observed on early or late images (Fig. 2).

Discussion

As early images on 123I-iomazenil SPECT correlate with brain perfusion images [6], our patient exhibited hyperperfusion in the affected cerebral hemisphere and CCH 2 days after seizure onset. This cerebral hyperperfusion may be related to subclinical seizure activity, and CCH may indicate reduced metabolism in the affected cerebral hemisphere. In the same region, BRBP was reduced on late images of 123I-iomazenil SPECT. Repeated 123I-iomazenil SPECT showed resolution of these abnormal findings. The results from our patient are consistent with the idea that a decrease in BRBP and metabolism in the affected cerebral hemisphere resolves along with the observed hyperperfusion. Other studies have reported similar results [12, 13]. Thus, the central benzodiazepine receptor system in the human brain can change due to seizures caused by epilepsy. However, reduced BRBP in the cortex usually suggests permanent damage in the cortical hemisphere [1, 3–5].

Several investigators also have reported that late images on 123I-iomazenil SPECT are correlated with images of the cerebral metabolic rate of oxygen on positron emission tomography [14, 15]. The correlation between the chronological changes in BRBP in the affected cerebral hemisphere and CCH in our patient corresponded with this previous finding.

Statement of Ethics

The protocol of this study was reviewed and approved by the institutional ethics committee, and written informed consent was obtained from the patient’s next of kin.

Disclosure Statement

The corresponding author (Kuniaki Ogasawara) declares the following potential conflicts of interest with respect to the research, authorship, and/or publication of this article: consigned research funds from Nihon Medi-Physics Co., Ltd., and Bristol-Myers Squibb.

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**Fig. 1.** \( ^{123} \text{I} \)-iomazenil SPECT images 2 days after seizure onset. Early images (upper row) revealed an increase and a decrease in tracer uptake in the left cerebral hemisphere and the right cerebellar hemisphere, respectively, compared with the contralateral hemispheres. Late images (lower row) showed a decrease in tracer uptake in the left cerebral hemisphere compared with the contralateral hemisphere and no difference in tracer uptake between the 2 cerebellar hemispheres.
Fig. 2. $^{123}$I-Iomazenil SPECT images 1 month after seizure onset. No difference was observed in tracer uptake between the 2 cerebral or cerebellar hemispheres in early (upper row) or late (lower row) images.