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Periodic Limb Movement During Sleep Following Cerebellar Infarct

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Introduction

Periodic limb movements during sleep (PLMS) are characterized by recurrent episodes of repetitive, stereotyped limb movements, predominantly occuring in the legs (American Sleep Disorders Association, 1997). It is observed in up to 30% of the general population (Trenkwalder, 2004). Uremia, iron deficiency, peripheral neuropathy, radiculopathy, spinal-cord and brainstem lesions are known to cause PLMS. PLMS has been reported after pontine lesion (Kim *et al*., 2003) or supratentorial cerebral infarction (Kang *et al*., 2004; Sechi *et al*., 2008). We present the first case in which PMLS has developed following cerebellar infarct.

Case report

An 87-yr-old right-handed man was admitted to our hospital emergency department with sudden onset of vertigo, nausea, and vomiting. He had bilateral dismetria and dysdiadokokinesia, more prominent on his right side. He also had ataxia. Brain computerized tomography was normal. Diffusion-weighted brain magnetic resonance imaging (MRI) revealed restricted diffusion in the right cerebellum. He was hospitalized at the Department of Neurology with a diagnosis of cerebellar infarction. On the first night after admission his wife reported abnormal movements in his feet during sleep. These involuntary movements recurred every 15-20 seconds and consisted of repetitive dorsiflexion of the bilateral ankles that were especially dominant in the right ankle. His wife had never observed such a movement before. His symptoms fulfilled the minimal criteria of the American Sleep Disorders Association for periodic limb movement disorders (American Sleep Disorders Association, 1997). A few days after admission brain MRI revealed a hemorrhagic infarct (intra-infarct hematoma) in the right cerebellum (Fig. 1). The patient had a history of hypertension, coronary artery disease, and acute myocardial infarction. He had been diagnosed with Parkinson's Disease (PD) two years ago. He had resting tremor in his left arm, bilateral rigidity, and minimal bradykinesia. He was not taking any medications for PD. He had no history of spinal cord disease or of obstructive apnea syndrome. Hemogram, serum electrolytes, erythrocyte sedimentation rate, glucose level, thyroid, renal, liver function, iron, ferritin, and vitamin B12 levels were all normal. EEG was also normal. Electromyography revealed

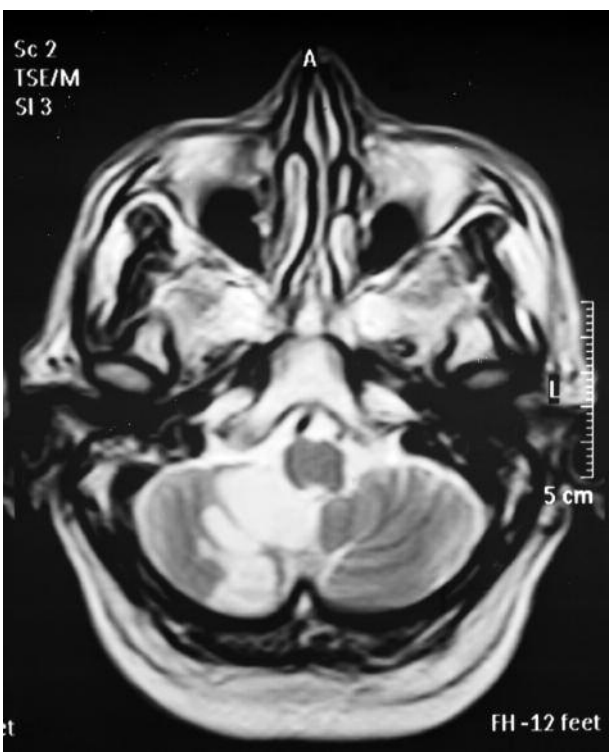

FIG. 1. — Axial T2-weighted brain magnetic resonance imaging scan shows hemorrhagic infarct in the right cerebellum.

no signs of peripheral neuropathy, myelopathy or lumbosacral radiculopathy. He was hospitalized for approximately a period of one month and his PLMS during sleep has continued during this period. Clonazepam therapy was started for PLMS, but no response was observed. Then levodopa therapy was started for both PD and PLMS. His symptoms and signs related to PD improved but his PLMS did not respond to levodopa. At follow-up two months after discharge there was no still improvement in his PLMS.

Discussion

Diverse conditions including uremia, iron deficiency, peripheral neuropathy, radiculopathy, spinal-cord and brainstem lesions are known to cause PLMS (Kim *et al*. 2003). Although PLMS can have several causes, the pathogenesis of PLMS has not yet been clarified. It is possible that PLMS can be produced by several independent mechanisms, and both central and peripheral mechanisms have been postulated (Bucher *et al.,* 1997). In view of its relationship to the sleep period, the generator of PLMS is presumed to be associated with sleep-related structures such as the reticular activating system (Kang *et al*., 2004). Several neurophysiologic and radiologic studies have indicated a role for brainstem generators in the pathogenesis of PLMS (Wechsler *et al*., 1986; Bucher *et al*., 1997). Wechsler et al. performed electrophysiological studies on six patients with PLMS; the most consistent electrophysiological abnormalities in PLMS patients were additional components of blink reflexes; these were found in all the studied patients. Both the PLMS and the blink reflex abnormalities were attributed to increased brainstem excitability (Wechsler *et al*., 1986). Two cases developing unilateral PLMS following pons infarcts have also been reported. It was suggested that the brainstem reticular formation is likely to play a role in the pathogenesis of PLMS (Kim *et al*., 2003). On the basis of findings from functional MRI Bucher and colleagues showed activation in the bilateral cerebellar and red nucleus in 12 patients with the combined sensory leg discomfort/PLMS (Bucher *et al*., 1997).

It is also possible that the nigrostriatal dopaminergic system could be involved in PLMS pathogenesis. PLMS is more common in patients with PD, a condition characterized by progressive nigrostriatal degeneration, than in the general population. Happe and colleagues used single-photon emission computed tomography (SPECT) and polysomnography to study eleven patients with idiopathic PD, and reported that PLMS numbers increased with the severity of striatonigral dopaminergic degeneration. They have suggested that nigrostriatal dopaminergic system might be involved in the pathogenesis of PLMS (Happe *et al*., 2003).

It has also been suggested that PLMS could be due to the loss of cortical or subcortical inhibition of a spinal and or brainstem pacemaker. Transcranial magnetic stimulation (TMS) studies have suggested that reduced cortical inhibition or an impairment of cortical–subcortical motor inhibitor pathways may take place in restless legs syndrome (RLS) (Provini et al., 2001; Quatrale *et al*., 2003). Quatrale and colleagues performed TMS examination on 15 untreated patients with primary RLS and 12 age-matched normal subjects, and an asymmetric distribution of sensorimotor symtoms and/or PLMS was found in 66% of RLS patients. Short interstimulus interval paired TMS showed significantly reduced inhibition and increased facilitation in the tibialis anterior muscles of patients compared to controls. These changes were evident in patients with RLS who had an asymmetric distribution of sensorimotor symtoms and/or PLMS. They suggested that the involvement of motor inhibitory pathways can cause disinhibition of the supraspinal network, and this could in turn influence the spinal cord generator, and thus motor inhibitory pathways are indirectly responsible for the appearance of PLMS (Quatrale *et al*., 2003). Some imaging studies have also suggested that loss of central descending pathway control over a spinal or brainstem pacemaker could be related to the mechanism of PLMS. For example, Iriarte *et al.* studied unilateral PLMS in the symptomatic limb of a patient with corticobasal degerenation in whom the pyramidal tract had undergone progressive degeneration. Positron emission tomography (PET) revealed hypometabolism in the left frontoparietal and subcortical areas in that patient. This supports the hypothesis that loss of central descending pathway control over a spinal or brainstem pacemaker is related to the mechanism of PLMS (Iriarte *et al*., 2001). In addition, Kang *et al.* reported PLMS development after supratentorial infarction. It was suggested that the close temporal relationship between the onset of PLMS and stroke, and unilateral PLMS in the paretic leg, support the idea that PLMS in that patient resulted from an ischemic stroke in the corona radiata. They proposed that PLMS is the result of a pyramidal tract lesion in which the loss of cortical or subcortical inhibition of the brainstem generator might cause PLMS (Kang *et al*., 2004). Sechi *et al.* reported a case of PLMS/RLS following ischemic infarction within the right lenticulostriate area, and therefore suggested that disinhibition of either the ascending sensori-

motor cortex or the descending inhibitory pathways might lead to RLS and PLMS (Sechi *et al*., 2008).

To our knowledge, this is the first case of PLMS following cerebellar infarction. It could be possible that PLMS might be a coincidental finding in our patient. Nevertheless, his wife and children had not noticed such leg movements before the stroke. Indeed, the close temporal relationship between the stroke and the onset of PLMS in our patient implies a cause–effect relationship rather than coincidence. We suspect that ischemia of the posterior circulation, or a mass effect of the lesion, could affect the the brainstem reticular formation and lead to the development of PLMS. In 19 patients with restless legs syndrome, Bucher and colleagues found with functional MRI bilateral activation of the cerebellum and contralateral activation of the thalamus during sensory leg discomfort and additional activation of red nucleus and brainstem during combined sensory discomfort and periodic leg movements (Bucher *et al*., 1997). The cerebellum is known to receive proprioceptive information from the periphery via the spinocerebellar tracts, and in turn projects via the cerebellar nuclei to the cells of origin of various descending motor pathways (Mitoma *et al*., 2000). The cerebellum might thus play a pivotal role in a condition like PLMS which combines sensory and motor abnormalities. Whether cerebellar lesions cause PLMS directly or via brain stem compression remains to be determined by further comprehensive studies of relevant patients.

REFERENCES

American Sleep Disorders Association, Periodic limb movement disorder. In: International classification of sleep disorders revised edition, (ICSD-R), Davies printing, Rochester MN; 1997:65-8.

Bucher SF, Seelos KC, Oertel WH, Reiser M, Trenkwalder C. Cerebral Generators involved in the pathogenesis of the restless legs syndrome. Ann Neurol. 1997;41:639-45.

Happe S, Pirker W, Klosch G, Sauter C, Zeitlhofer J. Periodic Leg movements in patients with Parkinson's Disease are associeted with reduced striatal dopamine transporter binding. J Neurology. 2003;250: 83-6.

Iriarte J, Alegre M, Arbizu J, Castro P. Unilateral Periodic Limb Movements During Sleep in Corticobasal Degeneration. Movement Disorders. 2001;16: 1180-3.

Kang SY, Sohn YH, Lee K, Kim JS. Unilateral periodic limb movement in sleep after supratentorial cerebral infarction. Parkinsonism&Related Disorders. 2004;10:429-31.

Kim JS, Lee SB, Park SK, Han SR, Kım YI. *et al*. Periodic limb movement during sleep developed after pontine lesion. Movement Disorders. 2003; 18:1403-5.

Mitoma H, Hayashi R, Yanagisawa N, Tsukagoshi H. Gair Disturbances in Patinets With Pontine Medial Tegmental Lesions. Archives of Neurology. 2000; 57:1048-57.

Provini F, Vetrugno R, Plazzi G, Solieri L, Lugaresi E. *et al*. Motor pattern of periodic limb movements during sleep. Neurology. 2001;57:300-4.

Quatrale R, Manconi M, Gastaldo E, Eleopra R, Tugnoli V. *et al*. Neurophysiological study of corticomotor pathways in restless legs syndrome. Clinical Neurophysiology. 2003;114:1638-45.

Sechı GP, Agnetti V, Galıstu P, Murgıa B, Marrosu F. *et al*. Restless legs syndrome and periodic limb movements after ischemic stroke in the lenticulositriate region. Parkinsonism & Related Disorders. 2008;14:157-60.

Trenkwalder C. Restless legs syndrome and periodic limb movements. Adv Neurol. 2002;89:145-51.

Wechsler LR, Stakes JW, Shahanı BT, Busıs NA. Periodic Leg Movements of Sleep (Nocturnal Myoclonus): An Electrophysiological Study. Ann Neurol. 1986; 19:168-73.

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