

Legend to the Video

Several spells of painful tonic spasm affecting the right side, with hand predominance. The electroencephalogram was normal during these spells.

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Periodic Limb Movement During Sleep Developed After Pontine Lesion

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Abstract: We describe 2 patients who suffered a pontine infarction and subsequently developed periodic leg movement (PLM). The temporal relationship between a stroke and subsequent PLM, as well as the absence of sleep-related disorders in patients' histories, favors the argument of a cause-and-effect

A videotape accompanies this article.

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relationship, with the observed association providing evidence for an anatomic substrate for PLM. © 2003 Movement Disorder Society

Key words: periodic leg movement (PLM); stroke; pons

Periodic limb movements during sleep are characterized by recurrent episodes of repetitive, stereotyped limb movements predominantly occurring in the legs.¹ They recur approximately every 30 seconds. They consist of dorsiflexion of the ankle and toes and flexion of the hip and knee. They usually last approximately 1.1 to 2.8 seconds. They occur in clusters while the subject is lying down or sleeping, primarily in non-rapid eye movement sleep.

Such periodic leg movements (PLM) can be found in normal individuals over 30 years of age and occur in 29% of those over 50 years of age.² Almost all patients with restless leg syndrome (RLS), whatever the cause, also have PLM during sleep.³ PLM with RLS has been reported to be associated with peripheral neuropathy, uremia, anemia, gastric surgery, chronic pulmonary disease, and chronic myelopathy.^{3–5} PLM without RLS has been reported in stiff-man syndrome, Issac's syndrome, Huntington's disease, and amyotrophic lateral sclerosis.^{5,6} However, it is difficult to say whether these reports indicate a causal relationship between PLM and these conditions, and the locus of generator is still unknown. In addition, their association with strokes has not been described previously. Here, we describe 2 patients who suffered a pontine infarction, with the subsequent onset of PLM.

Case Reports

Case 1

A 62-year-old, right-handed woman was admitted to our hospital complaining of an abnormal movement in her right foot and toes while sleeping. This movement had started approximately 1 month before her admission, when it was discovered she also had a transient ischemic attack, which manifested as a transient right hemiparesis. She had a 5-year history of hypertension, which was well controlled by diet and exercise therapy. There was no personal or family history of neurological diseases.

Her general and neurological examinations were unremarkable, with no extrapyramidal signs. On video monitoring during sleep, a mixture of repetitive dorsiflexion of the ankle, subsequent jerking of the knee and hip were observed. These involuntary movements occurred periodically, at 25- to 50-second intervals (see Video, Segment 1).

A brain magnetic resonance imaging (MRI), obtained 1 day after her admission, showed a small infarct in the left middle pons (Fig. 1). There were no other brainstem, cerebellar, or supratentorial lesions. After 50 mg of levodopa was started, the patient and her family reported an almost complete resolution of the involuntary movement during sleep.

Case 2

A 53-year-old right-handed man, previously in good health, was admitted to our hospital with a 5-hour history of hemiparesis of the right side. There was no personal or family history of medical or neurological diseases. He also denied any history of sleep disorders.

On examination, he was alert and oriented, with a blood pressure of 160/90 mm Hg, a regular heart beat of 85 beats/minute, and a temperature of 36.9°C. Physical and neurological examination demonstrated no pathological findings. A brain MRI, obtained on the day of admission showed an area of infarction in the left mid-pons (Fig. 2).

Two days after admission, his caregiver reported an abnormal movement of his right leg during sleep. These involuntary movements consisted of repetitive rapid dorsiflexion of the right ankle, which recurred every 15 to 25 seconds (see Video, Segment 2). A small dose of a dopamine agonist (0.15 mg of pergolide mesylate) led to a marked improvement within a week.

Discussion

Although the anatomical structure responsible for the PLM/RLS remains unclear, several reports have described anatomical substrates related to PLM/RLS. Through electrophysiological studies, an association between the dysfunction of the brainstem level and PLM has been strongly advocated.⁷ Recently, on the basis of the findings from functional MRI in idiopathic PLM/RLS patients, Bucher and colleagues indicated that the red nucleus and brainstem are involved in the generation of PLM in patients with RLS, and the cerebellum and thalamus play a role in the generation of sensory leg discomfort.⁸ Additionally, it has been suggested that a lesion in the brainstem was related to the development of secondary PLM.⁹ The underlying neurophysiological mechanisms are unknown, but the results of neurophysiological and radiological studies have revealed increasing evidence of the involvement of brainstem generators in the pathogenesis of PLM/RLS.

However, central nervous system generators, by themselves, do not sufficiently explain PLM/RLS. It was assumed previ-



FIG. 1. Axial T2-weighted magnetic resonance imaging scan of Patient 1. The infarction is seen adjacent to the left pontine reticular formation.

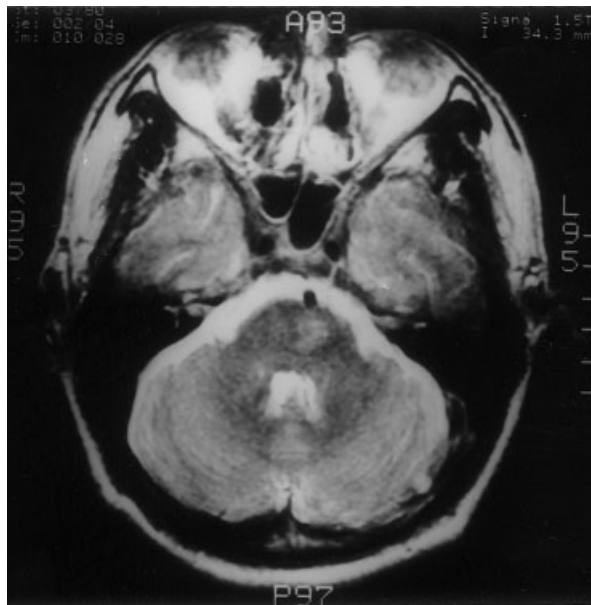


FIG. 2. Axial T2-weighted brain magnetic resonance imaging scan shows a small ischemic lesion in the left paramedian at the middle pontine level.

ously that diencephalospinal dopaminergic pathways might explain the beneficial effects of dopaminergic treatment in patients with PLM/RLS and the decrease of dopamine D2 receptor binding in the striatum.^{10–12} In addition, several reports have described the involvement of lumbosacral generators in the development of PLM, as they have been observed in patients with a spinal cord lesion.^{13–16}

Our 2 patients both experienced PLM during sleep, after ischemia involving the pons. There is a possibility that PLM are only coincidental findings in patients with a pontine ischemic lesion. However, the temporal relationship between a stroke and subsequent PLM, as well as the absence of a previous history of neurological and sleep disorders in our patients, favors the argument of a cause-and-effect relationship and against the simple coincidental occurrence.

Reticular formations in the brainstem directly influence the sleep-wake cycle in the transition from wake to sleep and the onset of rapid eye movement sleep.¹⁷ The disinhibition phenomena with reticulospinal excitatory responses in PLM/RLS patients may lead to a pathological recruitment in propriospinal or spinal jerks.¹⁸

In our cases, the lesions were located near the pontine reticular formation. The destructive lesion of the pons with PLM may reflect the disinhibition effects of the reticular formation on spinal pathways. In addition, the therapeutic responses to dopamine or dopamine agonist in our patients suggest that the dopaminergic paths were involved in the pathogenesis of PLM. From a clinical viewpoint, the occurrence of PLM in our 2 patients, after a pontine infarct, provides support for these symptoms having a biological and neuroanatomical substrate.

Legends to the Video

Segment 1. Patient 1 shows a mixture of repetitive dorsiflexion of the ankle and subsequent jerking of the knee and hip.

These involuntary movements occurred periodically at 25- to 50-second intervals, with durations of 1 to 2 seconds. The patient is snoring throughout the recording.

Segment 2. Patient 2 shows repetitive rapid dorsiflexion of the right ankle during sleep. The involuntary movements recurred every 15 to 25 seconds, with durations of 0.5 to 1 second.

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Adult-Onset Niemann-Pick Type C Disease: A Clinical, Neuroimaging, and Molecular Genetic Study

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Abstract: We report on a patient with adult-onset Niemann-Pick type C (NPC) disease, carrying the mutations P1007 and I1061T in the *NPC1* gene, presenting with marked psychiatric changes followed by dystonia and cognitive impairment. Filippin staining, single photon emission computed tomography perfusion, positron emission tomography metabolic, conventional magnetic resonance imaging, and magnetic resonance spectroscopy findings suggested a pathophysiological correlation with phenotype expression. This case expands the clinical and genetic spectrum of the rare adult-onset NPC disease phenotype © 2003 Movement Disorder Society

Key words: NPC1; adult-onset; neuroimaging studies

Niemann-Pick type C disease (NPC) is an autosomal recessive neurovisceral lipid storage disorder. Its frequency in the general population has been estimated at 1:100,000 live births. The phenotype of NPC (MIM 257220) is remarkably variable, including an acute, rapidly lethal form presenting at birth; an infantile and childhood form, presenting as a severe progressive disease leading to death in the second or third decade of life; an adolescent form, generally associated with a less aggressive phenotype. A rare adult-onset form with a slowly progressive course has been described in approximately 5% of patients. Recent biochemical data indicate three different metabolic defects: (1) sequestration of low density lipoprotein (LDL) -cholesterol in lysosomes, (2) premature pathological presence of cholesterol in trans-Golgi cisternae, and (3) altered intracellular sterols traffic.¹

Two complementation groups have been identified: (1) the NPC1 complementation group (>90% of patients) carrying mutations in the *NPC1* gene(18q11), which encodes a protein containing 13 transmembrane domains and a sterol-sensing

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