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CASE REPORT

Restless leg syndrome in spinal cord injury: case report

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CASE DESCRIPTION: Restless leg syndrome (RLS) is a condition infrequently reported in spinal cord injury that causes an uncomfortable sensation in the legs and an urge to move them. We report a case involving a 63-year-old man with incomplete paraplegia with an onset of RLS four years post injury.
FINDINGS: Based upon history, pramipexole was prescribed for the presumptive diagnosis of RLS, with good effect. Initial workup revealed an anemia (hemoglobin of 9.3 gram/deciliter (g/dl)) and iron deficiency (ferritin of 10 microgram/liter (µg/L)), necessitating further evaluation.
CONCLUSION: Due to the complexities in diagnosing RLS in patients with SCI, it is important to be cognizant of symptoms and to consider this diagnosis to initiate the appropriate work-up for an etiology, of which iron deficiency anemia is common.

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INTRODUCTION

Restless leg syndrome (RLS) is a sensorimotor disorder associated with an uncomfortable sensation in the legs, and the urge to move them, that may significantly affect quality of life [1]. RLS can either result from primary (idiopathic) or secondary causes, such as iron deficiency, pregnancy, peripheral neuropathy, and others [2]. While RLS affects approximately 5–10% of the general population, the diagnosis can be particularly challenging in persons with spinal cord injury (SCI) with absent or reduced motor activity [3], as well as the presence of altered sensation and spasticity. As a result, there have only been a few reported cases in the literature of RLS in SCI [4–10]. We report a case of RLS in a patient with incomplete paraplegia and discuss the clinical relevance for professionals in SCI Medicine.

CASE REPORT

A 63-year-old male with a history of incomplete paraplegia (T8 American Spinal Injury Association Impairment Scale C) presented for a chief complaint of "poor sleep". Initial SCI, four years prior to presentation, was related to thoracic spine myelopathy from degenerative arthritis, with progressive lower extremity weakness and thoracic back pain beginning. He underwent surgical decompression of a T10-T11 herniation and segmental spinal stabilization with a spinal fusion of T9-L1, followed by comprehensive rehabilitation. Additional pre-SCI medical history includes diabetes mellitus type II (HgbA1c 6.7), obesity, hypertension, as well as a history of kidney stones (predates SCI). Residua of his SCI includes lower extremity weakness, spasticity, neurogenic bowel and bladder (intermittent catheterization program) and wheelchair dependence for his mobility. His spasticity medications included baclofen 15 milligrams (mg) four/day. Additional medications include the following: Lisinopril 40 mg/day, Metformin 1000 mg BID, Tamsulosin 0.4 mg q/day, Rosuvastatin 5 mg/day, Amlodipine q/day, Pioglitazone 30 mg/day, Ozempic 0.5 mg q/week. Loratadine 10 mg/day, Vit D3, Colace, Senna, and Flonase q/day. No other medical issues or changes reported, and no significant family history or allergies.

Upon further questioning of his presenting symptoms, he reported uncomfortable sensations in his legs (right >left) in the evenings prior to sleeping. The duration of his symptoms before seeking treatment was approximately one month, with his symptoms gradually increasing in intensity. The sensations were described as spasm-like and caused the urge to stretch and move his legs, which offered some temporary relief. He had no complaints of cramping, and the symptoms reportedly only occurred at night when he rested. No report of sleep apnea symptoms, but the complaints of the described sensations and spasms would often wake him, leading to poor sleep, which reportedly significantly affected his ability to function. He increased his baclofen to 20 mg at night and later to 30 mg (on his own), with little relief. He reported no change in sensation or strength.

On examination, his sensory level remained unchanged at the T8 level. Motor examination showed no change from previous examinations. Upper extremity key muscles were intact (5/5), right hip flexors 2/5, knee extensors 4/5, ankle dorsiflexors, extensor halluces longus and ankle plantar flexors were 4/5. Left lower extremity key muscles were 0/5.

Initial diagnosis based upon symptoms and lack of change on his examination was RLS. No diagnostic challenges, such as those related to access to testing, financial considerations, or cultural reasons, were present. Pramipexole 0.125 mg/day was prescribed for one week, to be increased to 0.25 mg if no side effects occurred. Labs were ordered and key findings included a hemoglobin of 9.3 g/dL, hematocrit of 32.2%, and ferritin of 10 µg/L. The remainder of his complete blood count and chemistries were within normal limits. (BUN and creatinine were

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within normal limits at 12 mg/dl and 0.76 mg/dl, respectively). Once lab results were obtained (at day #10), the individual was called. He adhered to treatment with pramipexole, and he tolerated the medication well. He reported excellent improvement in his symptoms, although no scale was used to evaluate his symptom progression or resolution either before or after treatment with pramipexole.

His primary care physician was alerted to initiate a workup for his iron deficiency and anemia. Results of an endoscopy and colonoscopy 4 weeks later showed multiple prolapsed hemorrhoids and two mild bleeding gastric ulcers, and treatment with ferrous sulfate 325 mg once a day was initiated. Additional follow up one week later revealed complete symptom resolution, indicating great prognosis. His pramipexole dose was then decreased to ½ tablet (0.125 mg) per day because of symptom resolution. There were no adverse or unanticipated events during his care. The patient continues to be followed with plan to discontinue his pramipexole.

DISCUSSION

The diagnosis of RLS usually requires four criteria [11]. These include 1) an urge to move the legs due to unpleasant sensations associated with periods of rest or inactivity; 2) improvement with either passive or active movement (in SCI patients, even rubbing or washing the limbs can provide improvement in symptoms); 3) worsening of symptoms at rest; 4) worsening of symptoms in the evening or at night. Since many people with SCI have reduced or absent sensation and motor function of their lower extremities, as well as the presence of altered sensation and spasticity, it can be challenging to assess these criteria due to their inability to voluntarily move their legs. While challenging to notice and ultimately diagnose, it is extremely important for clinicians to consider RLS because of the effects on one's quality of life and the potential to find the underlying cause.

Kumru et al. [11] reported in a retrospective descriptive study that 35 of 195 (17.9%) patients with SCI who attended their routine annual follow up presented with symptoms that fulfilled the four criteria used to diagnose RLS. This percentage was greater than the prevalence of RLS in the general population (5–10%). Ten of the 35 patients with RLS were treated with a mean 0.19 ± 0.03 mg pramipexole, with improvement within 2 months of treatment. The majority of RLS cases (62.9%) occurred within the first year following SCI [11]. In our case, the individual did not present with symptoms until four years later, making this case rather unusual when considering the timeline. This case highlights the importance of keeping RLS in the differential diagnosis when SCI patients present with abnormal sensations of the limbs, even years after the initial SCI.

The pathogenesis of RLS is still unclear, but there are many factors that seem to play a role including genetics, the central dopaminergic system, and iron balance [12]. The central dopaminergic system has been considered due to evidence of clinical improvement following dopaminergic treatment [2]. Other factors that are involved in the pathophysiology of RLS include GABA and adenosine neurotransmitter pathway dysfunctions [12] and abnormal activation of brain areas such as the cerebellum, midbrain, dorsolateral prefrontal cortex, anterior cingulate cortex, pre- and post-central gyri and putamen [13–17]. Additionally, brain iron deficiency, specifically within the substantia nigra, is found almost universally in patients with RLS according to various human and animal model studies [12, 18–25]. Two studies by Earley et al. [21, 22] looked specifically at ferritin levels within cerebrospinal fluid and found an association between low ferritin levels and RLS. This overwhelming evidence suggests a major role of dopamine and iron within RLS.

The patient presented in this case report fulfilled the four criteria required for the diagnosis of RLS. A review of his bloodwork revealed a diagnosis of iron deficiency anemia with a low ferritin level of 10 µg/L (normal range: 12–300 µg/L). Workup for his anemia with endoscopy and colonoscopy revealed the presence of two mild bleeding ulcers and level 4 prolapsed hemorrhoids. It is possible that, in addition to his anemia, there exists either a dopamine imbalance or dysfunction within the central dopaminergic system that is also contributing to his symptoms. This is suggested due to his relief of symptoms following only 9 days of treatment with pramipexole, a dopamine agonist that acts in the brain. His iron deficiency anemia was also treated with ferrous sulfate, which likely provided further symptom relief alongside pramipexole. This clinical outcome provides a strength associated with this case report because he was likely accurately diagnosed and effectively treated.

Another possible etiology behind RLS is medication use, providing a source of limitation associated with this case report. A systematic review by Kolla et. al. found that antidepressants such as SSRIs, duloxetine, and tricyclic antidepressants slightly increased the risk of developing or worsening current RLS symptoms [26]. In addition to antidepressants, other medications found to be associated with the onset and/or exacerbation of RLS include many antipsychotics, such as olanzapine and quetiapine, and many antiepileptics, such as zonisamide and topiramate [27]. While this individual was not currently taking nor had he recently been taking an antidepressant, antiepileptic, or antipsychotic, he had been taking Loratadine, a common antihistamine, for over 10 years for treatment of seasonal allergies. Given his long-term treatment and relief, this medication was not initially discontinued. Antihistamines have been shown to be associated with RLS [28, 29], but given his symptom relief with pramipexole and ferrous sulfate, Loratadine was not believed to have played a role in his RLS. Lastly, Kumru et al. revealed many cases of comorbid neuropathic pain and RLS [10]. While our patient has a medical history of diabetes mellitus type II, his diabetic control was stable (HgbA1c 6.7) and his symptoms resolved with pramipexole and ferrous sulfate, suggesting his RLS was not directly related to diabetes.

PATIENT PERSPECTIVE

"A few years after developing a spinal cord injury, I had significant difficulty sleeping because of the uncomfortable sensations in my legs, mostly noted at night. I was started on a new medication and the symptoms improved. Blood tests were taken and then an endoscopy and colonoscopy were done.

I give permission to report my case to a journal with all my personal identifiers removed."

CONCLUSION

This case report of RLS in a person with SCI highlights the importance of considering this diagnosis in the SCI population. While symptomatology may vary from the non-SCI population his report emphasizes the benefit of treatment and the need to uncover the etiology of a very troubling yet treatable condition.

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COMPETING INTERESTS

The authors declare no competing interests.

ADDITIONAL INFORMATION

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