Case Report

Restless legs syndrome related to hemorrhage of a thoracic spinal cord cavernoma

Malik Hamdaoui¹, Elisabeth Ruppert^{1,2,3}, Henri Comtet^{1,2,3}, Ulker Kilic-Huck^{1,2,3}, Valérie Wolff^{3,4}, Marc Bataillard^{1,2,3}, Patrice Bourgin^{1,2,3}

¹Department of Neurology, Sleep and Electrophysiology Clinic, University of Strasbourg, Strasbourg, France,

²Institute for Cellular and Integrative Neurosciences, Strasbourg, France, ³Fédération de Médecine Translationnelle de Strasbourg (FMTS), Strasbourg, France, ⁴Department of Neurology, Stroke Unit, University of Strasbourg, Strasbourg, France

Context: Restless legs syndrome (RLS) is a common neurological disorder characterized by an irresistible urge to move the lower limbs often accompanied by unpleasant sensations in the legs, worsened at rest and in the evening. Symptoms are improved by movement. Its pathophysiology remains poorly understood. Lesion-related RLS has been reported, mainly in cases of stroke-related RLS involving the brainstem and lenticulostriate nuclei. Only few data of RLS in a context of spinal cord injury have been reported.

Findings: We report the case of a woman with secondary RLS due to hemorrhage of a spinal cord cavernoma located at T9-T10. Following recovery from the acute phase of the hemorrhage, the patient began to complain about restlessness in her legs causing impaired sleep and daytime somnolence. Polysomnographic investigations found a high index of periodic leg movements during sleep (71/hour), but no sleep disordered breathing. Iron stores were normal. Relief of symptom's severity was obtained with gabapentin 600mg in the evening.

Conclusion/Clinical Relevance: We hypothesize a possible involvement of the diencephalospinal pathway in the patient's RLS pathophysiology. A systematic study of focal lesions associated with RLS may contribute to improving our understanding of the pathophysiological mechanisms underlying this condition. The frequency of RLS associated with lesions of the spinal cord might be underestimated. Clinicians should be aware of spinal cord lesion-related RLS, especially as efficient treatments are available.

Keywords: Willis-Ekbom disease, Secondary restless legs syndrome, Lesion-related RLS, Lesion-related PLM, Lesion-associated RLS

Introduction

Restless legs syndrome (RLS) is a common neurological disorder, characterized by an urge to move limbs due to unpleasant or uncomfortable feelings in the legs. Symptoms occur at rest, are relieved by motor activity and are worsened in the evening or at night.^{1,2} RLS prevalence is estimated at 10% of the occidental populations.³ One distinguishes an idiopathic form with early-onset and frequent family history from a late-onset secondary form, but the neural substrates underlying its pathophysiology remain to be identified.^{2,4}

Some hypotheses are derived from the impact of different drugs on RLS severity, especially the therapeutic effect of dopaminergic agonists and secondary forms due to medications such as neuroleptics and antidepressants (tricyclic or selective serotonin reuptake inhibitors) or impaired iron stores.⁵ Few cases of stroke-related RLS have been reported,⁶⁻⁹ mainly involving the brainstem⁶⁻⁸ and lenticulostriate region.^{6,9} Cases of RLS in a context of spinal cord injury have been described.¹⁰⁻¹² We report the case of a patient who developed secondary RLS due to hemorrhage of a spinal cord cavernoma located at T9-T10. We discuss how this lesion could affect the diencephalospinal pathway, a dopaminergic circuit presumably implicated in RLS pathophysiology.¹³

Correspondence to: Elisabeth Ruppert; Centre des troubles du sommeil - Hôpital Civil, 1, place de l'Hôpital, BP 426, Cedex, 67091 Strasbourg, France. Ph: +33 3 88 11 64 30; Fax: +333 88 11 51 53. Email: elisabeth.ruppert@chru-strasbourg.fr

Report of case

A forty-seven-year-old woman complained of restlessness in her legs causing impaired sleep and daytime somnolence. Symptoms had appeared fourteen years earlier when she had presented hemorrhage of a spinal cord cavernoma revealed by a progressively regressive sensory-motor deficit of the lower limbs and sphincter control problems (Fig. 1). She had no other relevant medical history other than type 2 diabetes mellitus and high blood pressure, both without complications and well controlled using a low dosage of metformin (500mg daily) and telmisartan 40 mg daily. BMI was normal at 23.6 kg/m².

Following regression of the acute symptoms due to spinal bleeding, the patient described emergence of paresthesia in her legs with an urge to move that appeared at rest, transiently relieved by movements and worsened in the evening and at bedtime. RLS symptoms in the lower limbs were described as being clearly different from the initial sensory-motor deficits, and no other condition could explain the temporal relationship with the onset of RLS. The patient had no residual sensory symptoms from the spinal hemorrhage, but a slight paresis of the right lower limb persisted, as well as few neurogenic bladder discomforts. Concurrently, sleep had become non-restorative and total sleep time shortened because of sleep onset and sleep maintenance insomnia. Symptoms fulfilled the criteria of the International Classification of Sleep Disorders,² and RLS severity was evaluated as moderate (17/40) using the International Restless Legs Syndrome Severity Scale (IRLSS).¹⁴ Somnolence was evaluated as very severe using the Epworth Sleepiness Scale (21/24). The patient's body iron status was within the normal range with ferritin at 155µg/l (normal: 58–319). Video-polysomnography was performed and scored manually according to the criteria of the AASM scoring manual version 2.1. Sleep was highly

fragmented with an arousal index at 58.2/hour, mainly due to a high index of periodic leg movements during sleep (PLMS) at 71.0/hour. PLMS are frequently associated with RLS and characterized by stereotyped, repetitive movements of the lower limbs during sleep. Most commonly one observes an extension of the great toe and the ankle, with occasional flexion at the knee and hip.² Our patient had no sleep disordered breathing with a normal apnea-hypopnea index at 3.4/hour. Although RLS severity was only evaluated as moderate using IRLSS, rotigotine 2mg daily was introduced given the important daytime sleepiness with highly fragmented sleep due to PLMS. As symptoms remained insufficiently relieved, rotigotine 2mg was replaced by pregabalin 50mg in the evening. Six months later, the patient stopped pregabalin because of side effects and insufficient efficiency, replaced by gabapentin 600mg in the evening. As evaluated by clinical follow-up six months later, gabapentin therapy allowed a satisfactory partial relief of symptom's severity.

Discussion

Lesion-related RLS has been reported, mainly in cases of post-stroke RLS^{6–9} involving the brainstem^{6–8} and lenticulostriate nuclei.^{6,9} Only few cases of RLS or PLMS in a context of spinal cord injury have been reported.^{10–12,15,16} Frequency of spinal cord lesion-related RLS might be underestimated.¹²

As RLS emerged in the patient following spinal bleeding, we consider that she had lesion-related RLS, even though a recall bias cannot be excluded. Lesion-related RLS has been described to appear either as an initial symptom of the lesion,⁷ or concomitantly,^{8,9} or following the lesion symptoms after a certain delay,^{8,9} suggesting that a post-hemorrhage plasticity phenomenon could be involved.

How can a thoracic spinal cord lesion at T9-T10 impair pathophysiological pathways of RLS? We hypothesize a possible implication of the dopaminergic diencephalospinal pathway¹³ involving the dopaminergic neurons of the hypothalamic A11 area. These diencephalic neurons seem to have inhibitory actions and projections to multiple targets in the brain and throughout the spinal cord such as the neocortex, the serotonergic dorsal raphe nucleus, the sympathetic preganglionic neurons of the intermediolateral nucleus, the sensory dorsal horn of the spinal cord and interneurons. The interruption of such projections at the level of the thoracic spinal cord could contribute to both the sensitive symptoms of RLS and the motor phenomenon occurring during PLMS.^{12,13} However,

Figure 1 T2-weighted sequences in spinal cord MRI of a thoracic cavernoma (arrow) at T9-T10 in a transversal (a) and sagittal (b) section.

this is hypothetical, as the exact neural pathway remains poorly understood. The study of RLS associated with focal lesions may represent an original approach to improving our understanding of RLS pathophysiology.

Although the frequency of spinal cord lesion-related RLS is unknown,¹² clinicians should be aware of this condition, especially as efficient treatments are available.^{17,18}

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