Abstract

Two cases of hemiballism-hemichorea have been reported in woman patients with hyperglycemia; this was a feature of striatal hyperintensity on the T1-weighted MRI. In the first case, strict management of diabetes and treatment with pimozide effectively suppressed the movement disorder. The Z-score Imaging System revealed hyperperfusion in the bilateral dentate nuclei, left striatum, and bilateral motor cortices. In the second case, painful hemiballism-hemichorea limb, followed by the upper limb. The severity of HB-HC corresponded to the expansion of the striatal lesion. The mechanism of HB-HC by using statistical cerebral blood flow evaluation has also been discussed.

Case Reports

Case 1

The first case was an 85-year-old woman (body weight, 46 kg; height, 141 cm) who suffered from left facial hemichorea and showed a poorly controlled blood glucose level. She was admitted to the hospital on June 24, 2003. Initially, the Department of Metabolism and Endocrinology assumed the responsibility of this case. She had been medicated with an oral blood glucose depressant for 30 years but had developed diabetic retinopathy over the last 4 years.
and had oral dyskinesia for 2 to 3 months. The urine examination data, arterial blood gas data, and blood chemistry data that were observed on admission indicated poorly controlled diabetes mellitus and non-ketotic hyperglycemia, with a fasting blood glucose level of 324 mg/dl and hemoglobin A1c of 14.8%. Insulin therapy was administered immediately. The blood glucose level gradually improved; however, facial hemichorea worsened and grimacing increased. There was no abnormality in the cranial nerves, and the patient did not show any cerebellar symptoms. Muscle tone was normal; however, bilateral proximal muscle weakness was observed in the upper and lower limbs. An MRI study performed on June 30, 2003, showed a right, hyperintense putaminal lesion on the T1-WI (Fig. 1A), slight hypointensity on the T2-WI (Fig. 1B), and no abnormal signals on diffusion-weighted images. The hyperintense lesion on the T1-WI was not uniform, but it involved spotted hypointense regions. In mid-July, the facial hemichorea exacerbated and expanded to the chorea in the left shoulder and the upper arm, showing a HB-HC phenotype. The patient began to feel exhausted due to shoulder pain, HB-HC, and sleep disturbance. An MRI study performed on August 11, 2003, showed right putaminal atrophy in addition to hyperintensity besides in the ipsilateral caudate nucleus on T1-WI (Fig. 1C) and hypointensity on T2-WI (Fig. 1D). A gradient echo MRI showed the absence of apparent hemorrhages. SPECT of the brain revealed hot spots in the bilateral motor cortices and no laterality in the striatum. The eZIS revealed relative hyperperfusion in the bilateral dentate nuclei of the cerebellum (Fig. 2A), left striatum (Fig. 2B), and bilateral motor cortices (Fig. 2C and D) and hypoperfusion in the right dominant anterior lobe and left dominant temporal lobe in comparison with the average whole brain blood flow in a healthy volunteer. The Z-score that was expressed with reference to a color chart was as follows: +6, red; +5, yellow; +4, green; +3, blue; and +2, black. Strict blood glucose control was continued and a dopamine blocker, namely, pimozide, was administered in order to suppress HB-HC. Initially, a daily dose of 1 mg pimozide was administered and the patient’s condition was carefully monitored. Five days later, the dosage was increased to 2 mg per day, and subsequently, left facial hemichorea gradually diminished. After two weeks, HB-HC was cured. During that time, diabetes mellitus was well controlled, and her complaints decreased. A follow-up MRI study that was performed on September 10, 2003, showed hypointensity on the T2-WI (Fig. 1F), particularly on diffusion-weighted images of the striatum. The hyperintensity on the T1-WI in the right caudate nucleus almost disappeared but was slightly sustained in the putamen (Fig. 1E).

Case 2

The second case was a 52-year-old woman in whom non-insulin-dependent diabetes mellitus (NIDDM) was diagnosed in 1992. The patient was not administered sufficient medication, particularly for 8 months prior to admission to the hospital. On experiencing nausea, vomiting, and vertigo, she consulted a family doctor. She was admitted to the hospital on May 7, 2003. The blood chemistry data on admission showed ketosis (total ketone body, 2,895 mg/dl), hyperlipidemia (total cholesterol, 279 mg/dl; triglyceride level, 291 mg/dl), and hyperglycemia (blood glucose level, 659 mg/dl; HbA1c, 16.3%). Arterial blood gas examination showed the absence of acidosis (pH, 7.415; pCO2, 41.5 mmHg; pO2, 87.6 mmHg in room air). Insulin therapy was administered immediately and the blood glucose level decreased. However, the patient complained of a sleep disorder, hallucinations, and dysesthesia in both legs. The patient suffered from diabetic retinopathy, neuropathy, angiopathy, central retinal artery occlusion, and progressive visual loss. Ketosis diminished soon after intensive care. For the treatment of her complaint, metoclopramide and etizolam were administered. After two weeks, HB-HC occurred in the left upper limb, followed by an involvement of the lower limb after one more week. A CT scan performed on June 2, 2003, showed a slightly high density in the right striatum (Fig. 3A). A brain MRI study performed on June 5, 2003, showed hyperintensity on the T1-WI (Fig. 3B); FLAIR was limited to the right putamen, and a slight hyperintensity was observed on the T2-WI (Fig. 3C). The putaminal hyperintensity was irregular and contained several spotty hypointense areas. At that time, hallucinations worsened despite the glucose control; therefore, haloperidol treatment was initiated. Haloperidol is popular in the treatment of HB-HC; however, it was less effective in this case. The consciousness level improved in accordance with the therapy, and the patient’s performance on the Glasgow Coma Scale changed from 11 (E3, M5, V3) to 15 at one month after admission. Unfortunately, the patient accidentally aspirated during an evening meal on June 27, 2003, and lapsed into a deep coma (Glasgow Coma Scale-3). Emergency measures saved the patient’s life; however, they did not show a significant increase in the consciousness level. CT images taken on June 30, 2003, revealed brain edema, unclear basal ganglia, and slightly high density signals sustained in the right putamen (Fig. 4).

Discussion

The most common cause of HB-HC is a vascular lesion, ischemic stroke, or petechial hemorrhage. However, it is also associated with hyperglycemia, intraventricular cysts (12), tuberculosis (13), infectious diseases of the central nervous system such as those induced by the human immunodeficiency virus (14) or influenza A virus (15), thyrotoxicosis (16), and cerebral arteriovenous malformation (17). Some reports have stated that the reasons for the occurrence of T1-WI hyperintense basal ganglia lesions are petechial hemorrhage (18), partial calcification, demyelination (19), and characteristic cellular changes. T2-WI images showed some variations. A review of 42 patients with chorea associated with non-ketotic hyperglycemia and hyperintense basal ganglia lesion on the T1-WI studies revealed hypointensity in 24 patients, isointensity in 17 patients, and hyperintensity in 1
Partial calcification could explain the high densities obtained on the CT scans and, in part, explained the hyperintense lesions on the T1-WI; however, insignificant high densities on the CT scans were detected in the early phase of case 2. This discrepancy between the CT scan density and MRI intensity may indicate the involvement of another mechanism. The hyperintensity on T1-WI may also be due to the presence of abundant gemistocytes, which are located along the axons and persist for years. Shortening of the T1 relaxation time may be due to a protein hydration layer inside the cytoplasm of swollen gemistocytes, as reported in the case of gemistocytic astrocytoma (20). Gemistocytes are also found in some chronic diseases such as subacute sclerosing panencephalitis or epilepsy, thereby suggesting the presence of a long-lasting pathological reaction (10).

In case 1, right putaminal hyperintensity on T1-WI was present; this was followed by putaminal atrophy and ipsilateral caudate nucleus hyperintensity on the T1-WI. One month after the disappearance of HB-HC, the caudate nucleus showed isointensity while putaminal hyperintensity sustained. The progression of the MRI study suggested that there was a change in the striatum prior to the occurrence of HB-HC. In case 2, high density of the striatum diminished to only putamen, because of the fade out of HB-HC.
In both the cases, putaminal changes on the MRI or on the CT images were followed by caudate nucleus involvement. The putamen and caudate nucleus have the same origin; they chiefly consist of innumerous small cells, a few large cells, and the rest, consist of medium-sized cells. Therefore, variations in imaging studies may express the same cellular changes and indicate a part of the pathological cascade in HB-HC. Although functional changes in the striatum progressed gradually, HB-HC had a sudden onset. Therefore, there might be a threshold of HB-HC due to the suppression...
level of the striatum.

A SPECT study of case 1 revealed hot spots in the bilateral motor cortices and no laterality in the striatum. A previous report of SPECT scans in nine cases with HB-HC described that four cases showed a hypoperfusion at the basal ganglia contralateral to the HB-HC, four other cases showed hyperperfusion, and one was normal (8). The previously mentioned report stated that the SPECT study is merely qualitative and that the perfusion levels may be comparative. Therefore, the ezIS evaluation should be used for a quantitative analysis. In a previous study, healthy volunteers for the ezIS evaluation for the old age group comprised 40 subjects (19 men and 21 women aged 60–84 years). Performance for aged volunteers, i.e., over 55 years, was within normal limits on the Wechsler Memory Scale (Revised) as well as on the Wechsler Adult Intelligence Scale (Revised). The ezIS revealed hyperperfusion in the bilateral dentate nuclei of the cerebellum, left striatum, and bilateral motor cortices; it revealed hypoperfusion in the right dominant anterior lobe and left dominant temporal lobe. Hypoperfusion areas were consequences resultant from an age distribution of the normal control. A significant decrease in the ratio of blood flow in the basal ganglia contralateral to the chorea and a significant increase in the thalamus was reported using SPECT. Damage to striatal neurons leads to excessive inhibition of the subthalamic nucleus through disinhibition of the inhibitory neurons of the external segment of the globus pallidus. Structural lesions in the contralateral subthalamic nucleus and pallidosubthalamic pathway appear to play a critical role in the development of hemichorea and hemiballism. A widely accepted hypothesis is that loss of control exerted by the subthalamic nucleus on
the internal segment of the globus pallidus is followed by the disinhibition of the thalamus (21). In this condition, excitatory output for the cortex from the thalamus increases and consequently gives rise to hyperkinetic disorders such as HB-HC. Therefore, selective inactivation of the striatum should finally evoke an excitatory output for the motor cortex. On the other hand, hypokinetic disorders, including Parkinson’s disease (PD) are considered to have an opposite condition. In patients with advanced PD, a SPECT study showed that cerebral blood flow increased bilaterally in the putamina, globi pallidi, hippocampi, and cerebellar hemispheres (dentate nuclei) and in the left ventrolateral thalamus, right insula, and right inferior temporal gyrus (22). The PD-related pattern on using 18F-fluorodeoxyglucose positron emission tomography (FDG-PET) showed hypermetabolism in the globus pallidus, putamen, thalamus, and dentate nucleus of the cerebellum (23). In PD, the increasing neuronal activity in the internal segment of the globi pallidi is followed by the inhibition of the thalamus, thereby reducing the drive along the thalamo-motor cortex projection. Hypermetabolism and hyperperfusion of bilateral dentate nuclei were speculated to act as a compensation for the thalamic activity through dentate-thalamo-motor cortical projection, which is the excitatory neuron for the thalamus. The pathological cascade in HB-HC resulted in an increased thalamocortical drive. In case 1, compensatory reactions should have stimulated the left dentate nucleus to reduce the activity; however, bilateral hyperperfusion of dentate nuclei was observed. It was unclear whether or not hyperperfusion in the left dentate nucleus implied synergism with hypoactivity of the right putamen, thereby resulting in a sudden increase in HB-HC, another mechanism was involved. The reason behind the bilateral hyperperfusion of the motor cortices resulting only in the left HB-HC also remained unclear. A possible explanation for the eZIS findings is that right striatal failure instigates the left striatum hyperactive to suppress cortical hyperactivity and drives the activation of the right dentate nucleus for compensation. Further considerations of a SPECT (eZIS) or PET study will be necessary for analyzing HB-HC. Dopamine D2 receptor-blocking drugs may cause the tardive dyskinesia syndrome; however, rapid administration of pimozide might prevent the onset of this type of dyskinesia. Strict management of diabetes mellitus was carried out in both cases; medication with pimozide in case 1 effectively suppressed this movement disorder.

We have presented two patients with HB-HC and have evaluated serial signal changes expanding from the striatum to the caudate nucleus, which are in accord with the severity of HB-HC. A quantitative SPECT (eZIS) study also described the focal neuronal activities suggesting the underlying pathomechanism of HB-HC.

References