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RESTLESS EYES AT NIGHT: A NOVEL VARIANT OF RESTLESS LEGS SYNDROME

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ABSTRACT

Introduction: Restless legs syndrome (RLS) is a common sensorimotor disorder that primarily affects the lower extremities. This condition is characterized by unpleasant sensations and an irresistible urge to move the affected body regions, typically during periods of rest or at night. While RLS most commonly involves the legs, atypical variants affecting other body parts, including the arms, abdomen, face, and even the head, have increasingly been reported. This has led to the emergence of a broader diagnostic concept termed "restless X syndrome". However, no prior cases involving the ocular region have been documented.

Case description: Herein, we report a novel case of a 57-year-old woman who experienced chronic, nocturnal ocular pain for over 10 years, which repeatedly woke her from sleep. The pain, described as heavy and crushing, was not associated with any known ocular or neurologic pathology, and could be consistently alleviated by eye movements or eyelid stimulation. Multiple treatments for presumed dry eye syndrome and atypical facial pain were unsuccessful. After extensive evaluation, the condition was identified as a novel variant of RLS affecting the eyes. The patient showed no response to a dopamine agonist (pramipexole), but experienced marked and sustained relief with gabapentin enacarbil.

Conclusion: This case highlights the potential for RLS to present in non-traditional locations, including the eyes. Clinicians should maintain a high index of suspicion for RLS variants in patients with nocturnal sensory discomfort that can be relieved by movement, even in the absence of limb symptoms.

KEYWORDS

Restless leg syndrome, ocular pain, gabapentin enacarbil, RLS variant

LEARNING POINTS

- Restless legs syndrome (RLS) variants can affect body parts beyond the lower limbs, including the eyes.
- Symptoms are typically nocturnal and relieved by voluntary movement or sensory stimulation.
- Gabapentin enacarbil may be effective in treating these atypical RLS presentations.

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INTRODUCTION

Restless leg syndrome (RLS) is a neurological disorder characterized by an overwhelming urge to move the legs, generally accompanied by sensations of discomfort. These symptoms typically arise during periods of rest, particularly in the evening or at night, and can be temporarily relieved by movement. The exact pathophysiology is not fully understood but is believed to involve dopaminergic dysfunction and abnormalities in iron metabolism[1].

Although RLS is predominantly described in relation to the lower limbs, growing evidence supports the existence of atypical forms involving other regions of the body[2,3]. This has led to the emergence of a new term: "restless X syndrome," where "X" represents the various potentially affected body parts, including the arms, face, or abdomen. Such variants may present diagnostic challenges, particularly when the affected area deviates from classic limb involvement, and they are commonly underrecognized in clinical practice.

To date, no published cases have documented RLS manifesting as ocular pain or discomfort. Herein, we present the first reported case of what we term "restless eyes syndrome" a rare variant of RLS characterized by nocturnal ocular discomfort relieved by voluntary movement of the eyes or stimulation of the eyelids. This case adds to the expanding spectrum of RLS variants and underscores the importance of considering non-limb presentations when evaluating unexplained nocturnal symptoms. Moreover, it highlights the potential utility of gabapentin enacarbil as a therapeutic option for such atypical cases[4].

CASE DESCRIPTION

A 57-year-old woman presented to our department with a 10-year history of nocturnal pain in both eyes and cheeks that occurred during sleep. Three years prior to presentation, she began experiencing pain in the temporal regions that caused her to wake up 3–4 times per night. Glaucoma was initially suspected but was ruled out based on normal intraocular pressure and fundus examinations performed by ophthalmologists. Subsequently, dry eye syndrome and atypical facial pain were also considered, and the patient was treated by several departments, including neurology, but none of the prescribed medications were effective. She reported no difficulty falling asleep, and when she woke up during the night, she was able to return to sleep by blinking, closing her eyes, massaging her eyelids, or shifting her gaze. She described the pain as a "heavy, crushing sensation" and denied any sharp, stabbing, or tingling pain. She was asymptomatic during the day. Medical history included iron deficiency anaemia. Medications included amitriptyline and ferric citrate. Physical examination revealed no abnormalities. Her blood test results, including ferritin, were normal.

Although dry eye syndrome and atypical facial pain were suspected due to prolonged diagnostic difficulty, the former was inconsistent with nocturnal pain during sleep with closed eyes, and the latter typically presents as persistent unilateral pain below the cheek area unrelated to specific nerve distributions. Therefore, the prolonged nature of her pain and the involvement of both eyes made these diagnoses less likely. Given that the condition was predominantly nocturnal and could be relieved through specific movements, we suspected a variant of RLS that primarily affected the eyes. We initially prescribed pramipexole (0.125 mg/day); however, her symptoms did not improve. She was subsequently switched to gabapentin enacarbil (600 mg/day), which led to marked improvement within 2 days. The maintenance dose was set at 600 mg/day because her symptoms recurred with dose reduction to 300 mg/day. Discontinuation of amitriptyline did not lead to symptom recurrence.

DISCUSSION

Restless leg syndrome (RLS) is characterized by unpleasant sensations in both lower limbs that occur at night or during rest and are relieved by certain movements or sensory stimulation. Although the patient's legs were not involved, her presentation met the following four diagnostic criteria established by the International RLS Study Group[1]: 1) an urge to move the legs, typically accompanied by uncomfortable sensations; 2) symptoms that begin or worsen at rest; 3) symptom relief from certain movements; and 4) symptoms that worsen or occur exclusively during the evening or night. There are several RLS subtypes that are not confined to the lower limbs[2]. Consequently, the term "restless X syndrome" with X representing any body part, has been proposed to describe these cases as a new diagnostic category *(Fig. 1)*[3]. Although these conditions can theoretically affect any part of the body, there are no reports yet of variants affecting the eyes. Dopamine agonists are typically used to treat these conditions; however, because of augmentation issues, gabapentin enacarbil has recently become the first-line drug for treating moderate-to-severe RLS[4]. Both pramipexole and gabapentin enacarbil exhibit dose-dependent efficacies[4,5]; therefore, increasing the

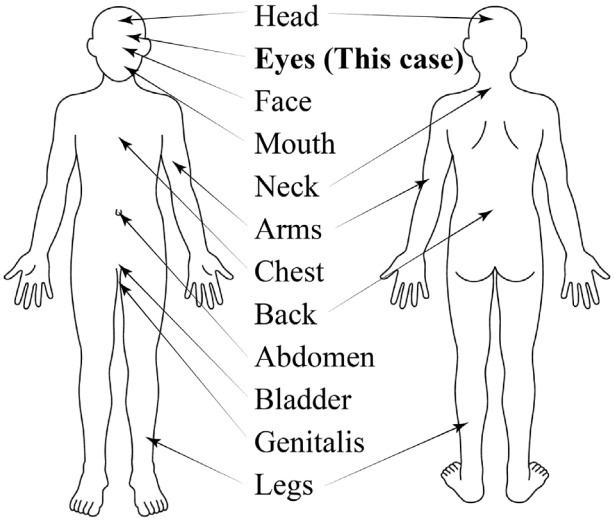


Figure 1. Parts of the body currently known to be affected by restless X syndrome (modified from Sato et al.[3]).

pramipexole dose was a potential option. However, given that gabapentin enacarbil is associated with a lower risk of augmentation, we chose to switch to it instead. This case represents an RLS variant presenting as eye pain. When symptoms worsen at night and are relieved by movements, differential diagnoses should include RLS variants. Taking into account our patient's clinical course and favorable response to treatment, we diagnosed her with a variant of RLS manifesting as ocular pain. Gabapentin enacarbil can be considered as a trial therapy in such cases, with careful dose titration according to the patient's condition, tolerability, and preferences.

This case highlights the potential for RLS to present in non-traditional locations, including the eyes. Clinicians should maintain a high index of suspicion for RLS variants in patients with nocturnal sensory discomfort that can be relieved by movement, even in the absence of limb symptoms.

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