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Crossed cerebellar glucose hypermetabolism demonstrated using PET in symptomatic epilepsy —Case report—

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A 65-year-old male with an old cerebral contusion in the frontal lobes had suffered from status complex partial seizures. Ictal positron emission tomography with an F-18 fluorodeoxyglucose ([^{18}F]FDG-PET) scan revealed hypermetabolism in the frontal, temporal and parietal lobes and the contralateral cerebellar hemisphere. The patient underwent a next-day PET scan with the ^{15}O-labeled gas inhalation technique, which showed mild hyperperfusion and oxygen hypermetabolism in these areas. An interictal [^{18}F]FDG-PET scan 17 days after the initial epilepsy demonstrated glucose hypometabolism of the frontal, temporal and parietal lobes and the contralateral cerebellar hemisphere. Increased glucose metabolism on the ictal PET scan and decreased glucose metabolism on an interictal PET scan in the epileptogenic supratentorial zones and the contralateral cerebellar hemisphere are interesting observations for understanding the pathophysiology in long-standing partial seizures.

Key words: epilepsy, crossed cerebellar hypermetabolism, crossed cerebellar hyperperfusion, PET (positron emission tomography)

INTRODUCTION

CEREBELLAR HYPERPERFUSION CONTRALATERAL to the supratentorial epileptogenic area is frequently observed on ictal/postictal SPECT scans in epilepsy patients,[1–5] reflecting an alteration of blood flow through a neuronal connection during seizures. This phenomenon is rarely observed interictally in most cases.[6] This observation has been called "reverse crossed cerebellar diaschisis" or "crossed cerebellar hyperperfusion." Classically, during neuronal activation such as seizures, the cerebral perfusion and glucose metabolism are closely coupled.[7] Recently, we experienced a case that had suffered from complex partial seizures. Ictal positron emission tomography with F-18 fluorodeoxyglucose ([^{18}F]FDG-PET) revealed hypermetabolism in the epileptogenic supratentorial zones and the contralateral cerebellar hemisphere. An interictal [^{18}F]FDG-PET scan 17 days after the initial epilepsy attack demonstrated glucose hypometabolism in these areas. To our knowledge, this is the first report to describe crossed cerebellar glucose hypermetabolism and hypometabolism on ictal and interictal PET scans, respectively.

CASE REPORT

The patient was a 65-year-old right-handed man who had suffered a severe head injury at the age of 18 years. He had suffered from complex partial seizures and had been treated with sodium valproate at our outpatient clinic. The frequency of seizures was once or twice per year. The patient's seizure was characterized by left-sided head deviation (adversive seizure), loss of consciousness, and sometimes generalized tonic-clonic movements, with a duration of 5–10 minutes. An interictal EEG recording from the scalp demonstrated intermittent θ waves in the right frontal lobe but no epileptiform activity. On the morning of June 27, 2004, he was transported to our hospital by ambulance because of convulsive seizures. On admission, he exhibited characteristic convulsions with

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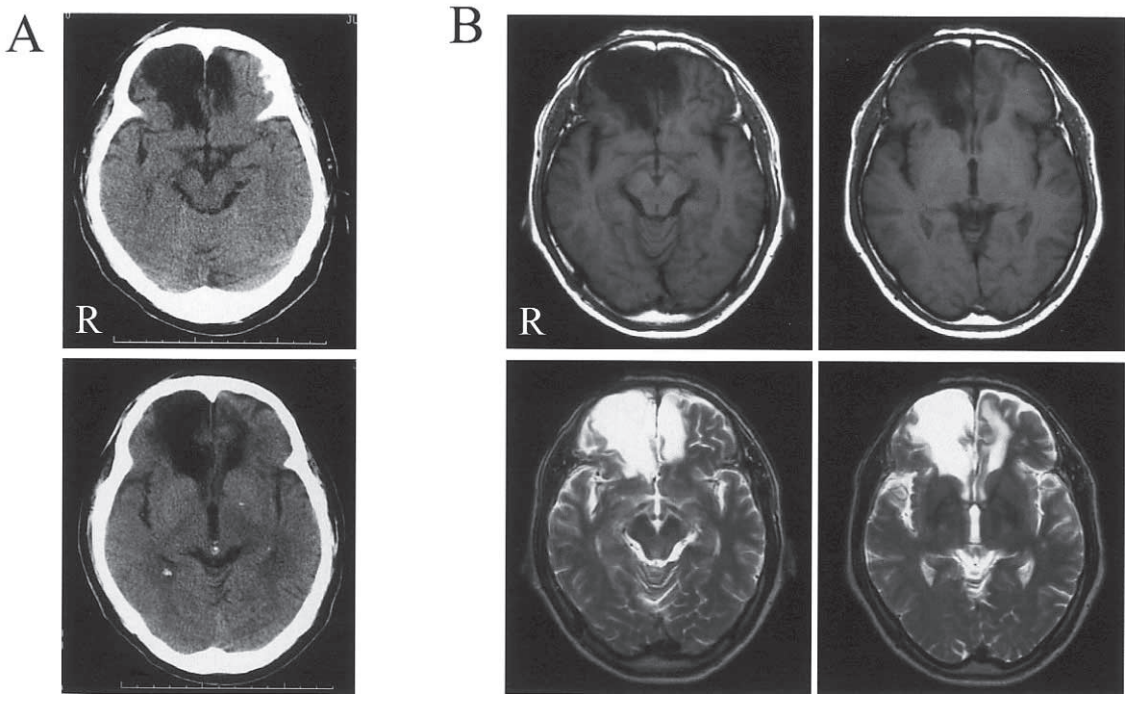

Fig. 1 (A) CT scan immediately after admission showing large and small low density areas in the right frontal and left frontal lobes respectively. (B) Axial T1- and T2-weighted MRI images on the day after admission showing low and high intensity lesions in the same area as that shown in the CT scan.

tonic-clonic movements in his left face and limbs. Diazepam was administrated intravenously to control the seizures. An emergency CT scan showed old brain lesions after cerebral contusion in the bilateral frontal lobes (Fig. 1A). After admission, he received anticonvulsant therapy. Although he regained consciousness and his tonic-clonic movement had ceased by the following morning, he presented left hemiparesis and showed intermittent left-sided head deviation followed by unresponsiveness for 1–2 minutes. Magnetic resonance imaging (MRI) did not detect any fresh lesion in the brain (Fig. 1B). On June 29, 2004, he still showed infrequent typical adversive seizure followed by unresponsiveness. A PET scan with F-18 fluorodeoxyglucose (216 MBq) was performed. The ictal [^{18}F]FDG-PET images showed significant diffuse glucose hypermetabolism in the right frontal, temporal and parietal lobes, the right basal ganglia, and the left cerebellar hemisphere (Fig. 2A). EEG monitoring was not performed during the PET scan. The radioactivity ratio between right/left was 3.15:1 in the frontal lobe, 3.28:1 in the parietal lobe, and 1:2.78 in the cerebellum. Thereafter, he received continuous midazolam administration (0.12 mg/kg/hr) and then had no epileptic episodes. The patient underwent a next-day PET scan with the ^{15}O-labeled gas inhalation technique, which showed mild hyperperfusion in the right frontal, temporal and parietal lobes and the left cerebellar hemisphere and oxygen hypermetabolism in the right temporal and the left cerebellar hemisphere (Fig. 3). Interictal [^{18}F]FDG-PET images 17 days after the initial ictus demonstrated glucose hypometabolism in the right frontal, temporal and parietal lobes and the left cerebellar hemisphere (Fig. 2B). The radioactivity ratio between right/left was 0.49:1 in the frontal lobe, 0.68:1 in the parietal lobe, and 1:0.66 in the cerebellum. The patient was referred to an affiliated hospital to await surgical resection of the epileptogenic focus without any new neurological deficits on day 35 of hospitalization.

DISCUSSION

Contralateral cerebellar hyperperfusion, a condition in opposition to crossed cerebellar diaschisis, can occur because of cerebral hyperperfusion or hypermetabolism of the epileptic focus. This phenomenon is revealed on ictal/postictal and interictal SPECT in epilepsy patients,[1–6] reflecting an alteration of blood flow through a neuronal connection during seizures. The cerebellum receives a significant input from the cerebral hemispheres by the corticopontocerebellar pathway, which arises in the motor, premotor, parietal, and occipital cortices.[8] Because the corticopontine projection provides a predominant excitatory input in the contralateral cerebellar hemisphere, activation of the corticopontocerebellar pathway is considered to be the principle mechanism of cerebellar hyperperfusion from the supratentorial lesions. Classically, during neuronal activation such as seizures, the cerebral perfusion and glucose metabolism are closely coupled.[7] The focal glucose hypermetabolism during

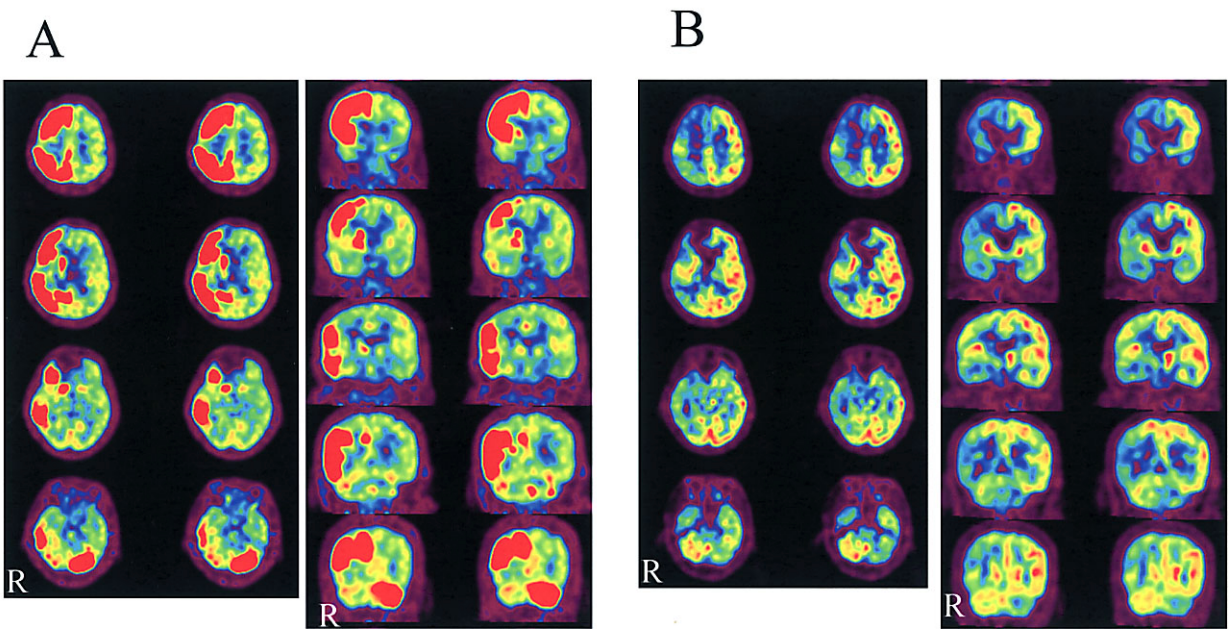

Fig. 2 (A) Ictal [^{18}F]FDG-PET axial and coronal images obtained soon after an epilepsy attack showing diffuse glucose hypermetabolism in the right frontal, temporal and parietal lobes, right basal ganglia, and left cerebellar hemisphere. The radioactivity ratio between right/left was 3.15:1 in the frontal lobe, 3.28:1 in the parietal lobe, and 1:2.78 in the cerebellum. (B) Interictal [^{18}F]FDG-PET axial and coronal images obtained 17 days after the initial ictus showing diffuse glucose hypometabolism in these areas except for the basal ganglia. The radioactivity ratio between right/left was 0.49:1 in the frontal lobe, 0.68:1 in the parietal lobe, and 1:0.66 in the cerebellum.

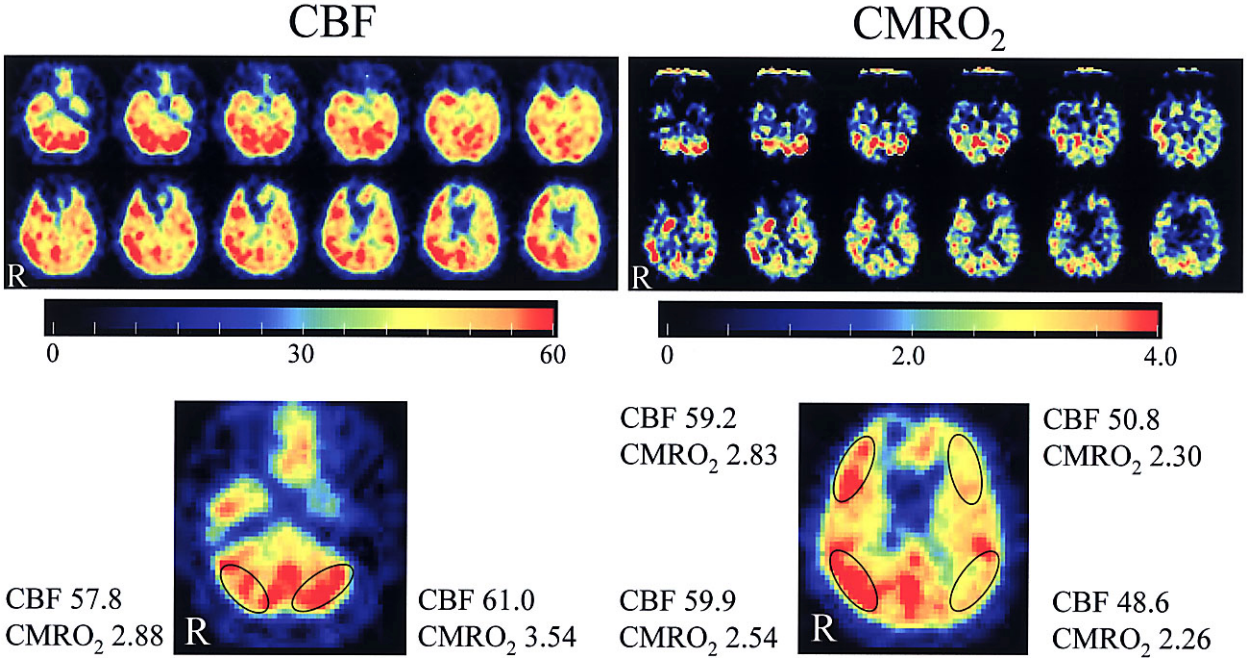

Fig. 3 CBF and $CMRO_2$ examined by an ^{15}O-labeled gas inhalation PET study showing mild hyperperfusion in the right frontal, temporal and parietal lobes and the left cerebellar hemisphere and oxygen hypermetabolism in the left cerebellar hemisphere. $CMRO_2$ in the contralateral cerebral hemisphere shows low oxygen metabolism (≈ 2.3 m*l*/100 g/min) due to continuous midazolam administration.

ictal and early postictal hyperactivity is most likely related to increased glucose demand within an epileptic focus and this has been demonstrated by PET studies.[7,9–11] In this report, we describe an interesting phenomenon, "crossed cerebellar glucose hypermetabolism," demonstrated by ictal [^{18}F]FDG-PET images in a symptomatic epilepsy patient. To our knowledge, this phenomenon has not been reported previously. Crossed cerebellar glucose hypermetabolism observed in this case seems to be primarily responsible for the crossed cerebellar hyperperfusion. Unfortunately, we could not obtain a same-day cerebral hemodynamic study on PET. The next-day PET scan with the ^{15}O-labeled gas inhalation method showed mild hyperperfusion and oxygen hypermetabolism in the contralateral cerebellar hemisphere in spite of continuous midazolam administration. The ictal [^{18}F]FDG-PET images demonstrated diffuse supratentorial glucose hypermetabolism in the right hemisphere except for occipital lobe. Neuronal overactivation of the epileptic focus in the unilateral cerebral hemisphere spreads through the intrahemispheric associative white matter fiber bundles,[12] such as superior longitudinal fasciculus, superior frontooccipital fasciculus, and uncinate fasciculus, and this neural overactivation may have led to the ictal hypermetabolism in the ipsilateral temporal and parietal lobes in this case. Generally, an interictal PET scan shows hypometabolism in the epileptic focus.[13,14] In this case, the ictal glucose hypermetabolism in the right frontal, temporal and parietal lobes and the contralateral cerebellar hemisphere became hypometabolic 17 days after the ictus. The exact reason for the diffuse supratentorial hypometabolism on interictal PET images cannot be determined. Of course, the patient had no new neurological symptoms and no new radiological abnormalities involving the right cerebral hemisphere after this event. Although it is possible that frequent neuronal overactivation produced a secondary epilepsy focus in these areas,[15,16] less energy expenditure in the exhausted brain after a long-standing epileptic event is more likely to cause this phenomenon. Based on the repeated PET findings and his characteristic convulsions, the right frontal lobe was likely responsible for his epilepsy. However, more specific examinations including a subdural electrode recording must be performed to identify the precise localization of the epileptogenic focus.

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