CASE REPORT

Acute exacerbation of restless legs due to cervical spinal cord ischaemia

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SUMMARY

We present a 60-year-old male patient with an acute exacerbation of restless legs due to cervical spinal cord ischaemia. This case supports the hypothesis that interruption of spinal cord pathways are part of the aetiology of restless legs syndrome.

BACKGROUND

The restless legs syndrome (RLS) is a disorder characterised by an unpleasant sensation in the legs, accompanied by a strong urge to move them.¹ It is most prominent at rest and has a circadian rhythm. RLS affects 5–10% of the general population, and it may be a primary (idiopathic) or secondary disorder. Secondary types are mainly associated with iron deficiency, uraemia, pregnancy, neuropathy and myelopathy. Relevant literature describes a small number of RLS cases associated with spinal cord lesions, of which only one is due to spinal cord infarction.^{2–3} To our knowledge, this is the first case report of an acute exacerbation of RLS as a presentation of cervical spinal cord ischaemia.

CASE PRESENTATION

A 60-year-old male patient with a 30-year history of RLS presented at the emergency department with an extreme urge to move his legs. This patient had already been diagnosed with RLS, according to the international RLS (IRLS) criteria, 2 years previously at our outpatient clinic. His IRLS score at that time was 24/40, which is classified as severe. A dose of 0.25 mg/day of ropinirole has clearly improved his symptoms.⁴ Neurological examination showed no clues pointing to a secondary form of RLS. The day before presentation, he had experienced sudden and severe neck pain, which radiated to both the shoulders. The pain decreased in the supine position and re-emerged in the upright position. It was accompanied by a weakness of his proximal shoulder muscles with a feeling of 'light-headedness'. To relieve the pain he favoured the supine position, but in the supine position a very unpleasant leg sensation started, and this came with an extreme urge to move his legs. He recognised this leg sensation as the same as his RLS leg sensation; however, it was much worse than he had ever experienced before. The patient decided to go to the emergency room (ER) when this acute and very disturbing exacerbation of his already established RLS started. When he presented at the ER, his IRLS score was 40/40, which is classified as very severe.

On examination, it was evident that the patient was completely unable to sit or to lie still. His blood pressure was 110/80 mm Hg in the supine position with a drop of 40 mm Hg systolic blood pressure in the upright position (orthostatic hypotension). There was a decreased sense of pain in the C4–C6 dermatomes, but touch and vibration senses were normal. Muscle strength and tonus in his arms and legs were normal, but his gait was spastic and his tendon reflexes were normal with bilateral extensor plantar responses. Bladder catheterisation showed 1 litre urinary retention. A cervical spinal cord lesion was suspected.

INVESTIGATIONS

MRI study of the cervical spine revealed signal hyperintensities on T2-weighted images and diffusion-weighted images, with reduced signal intensity on the apparent diffusion coefficient images (ADC) at the centre of the C3–C6 levels of the spinal cord (figure 1A,B). A diagnosis of cervical spinal cord infarction was made. In order to identify the cause of stroke, extensive diagnostic work was done. Laboratory testing and cerebrospinal fluid examination showed no abnormalities. CT angiography showed no vascular abnormalities and a dissection of the vertebral arteries was specifically excluded.

OUTCOME AND FOLLOW-UP

Four months later, he still experienced constipation and difficulty with voiding (a delayed urge). His gait was normal and there were no signs of orthostatic hypotension. With the application of the rotigotine transdermal patch (2 mg) and 0.25 mg a day of ropinirole, the patient no longer experienced the urge to move.

DISCUSSION

We presented a 60-year-old male patient with an acute and extreme exacerbation of RLS due to cervical spinal cord ischaemia. The relevant literature describes a small number of RLS cases associated with spinal cord lesions. To our knowledge, this is the first case report of a patient in whom an acute exacerbation of RLS was the first symptom of cervical spinal cord ischaemia. There is another case report of RLS due to spinal cord ischaemia by Tings *et al.*² Their patient presented with a paraparesis and hypaesthesia of both the legs and his RLS symptoms occurred 4 weeks later. Therefore, spinal cord ischaemia should be in the differential diagnosis in the case of an acute exacerbation of RLS and 'acute' or semi-acute new-onset RLS.

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Figure 1 (A) Axial MRI of T2-weighted images made 36 h after symptom onset showing increased signal in the spinal cord at level C3–C6. (B) Axial MRI of T2-weighted images showing increased signal in the spinal cord at level C3–C6, 3 days after symptom onset.

Several other cases of secondary RLS due to spinal cord lesions induced by diverse causes such as multiple sclerosis, cervical spondylotic myelopathy, spinal cord injury, Lyme borreliosis and herpes zoster myelitis have been reported.^{2 3 5 6}

Our case supports the hypothesis that spinal pathways are involved in the pathogenesis of RLS.

The exact pathophysiology of RLS is uncertain. However, RLS is a network disorder. Many regions of the nervous system contain structures that are involved in somatosensory perception and the generation of movement.¹ This diversity makes it reasonable to assume that changes in different parts of the nervous system may cause RLS. Currently, it is unclear as to whether RLS originates from the cortical, subcortical or in the spinal cord. Several experimental animal studies as well as case reports of patients who developed RLS in association with spinal cord lesions have given rise to the hypothesis that interruption of the spinal pathways is a part of the aetiology of RLS.^{2 3 5 6} However, the exact role of the spinal cord in the origination of RLS is not yet completely understood. What we do know is that dopamine and iron deficiency seem to be critical in the RLS aetiology.^{1 7} Links between iron deficiency and reductions in the central dopaminergic state are clues that RLS reflects changes in dopamine signalling. It has been suggested that A11 neurons play a central role. These neurons are located in the hypothalamus and are the only source of dopaminergic innervation to the spinal cord.⁸ Dysfunction of the A11 is hypothesised to change the sympathetic activity on muscle afferents and spinal sensory signalling in a way that induces RLS symptoms. The A11 neurons project to the sensory dorsal horn and the intermediolateral nucleus (IML). The dopaminergic projections of the A11 on the IML exert direct inhibitory actions on sympathetic preganglionics. Thus, an impairment of the A11 inhibitory function would shift the balance of descending control of the sympathetic preganglionics towards excitation. This leads to the activation of high threshold muscle afferents and focal akathisia. In an animal experimentation study, A11-lesioned mice showed increased locomotor activity in a dark room.⁷ The cervical spinal cord ischaemia in our patient possibly interfered with the descending A11 dopamine pathway to the spinal cord and may thus have caused the RLS exacerbation and the autonomic dysfunction in our patient.

It is also possible that the impairment of the sensory spinal pathway, as seen in our patient, influences the RLS exacerbation. Alteration of sensory information reaching the brain may cause a 'bias shift', especially in this patient who is prone to restless legs. Damage of the sensory spinal pathway as a cause of RLS has been described before as well.^{2 3 9–11} As was mentioned

above, the dysfunction of A11 spinal dopaminergic spinal projections is thought to contribute to altered sensory signalling. Normally, A11 projections exert inhibitory control over ascending nociceptive input via D2-like receptor-depending mechanisms. Thus, less A11 function could lead to increased ascending nociception. Indeed, with neurophysiological testing, evidence was found for hyperexcitability and disinhibition of the sensory spinal cord structures shown by Hoffmann's reflex and flexor reflex studies in RLS patients.^{10 12} The observation that RLS patients show hyperalgesia but no dynamic mechanical allodynia illustrates central sensitisation within the spinal cord.⁹

According to the 2012 European guidelines on the management of RLS, dopaminergic agents are the first-line treatment for primary RLS. Although their working mechanisms are not fully clarified as yet, it is assumed that dopaminergic agents stimulate D2-like (D2, D3 and D4) receptors. This stimulation, just like endogenous dopamine, exerts direct inhibitory actions on sympathetic preganglionics and inhibitory control over the ascending nociceptive input.

For our patient, the application of a rotigotine transdermal patch and 0.25 mg a day of ropinirole proved to be very effective. This good effect of dopamine agonists has been described before in patients with secondary RLS due to spinal cord lesions.³ The assumed central role of the dopaminergic A11 neurons in the pathophysiology of RLS and specifically in the origin of the RLS exacerbation of our patient is described above. The terminals of A11 neurons lack D2 receptor-mediated presynaptic regulation of dopamine synthesis; thus, we presume that in our patient the dopamine agonists exert postsynaptic actions on the D2-like receptors in the spinal cord itself.^{1 13}

For our patient, an acute RLS exacerbation was the alarming symptom that brought him to the ER, where it turned out to be the presenting symptom of cervical spinal cord ischaemia. Spinal cord ischaemia is rare. It has a diverse presentation and the symptoms depend on the affected spinal cord level. It may be difficult to distinguish spinal cord ischaemia from other causes of spinal cord disorders, such as myelitis transversa, multiple sclerosis or spinal cord compression. Clues that point to a vascular origin are acute onset, acute pain and often symptoms that worsen after exercise. An MRI scan with diffusion, ADC mapping and the administration of gadolinium is essential to make the correct diagnosis.¹⁴

In summary, this case describes an acute exacerbation of restless legs due to spinal cord ischaemia. Our case supports the hypothesis that interruption of the spinal cord pathways are part of the aetiology of RLS. Further research is needed to unravel the complex RLS pathophysiology.

Learning points

- ▶ An acute exacerbation of restless legs syndrome (RLS) can be the presenting symptom of cervical spinal cord ischaemia.
- ▶ It is currently unclear as to whether RLS originates from the cortical, subcortical or in the spinal cord.
- ▶ Dopamine and impairment in iron availability seem to be critical in the RLS aetiology and A11 neurons are the only source of dopaminergic innervation to the spinal cord.
- ▶ The dopaminergic projections of A11 on the intermediolateral nucleus exert direct inhibitory actions on sympathetic preganglionics, and impairment of the A11 inhibitory function shifts the balance of descending control of the sympathetic preganglionics towards excitation.
- ▶ The cervical spinal cord ischaemia in our patient possibly interfered with the descending A11 dopamine pathway to the spinal cord and thus may have caused the RLS exacerbation.

Competing interests None.

Patient consent Obtained.

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