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Unilateral RLS with predominantly ipsilateral PLMS and variable response to dopaminergic drugs: a variant of idiopathic RLS?

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ABSTRACT

Restless legs syndrome (RLS) is characterized by sensorimotor symptoms that usually are localized in both legs, but may present considerable asymmetry. Patients with strictly and persisting unilateral manifestations have not yet been reported. We describe the clinical und electrophysiological characteristics of three RLS patients with unilateral symptoms. All essential RLS criteria were fulfilled in each patient. Neuroimaging and electrophysiological studies did not reveal structural lesions. All patients showed a predominance of periodic limb movements in sleep (PLMS) ipsilaterally to the RLS symptoms. Treatment response to dopaminergic drugs was favourable only in one patient. Our observations suggest the existence of unilateral RLS with predominantly ipsilaterally PLMS as a (so-far unrecognized) variant of RLS.

Key words: Restless legs syndrome • periodic leg movements in sleep • unilateral

INRODUCTION

Restless legs syndrome (RLS) is characterized by sensorimotor symptoms that occur with a circadian pattern and improve in response to movement. Although often symmetric, a transient presentation of discomfort with unilateral dominance is not infrequent (29% of the 55 RLS patients reported in one series) [1]. To the best of our knowledge, patients with persisting unilateral RLS symptoms have not yet been reported.

The aim of this paper is to describe the clinical and polysomnographic findings of three patients (out of 1156 patients with sleep-wake disorders seen 2003-2005 in our neurological sleep clinic, including 117 patients with RLS), who presented for years RLS symptoms exclusively on one side.

Case 1

A 21-year-old man complained for five years of daily, persisting and drawing painful sensations in the right calf and sole, appearing at rest and worsening in the evening and night, accompanied by an urge to move the right leg and relieved by massage or movement. In addition, frequent muscle twitchings were reported. The Epworth Sleepiness Scale (ESS) score was 6 of a scale from 0 to 24 and the RLS-Score was 29 on a scale from 0 to 40 [2]. Family history was positive for RLS (with bilateral RLS symptoms). Physical examination revealed mild tenderness of the right lower back and diffuse fasciculations of all four limbs; neurological examination was otherwise unremarkable. Results of laboratory tests, including iron status (ferritine), were normal. Magnetic resonance imaging (MRI) of the thoracic and lumbar spine revealed a tumour of the paraspinal autochthonous dorsal musculature on the right side, extending from the 11th thoracic to the 1st lumbar segment, however without infiltration of intradural structures and with normal appearance of the myelon. Pathologic findings of a biopsy specimen were compatible with a schwannoma. The patient did not report

any change of his symptoms five months after removal of the schwannoma. Electroencephalography (EEG), brain MRI scans as well as electroneuromyographic (ENMG) examination and somatosensory evoked potentials (SEP) were normal. Video-polysomnography (PSG) showed predominantly right-sided periodic limb movements in sleep (PLMS) (23/h right vs. 13/h left leg) and a normal sleep architecture. No improvement was obtained with dopaminergics, antiepileptics and benzodiazepines. Only dihydrocodein was accompanied by some relief of symptoms.

Case 2

A 52-year-old man presented with a two-year history of unpleasant, "pulling" sensations in his right lower leg when sitting or laying down. Initially, symptoms were present on 3-4 days per week, but soon appeared every day. He noticed repetitive involuntary muscle jerks in his right calf and a sense of intense restlessness with a compelling need to move his right leg. Symptoms were restricted to evening and night-time and were relieved by movement. The patient complained of insomnia, but not of daytime sleepiness (ESS 5). Family history was negative for RLS. Neurological examination was unremarkable. Laboratory findings, including iron status (ferritine), were normal. Video-PSG showed exclusively right-sided PLMS (21/h right vs. 0/h left leg) with otherwise normal sleep architecture. The patient reported a short-lived improvement with levodopa at a dosage pf 250mg/d. With ropinirol at dosage of 1.5mg/d, RLS symptoms completely subsided.

Case 3

A 68-year-old man presented with a 30-year history of unpleasant, burning sensations in his right lower abdomen and groin with further extension to his gluteal region and right leg. Symptoms were present only at rest, were initially restricted to night-time, accompanied by

mild restlessness and improved by movement. He had difficulty to get asleep, but had no daytime sleepiness (ESS 0). RLS-Score was 21. Family history was negative for RLS. Neurological examination was normal, in particular no signs suggestive of myelopathy, radiculopathy or peripheral neuropathy were found. Laboratory findings, including iron status (ferritine), were normal. Spinal MRI scans, repeated twice within two years, were normal. Video-PSG (*figure 1*) showed predominantly right-sided PLMS (99/h right vs. 7/h left leg), prolonged sleep latency (46') and reduced sleep efficiency (73%). Treatment response to dopaminergics, opioids and antiepileptics was unsatisfactory. After abrupt withdrawal of gabapentine (at a dosage of 2.7g/d) the patient experienced a worsening of his symptoms, which involved for the first time transiently also the proximal part of his left leg.

DISCUSSION

We describe three patients with strictly unilateral RLS symptoms, predominantly ipsilateral PMLS and variable response to dopaminergic drugs.

All four essential diagnostic criteria for RLS - as established and recently revised by the International Restless Legs Syndrome Study Group (IRLSSG) [3] - were fulfilled in each patient. Furthermore, both patients 1 and 2 satisfied two (PLMS + positive family history for RLS, and PLMS + positive response to dopaminergic treatment, respectively) and patient 3 one supportive criteria (PLMS). The negativity of the ancillary tests additionally supports the hypothesis that the three patients have idiopathic RLS. The schwannoma in patient 1 was considered a fortuitous finding.

Although the exact pathophysiology of RLS remains unknown, the good response to levodopa and dopamine agonists, and the exacerbation of RLS symptoms when taking dopamine antagonists, suggests a deficiency of dopamine transmission in RLS [4]. Other data support also a role of iron deficiency [5], which could interact with dopaminergic

transmission [6]. Thus, the failure of dopaminergic treatment in two of our patients raises doubts about the idiopathic origin of unilateral RLS. It might be caused by a subtle peripheral or spinal lesion, which was not detectable by the neuroimaging and electrophysiological studies that were performed.

A diagnosis of painful legs and moving toes (PLMT), which sometimes can also present with strictly unilateral symptoms, was also considered [7, 8]. However, the absence of the characteristic involuntary toe movements and the normal electrophysiological studies made PLMT highly improbable.

We suggest that unilateral RLS pathogenetically may reflect similar mechanisms underlying idiopathic RLS. The striking predominance of PLMS ipsilaterally to the RLS symptoms (Table 1) suggests the unilateral disinhibition of the spinal cord generator recently postulated to exist in RLS/PLMS [9]. The clinical overlap between RLS/PLMS, unilateral RLS/PLMS and PLMT may arise from a common (or at least similar) underlying pathophysiology.

Unilateral PLMS without RLS symptoms, have been observed in the paretic leg of patients with supratentorial cerebral infarction [10], pontine lesion [11], parietal hemorrhage [12], and in the affected limbs of patients with corticobasal degeneration [13]. In these cases, unilateral PLMS have been attributed to the pyramidal tract lesion with subsequent disinhibition of a PLMS generator.

In conclusion, this report on unilateral RLS/PLMS represents a further contribution to our knowledge about the broad and pleomorphic clinical spectrum of RLS. Considering the normal iron laboratory findings in each patient and the absence of detectable structural lesions, we believe these cases of unilateral RLS to represent a variant of idiopathic RLS.

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