

Case Report

Dopa responsive headache: Restless head syndrome or a cephalic variant of restless legs syndrome?

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ABSTRACT

Restless legs syndrome (RLS) is a common but highly undiagnosed sensorimotor disorder. It typically affects the lower extremities. However, various other parts of the body can be involved, such as the arms, the abdomen, the face, the oral cavity, head-neck, and the genital area. In addition, RLS is linked with a large number of comorbid conditions, including various headache disorders. Herein we are reporting two cases of RLS who also had headaches. The headaches fulfilled the criteria of chronic tension-type headache (CTTH). The administration of levodopa provided improvement in both RLS and CTTH. We suggest that that headache in a subset of patients with RLS may be the part of RLS symptoms complex.

Keywords: Dopamine, headache, restless legs syndrome

Introduction

Restless legs syndrome (RLS) typically involves legs. However, several reports suggest that other body parts such as arms, abdomen, face, oral cavity, and genital area may be involved.^[1] In addition, RLS is linked with a large number of comorbid conditions, including various headache disorders.^[2-3] Herein, we are reporting two cases of RLS who also had tension-type headache (TTH). Both headaches and RLS responded to levodopa therapy. The study did not need approval by the ethics committee as per the local regulations for the retrospective case reports. Written informed consent was taken from the patients to publish this observation.

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Received: 16-04-2020

Revised: 10-06-2020

Accepted: 01-07-2020

Published: 25-08-2020

Case-1

A 35-year old woman had an unpleasant sensations in both legs for the last 4-year. She described an unpleasant sensation as a combination of burning feelings, pulling sensation, ants-crawling, and pain. The patient noted symptoms usually while relaxing, especially in the evening and during night. The unpleasant sensations were relieved by walking and movement of the limbs. Occasionally, she had an unpleasant sensation even in both arms. The discomfort interfered her sleep and it was accompanied with frequent wake up at night. Her husband confirmed the presence of irritability and restlessness while sleeping. Her sleep was not refreshing and used to take several naps during daytime. The symptoms were infrequent earlier, and it increased to almost daily for the last 12 months. She also had headaches for the several years. The headache was holocephalic and non-throbbing. It was infrequent earlier and gradually increased to 4–5 times per week for the last 6 months. The headache attacks varied for 2–6 hours. The headache mostly fluctuated from mild to moderate in intensity and the patient could continue her routine activities as usual. The headache used to be more severe in the evening

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DOI:
[10.4103/jfmpc.jfmpc_640_20](https://doi.org/10.4103/jfmpc.jfmpc_640_20)

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How to cite this article: Prakash S, Prakash A. Dopa responsive headache: Restless head syndrome or a cephalic variant of restless legs syndrome? J Family Med Prim Care 2020;9:4431-3.

and night. There was no nausea, vomiting, phonophobia, or photophobia. She consulted several physicians for her lower limb symptoms, but never for headache. Prior treatment with various drugs (including antidepressants, painkillers, and multivitamins) did not provide any remarkable and consistent effects on lower limb symptoms. Physical examination and laboratory investigations were unremarkable. The unpleasant sensations of the legs met the International Restless Legs Syndrome Study Group (IRLSSG) criteria for RLS, and headache fulfilled ICHD-3 criteria for CTTH.^[4,5]

We prescribed levodopa plus carbidopa (110/10 mg) and subjected the patient for various investigations to identify the secondary cause of RLS and associated headaches. The patient reported after 3 weeks, and she noted a marked response in her lower legs' symptoms and associated insomnia. There were just 2–3 episodes of RLS symptoms over 3 weeks. Moreover, she noted a response in the headache frequency. There were just 2 headache episodes over the same period. We followed the patient for 18 months. She discontinued the drug for at least six occasions over the follow-up period. Skipping of the drug always led to the reappearance of both RLS and headaches in a few days. Reinstitution of the drug provided complete relief in both RLS and headaches on each occasion.

Case-2

A 36-year-old man had a 6-year history of headache. The frequency gradually increased over the years and had almost daily headaches for the past 12 months. The headache was holocephalic, constricting in character, and mostly fluctuated from mild to moderate in intensity. However, it used to be more severe in the evening and night. On questioning, the patient admitted having uncomfortable sensation in both legs for 7–8 years. It was occasional in the early stage (4–5 days in a month). However, it increased to become daily for the last 12 months. The uncomfortable sensation was severe in the evening and night-time. The uncomfortable sensation was continuous with worsening in the evening and night-time. He felt the need to move his legs. Walking improved the symptoms. He also had a complaint of increasing insomnia for the past 8–9 months.

The patient didn't get any significant responses on the headaches by previous therapies. The patient considered his lower limbs symptoms because of overwork or excessive physical activities and never consulted any physicians for it. Physical examinations and laboratory investigations were unremarkable. The lower limbs' symptoms met the criteria for RLS. He also fulfilled the ICHD-3 criteria for CTTH. Based on our Case 1 experience, we started levodopa/carbidopa (110/10 mg) for RLS. Within a few days of initiating the treatment, RLS started to improve, and there was almost complete response in about a 2-week duration. In parallel, the headache frequency also declined markedly, just 3–4 attacks in a month. The patient was followed-up for 12 months, showing a consistent and complete response. Skipping of the drug always led to the reappearance of RLS,

headaches, and insomnia in a few days. Re-initiation of the drug always provided complete relief in both RLS and headaches.

Discussion

Both cases fulfilled the IRLSSG criteria for RLS and ICHD-3 criteria for CTTH.^[4,5] A response to dopamine agonist was noted in both RLS and CTTH. A possibility of a placebo response cannot be excluded completely. However, it is less likely as there was a temporal relation in the administration of the drug and response, and a withdrawal of the drug led to reappearance of the symptoms (both RLS and headaches) on the several occasions in the follow up. It indicates that dopamine agonist was pivotal in the improvement of both syndromes.

Several studies have demonstrated a significant association between RLS and pain of different origins, including different types of headaches. A meta-analysis has demonstrated a strong evidence of increased prevalence of RLS among individuals with migraine than controls.^[2] A recent study have demonstrated structural neuroimaging changes in migraine patients having RLS, indicating a close interrelation between two.^[6] An association between TTH and RLS has also been explored in the literature.^[2,3] Yang *et al.*, in a nationwide, population-based, retrospective cohort study have demonstrated an increased risk of RLS among patients with TTH.^[7] Chung *et al.* have also demonstrated increased prevalence of RLS in TTH patients in another population-based study.^[3] Associated comorbidities can complicate or modify the different aspects of RLS, and treatment may include both RLS and associated comorbid conditions.^[8]

Abnormalities in the dopaminergic system have been demonstrated in patients with RLS and dopaminergic medications improve RLS symptoms.^[4] Headache in TTH patients may also be because of dopaminergic dysregulation. A therapeutic response to intravenous metoclopramide in TTH suggest dopaminergic abnormalities in the generation of headache in TTH.^[9] The response of dopamine in both RLS and headaches raises a question if the headache was the part of RLS symptom complex.

Several studies have reported restlessness in various other body parts, such as arm, genital, mouth, restless abdomen, and bladder. RLS spreading to the head and neck has also been reported. Restlessness in atypical body parts usually coincides with the classical RLS of lower limbs.^[1] However, atypical body parts may be involved in isolation (i.e., without the involvement of legs).^[4] Restless arm syndrome is the most common variant in this regard.^[4] Restlessness genital syndrome, Restless mouth syndrome, restless abdomen syndrome, restless bladder syndrome are other few variants in this regard.^[8,10–12] Insomnia is one of the important accompanying symptoms in patients with RLS. Isolated insomnia has also been described as a variant of RLS.^[13]

So, the review of the literature suggests that any part of the body may be involved in RLS. Dopaminergic abnormality of RLS may also affect the head or its various connections. Hence,

involvement of the head cannot be ruled out in RLS. Pain or any sensory phenomenon in the head is called as headache. So, if RLS-like phenomenon occurs in the head, it will be mistaken as a headache. We hypothesize that the headache in our patients was the part of the RLS symptom complex. Both patients may have a few attacks of TTH, but most of the symptoms pertinent to the head was probably the extended form of RLS. A therapeutic response to dopamine on several occasions in both patients is the main feature to support this assumption. Urge to move is an essential feature of RLS and it has been noted even in RLS variant with atypical locations.^[4] However, it is not possible to show this phenomenon if RLS involve the head. However, headache aggravation mainly in the evening and night may be an indirect hint that inactivity increased the head symptoms.

To the best of our literature, this is the first report showing a positive response of dopaminergic drug in headache patients. So, our case reports suggest that there is a need to evaluate headache in patients with RLS. We suggest that headaches in a subset of patients with RLS may be the part of RLS spectrum. Both symptoms may respond to dopamine agonists. In clinical practice, physicians frequently encounter patients having both headaches and RLS. We hope our observations may serve as a catalyst for further investigations to clarify the issue.

In conclusion, our case reports and review of the literature suggests that headache in a subset of patients with RLS may be the part of RLS symptoms complex, and headache in such patients may respond to dopaminergic drugs.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

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