Rapidly Progressive Cognitive Disturbances
Due to Nonconvulsive Status Epilepticus
Associated with a Cerebral Microbleed:
Clinical Application of FDG-PET

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Abstract

Cerebral microbleeds (CMBs) usually produce no symptoms. We encountered a patient who developed cognitive decline and psychotic symptoms associated with nonconvulsive status epilepticus (NCSE), with presumptive epileptogenic focus possibly caused by a CMB. A 70-year-old man developed progressive cognitive disturbances including disorientation and hallucinations two months after a mild head injury. He was admitted to our hospital three months after the trauma, because of progression of symptoms. The first positron emission tomography (PET) with [18F]fluoro-2-deoxy-d-glucose (FDG)
demonstrated intense FDG uptake in the left occipitoparietal region, in which a CMB was detected by T2*-weighted magnetic resonance imaging (MRI). Electroencephalography showed continuous slow waves in the left occipital and parietal areas. After anticonvulsive therapy, his symptoms completely disappeared, accompanied by change in FDG uptake. Our case suggests that CMBs may be an epileptogenic focus of NCSE, and that FDG-PET is useful for the diagnosis of NCSE and assessment of therapeutic efficacy.

Introduction

With the development of neuroimaging technology, research regarding cerebral microbleeds (CMBs) has progressed. T2*-weighted magnetic resonance imaging (MRI) is useful for the detection of CMBs as small dot-like low-intensity lesions [1, 2]. CMBs produce no clinical symptoms in most cases, and a few reports suggested that CMBs may be related to epilepsy [3-5].

Nonconvulsive status epilepticus (NCSE) is status epilepticus not accompanied by motor symptoms. NCSE may be caused by various conditions, and the symptoms are diverse, ranging from subtle clinical signs to coma [6, 7]. Because of the variety of causes and manifestations, a diagnosis of NCSE is sometimes missed. Electroencephalography (EEG) is useful for the diagnosis, with typical findings of spike-and-wave discharges. However, EEG findings in NCSE frequently lack epileptiform patterns [6-8]. Nuclear imaging such as [18F]fluoro-2-deoxy-d-glucose positron emission tomography (FDG-PET) and single photon emission computed tomography (SPECT) are useful to determine the location of the epileptogenic focus of NCSE [7, 9]. To the best of our knowledge, there is no neuroimaging report demonstrating that CMBs may be a cause of NCSE. Here, we report the first case in which a CMB is considered to be associated with NCSE. In this case, FDG-PET was useful for the diagnosis of NCSE and identification of its underlying cause, as well as for evaluation of therapeutic response.

Case report

A 70-year-old, right-handed man fell from a bicycle, hitting the back of his head on the ground. He lost consciousness for 15 min after the accident. Neurological examinations and a CT scan at a nearby hospital revealed no abnormalities, and he returned home. Three days later, the patient experienced nausea and dizziness. Two weeks after the accident, he developed urinary incontinence, insomnia, and gait disturbance. Two months after the accident, the patient experienced cognitive disturbances; he was unable to recall his age or the name of his wife, or write his own name. The patient also developed auditory and visual hallucinations, saying that he saw many horses running around and heard their steps.

The patient was admitted to our hospital at
three months after the accident, because of cognitive disturbances. While neurological assessments indicated no significant physical abnormalities, he showed agraphia, acalculia, finger agnosia and left-right disorientation. The Mini Mental State Examination (MMSE) score was 18, indicating moderate cognitive impairment. The psychotic symptoms were intermittent; hallucinations and delusions appeared from time to time without lucid intervals. T2*-weighted MRI revealed a small spot of low signal intensity with a diameter of 4 mm in the left occipitoparietal region. However, there were no significant abnormalities on T2-weighted, FLAIR, and diffusion-weighted images in the same area. These MRI findings suggested that the lesion in the left occipitoparietal region was a CMB. Cerebrospinal fluid examination was normal. FDG-PET analysis demonstrated intense FDG uptake in the left occipitoparietal region (Figure 1A), which was spatially congruent with the spot diagnosed as a CMB on T2*-weighted MRI (Figure 1B). EEG showed continuous slow waves in the left occipital and parietal areas with no obvious epileptic discharges (Figure 2A). Based on these examinations and the course of the patient’s symptoms, he was diagnosed as having NCSE. These findings suggested that the epileptogenic focus of NCSE was located in the left occipitoparietal region, and possibly associated with a CMB.

We started treatment with levetiracetam at a dose of 500 mg per day, and increased the dose to 1000 mg per day. The patient responded to treatment. The second FDG-PET conducted three weeks after the initiation of medication showed reduced FDG uptake in the left occipitoparietal region (Figure 1C). The EEG findings of continuous slow activities improved to dominant rhythm of 8 Hz (Figure 2B). At the time of discharge, his MMSE score improved to 29, and all the symptoms including hallucinations and urinary incontinence also disappeared.

**Discussion**

We report an elderly patient with rapidly progressive cognitive impairment and psychosis associated with NCSE and its postictal state, with a presumptive epileptogenic focus possibly associated with a CMB. The diagnosis of NCSE was difficult because of a lack of specific epileptiform EEG activity. Neuroimaging techniques such as T2*-weighted MRI and FDG-PET were useful for the diagnosis. In addition, FDG-PET allowed evaluation of therapeutic response. Anticonvulsant medication was effective in the treatment of the patient’s cognitive disturbances and psychosis.

The etiology of NCSE is variable. NCSE can be classified as follows [6]: NCSE in metabolic disorders, NCSE in individuals with preexisting epilepsy with or without epileptic encephalopathy, NCSE in acute cerebral lesions, and NCSE in coma. In the present case, the clinical course and neuroimaging findings imply that the etiology of NCSE was an acute cerebral lesion due to...
mild brain injury.

The diagnosis of NCSE generally depends on EEG findings. For example, frequent generalized spike wave discharges or focal ictal patterns with waxing and waning may indicate NCSE. However, some cases lack definitive epileptiform discharges, and diagnosis can be difficult [6-8]. In such cases, nuclear imaging (such as FDG-PET and SPECT) may help to diagnose NCSE and to locate the epileptogenic focus of NCSE [7, 9], as demonstrated in the present case.

While the mean duration of NCSE is 15-54 hours [10], the abnormal behaviors and cognitive disturbances in this patient continued for months. The prolonged symptoms may be attributed to seizure clustering and prolonged postictal state [11]. In fact, the symptoms of this patient changed from time to time, including cognitive disturbances, Gerstmann syndrome (agraphia, acalculia, finger agnosia, left-right disorientation), hallucinations and delusion, without lucid intervals. Because of the diverse symptoms, it is difficult to differentiate ictal symptoms from a postictal state such as postictal delirium and psychosis. On the other hand, the patient had a specific sign indicating the ictal lesion; Gerstmann syndrome in our case might be related to the epileptogenic focus of NCSE, which included the left angular gyrus.

CMBs are characterized by small, round, homogeneous, low-intensity lesions detected on T2*-weighted MRI that is highly sensitive to detect hemosiderin deposits [1, 2]. Although there is no global consensus regarding their size, these lesions are typically between 2 and 5 mm in diameter, and many previous studies on CMBs have excluded lesions with diameters greater than 10 mm [2]. In this case, the lesion diameter was 4 mm, which is consistent with previous studies. The prevalence of CMBs is 5% in an asymptomatic population (mean age 60 years), and higher than 7% in individuals older than 70 years [2]. The main causes of CMBs are hypertension-related arteriopathy and cerebral amyloid angiopathy [1]. In our case, the clinical course suggested that a mild head injury may have caused the CMB. Traumatic CMBs tend to occur in subcortical white matter, while hypertension-related CMBs tend to occur in the basal ganglia or thalamus [2, 12]. This characteristic distribution pattern is in agreement with our case.

CMBs are usually asymptomatic and are used as a clinical marker of cerebral small-vessel disease [1]. A few reports suggested that CMBs, which include hemosiderin deposits, may be related to epilepsy. However, clinical and animal model studies imply that hemosiderin per se may be related to epilepsy. In epilepsy surgery, removing hemosiderin-stained brain is important to achieve good seizure outcome after resection of vascular malformations [13]. In an animal model, injecting iron into the cerebral cortex induced seizure [14]. In addition, a recent prospective cohort study of 325 patients showed an association between CMBs and
late seizures [5]. These reports serve as an etiological support to the notion that CMBs may be related to epilepsy, while our neuroimaging findings that a high FDG uptake area spatially included a CMB may provide clinical support. Further studies are needed to establish the possible relationship between CMBs and epilepsy.

This case suggests that CMBs may be an epileptogenic focus of NCSE and that assessments with brain MRI and FDG-PET are important for the diagnosis of NCSE and for understanding the pathological mechanisms of the condition, which can be overlooked as a cause of progressive cognitive impairments, especially in elderly individuals with CMBs.

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Figure 1.
(A) A FDG-PET image obtained 4 days after admission demonstrates intense FDG uptake in the left occipitoparietal region.
(B) A T2*-weighted MRI depicts a cerebral microbleed as a small spot of low signal intensity in the region showing increased FDG uptake.
(C) After 3 weeks of antiepileptic medication, FDG-PET reveals reduced FDG uptake in the same area. R, right; L, left.
Figure 2.
(A) EEG shows continuous slow waves in the left occipital and parietal areas, corresponding to a MMSE score of 18.
(B) EEG shows dominant rhythm of 8 Hz without any epileptiform discharge or slow wave, corresponding to a MMSE score of 29.

References


