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Case Report

Periodic Limb Movement Disorder Caused by a Pontine Infarction

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ABSTRACT

An 81-year-old woman sustained an infarction in the right side of the ventral pons, after which she experienced periodic involuntary bilateral movements of the lower extremities. Polysomnography revealed that the involuntary movements were periodic limb movements in sleep (PLMS). The location of the neural substrate that causes PLMS is a major subject of debate. This case suggests that the pontine nuclei play a major role in the pathophysiology of PLMS.

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Key words : nocturnal myoclonus syndrome, pons, polysomnography, sleep disorders, infarction

INTRODUCTION

Periodic limb movements in sleep (PLMS) are involuntary, jerking movements of the lower extremity which occur regularly. These movements often accompany restless legs syndrome (RLS) and lead to sleep fragmentation and daytime fatigue. Numerous disorders have been reported to cause PLMS, but the location of the neural substrate that causes PLMS is still unclear[1-5]. In this paper we describe a patient with PLMS triggered by a pontine infarction.

CASE REPORT

An 81-year-old woman with dysarthria was transported to our hospital. Before she arrived, a magnetic resonance imaging (MRI) examination of the brain by the family's physician had shown an acute ischemic lesion in the right side of the ventral pons.

When the patient arrived at our hospital, speech was slurred and the tongue was positioned towards the left side of the mouth. She had left-sided hemiparesis in both the upper and lower extremities and exhibited a Babinski sign in the left foot. She also had mild ataxia in the left extremities. We believed parkinsonism was not present because there was no rest tremor, rigidity, or akinesia. The past history included hypertension, dyslipidemia, osteoporosis, and anemia. Laboratory studies revealed mild renal failure, iron deficiency anemia, mild hyponatremia, and elevated fibrin degradation products and D-dimer levels (Table 1).

Treatment was started with edaravone, argatroban, and cilostazol. Motor functions improved on a daily basis. An MRI examination of the brain performed 3 days after admission showed obvious hyperintense signals in the right ventral pons on both diffusion-weighted images and T2-weighted images (Fig. 1).

On the day MRI was performed, the patient com-

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Table 1. Laboratory results on admission

Aspartate aminotransferase	16 U/L
Alanine aminotransferase	9 U/L
Blood urea nitrogen	16 mg/dL
Creatinine	0.82 mg/dL
Triglyceride	33 mg/dL
Low-density lipoprotein cholesterol	72 mg/dL
High-density lipoprotein cholesterol	85 mg/dL
Thyroid-stimulating hormone	4.17 μIU/mL
Free triiodothyronine	1.91 pg/mL
Free thyroxine	0.96 ng/dL
Sodium	132 mmol/L
Potassium	3.9 mmol/L
Chlorine	99 mmol/L
Magnesium	1.8 mg/dL
Iron	57 μg/dL
Unsaturated iron binding capacity	293 μg/dL
Ferritin	13 ng/mL
Vitamin B_{12}	805 pg/mL
Folic acid	8.2 ng/mL
C-reactive protein	0.1 mg/dL
Fasting plasma glucose	109 mg/dL
Hemoglobin A_{1C}	6.1 %
Hemoglobin	9.2 g/dL
White blood cell	5,100 /μL
Platelet	143,000 /μL
Prothrombin time	90%
International normalized ratio	1.06
Activated partial thromboplastin time	26.5 s
Fibrin degradation product	6 μg/mL
D dimer	2.2 μg/mL

plained of peripheral dominant periodic involuntary extensions in the left lower extremity. The extensions occurred at night and disturbed her sleep. The movements gradually became more frequent and also started to occur in the right lower extremity. Treatment was started with clonazepam, which helped to alleviate the extensions. On the 19th day after admission we performed a surface electromyography of the left lower extremity. Both extensors and flexors contracted continuously for 3 to 4 seconds approximately every 15 seconds. The extensors exhibited stronger contractions than did the flexors. After treatment with clonazepam had been started, the movements subsided and the patient was discharged from our hospital.

We suspected the symptoms were consistent with PLMS caused by a pontine infarction. Thirty-nine days after the patient had been admitted, we used screening examination scales (Table 2) to evaluate her sleep disorder. The evaluation revealed excessive sleepiness in the daytime and mild depression, which in turn led to social disability.

Sixty-three days after she had been admitted to our hospital, the patient underwent polysomnography. Medication was withheld for the 24-hour period before polysomnography. The sleep stages observed with polysomnography were scored on the basis of the standard Rechtschaffen and Kales classification system[6]. We identified periodic bilateral involuntary movements that fulfilled the diagnostic criteria for PLMS (Fig. 2)[7]. The periodic leg movement index was 93.8 and indicated the severe periodic limb

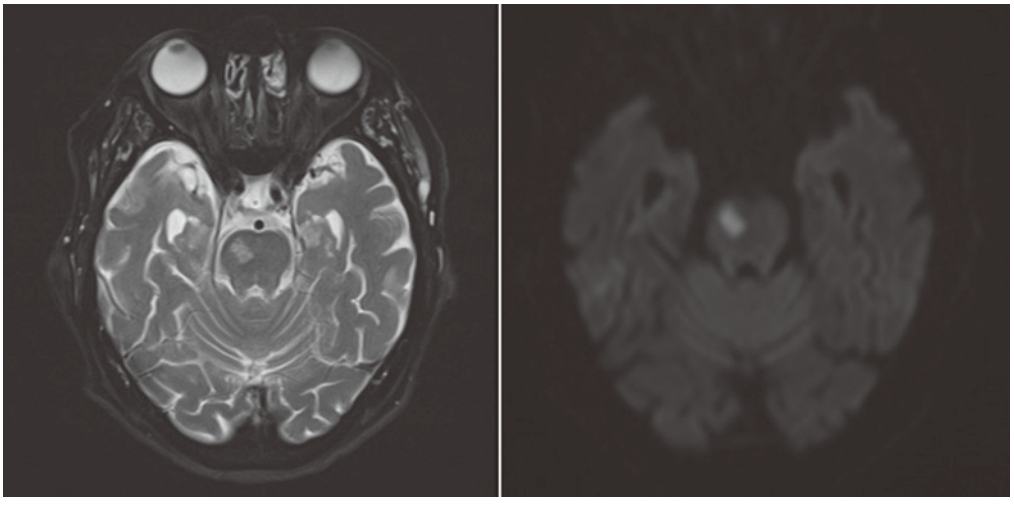

Fig. 1. Magnetic resonance imaging of the brain reveals an acute ischemic stroke in the right ventral pons.

Table 2. Results of sleep disorder screening examinations

Examination scale	Score	Evaluation
Japanese version of Epworth Sleepiness Scale	13	Abnormal sleepiness
Japanese version of the Insomnia Severity Index	14	Subthreshold insomnia
Self-Rating Depression Scale	56	Mildly depressed
Sheehan Disability Scale	Work : 6 Social life : 2 Family life : 5	Mild functional impairment

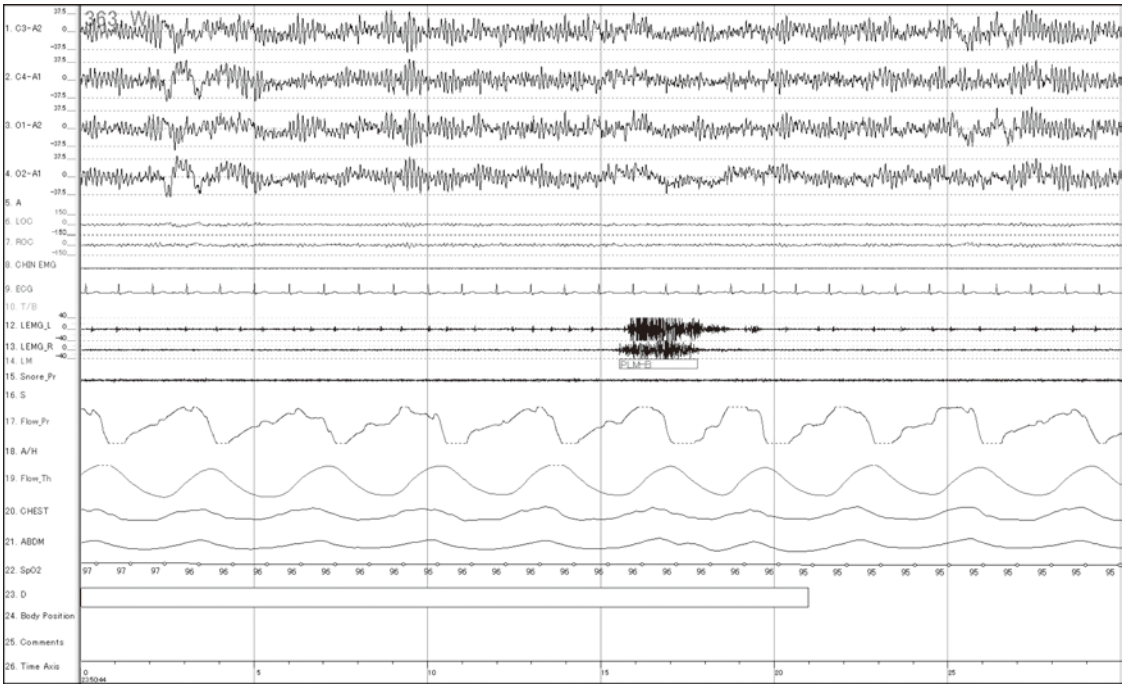

Fig. 2. Periodic limb movements in sleep seen with polysomnography.

movement disorder (PLMD) consistent with the international classification of sleep disorders[7]. The total sleep time was 281.5 minutes, and the arousal index was 14.1 per hour. The patient did not complain of discomfort or unpleasant sensations of the lower extremities, and, therefore, the criteria for RLS were not fulfilled[7].

Whole-spine MRI and nerve conduction studies performed after polysomnography showed no significant changes.

We concluded that the involuntary movements in this patient were PLMS triggered by a pontine infarction. The symptoms were well controlled through the administration of clonazepam, which enabled her to sleep.

Discussion

Both PLMS and RLS have been reported to be caused by a wide range of disorders, such as iron deficiency, multiple sclerosis, peripheral neuropathy, spinal cord lesions, and Parkinson's disease[1-5]. In the present patient, the findings of whole-spine MRI and nerve conduction studies were normal and, other than the pontine infarction, no organic changes were found in the central nervous system or peripheral nerves. Furthermore, the patient did not fulfill the Japanese diagnostic criteria for Parkinson's disease which require the symptoms of parkinsonism[8]. Despite ^{123}I-metaiodobenzylguanidine scintigraphy and dopamine transporter imaging not being performed, Parkinson's disease was ruled out[8]. The PLMS occurred just after pon-

tine infarction, and laboratory studies revealed iron deficiency anemia. These findings suggest that the pontine lesion had triggered PLMS based on iron deficiency.

Because of the variety of potential causes, there has been much debate about the location of the neural substrate that causes PLMS. The present case suggests an association between PLMS and nuclei in the pons. This association indicates that the neural substrate of PLMS is located in the brainstem.

Some evidence suggests that the pathophysiology of PLMS is associated with brainstem nuclei. One study has found that patients with PLMS exhibit an increased excitability of the late component of the blink reflex[9]. This phenomenon indicates that the neural substrate of PLMS is localized on the pontine level or more rostrally. One functional MRI study has shown activation of the cerebellum, thalamus, red nucleus, mesencephalon, and pons when patients with RLS experience involuntary movements[10]. The brainstem neuronal loop, together with the nuclei it contains, has been proposed to be responsible for PLMS[11].

In the present patient, the lesion was located on the right side of the ventral pons, where pontine nuclei exist and project pontocerebellar fibers to the contralateral cerebellum. This lesion might have damaged the right pontine nuclei and fibers from the left side, an assumption that is consistent with the bilateral symptoms of this case (Fig. 3). The pontine nuclei might play an important role in the pathophysiology of PLMS.

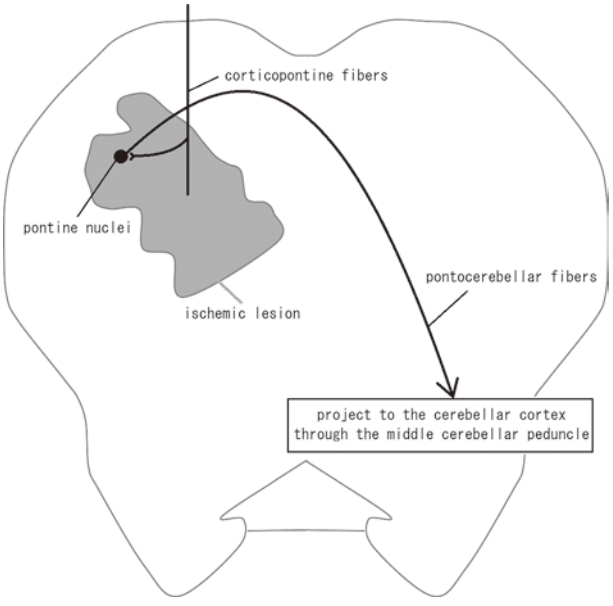

Fig. 3. Hypothetical scheme of the damaged tracts in the pons.

In addition to the present case, at least 2 cases of PLMS have been reported to be caused by pontine stroke[12]. Although the 2 cases were not evaluated with polysomnography, they do support our theory.

The etiologies of RLS and PLMS have not been fully clarified. Nevertheless, we believe that the present case provides clinical evidence that the neural substrate that causes PLMS is located in the brainstem.

Authors have no conflict of interest.

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