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Letter to the editor

# Spasticity or periodic limb movements? Lessons from a not-uncommon case report

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*Dear editor*

After traumatic spinal cord injury (SCI), patients experience different kinds of movement disorders such as spasticity and spasms that significantly alter their quality of life [1]. The management of spasticity and spasms is well established and consensual among the physical and rehabilitation medicine (PRM) community [2]. However, some patients still report disabling spasms while under high doses of intrathecal baclofen (ITB), which represents a diagnostic and therapeutic challenge for PRM physicians.

Here, we report the case of a 48-year-old man with complete D4 paraplegia secondary to gunshot wounds in 2004 who was referred to our spasticity consultation for intractable spasms despite ITB therapy. The patient received the first pump implantation in 2007 for disabling, diffuse lower-limb spasticity, with satisfactory relief of the spasticity. The pump was replaced in 2012, without any concerns, until 2014. The patient was progressively hampered by disabling spasms, occurring mostly in the afternoon while fishing. He first consulted his referral PRM specialist, who clinically ruled out an irritative factor. Abdominal and spinal X-rays showed the catheter's top extremity reaching D11 without disconnection of the device (Fig. 1A). Indium scintigraphy revealed an appropriate infusion of baclofen in the intrathecal space, and MRI of the spinal cord showed a known and stable syringomyelic cyst (Fig. 1B, C).

With lack of evidence of pump dysfunction, the ITB dosage was progressively increased up to 960 μg/day in continuous mode, without significant change. It was then decided to replace the catheter and pump, considering the strong suspicion of dysfunction of the device. The infusion mode was secondarily switched to discontinuous boluses, up to 1200 μg/day by the end of 2016, without efficacy. The patient was then referred to our consultation.

By the time of our clinical evaluation, the Penn score for spasms was 3 and we did not find any irritative factor either. A direct intrathecal injection of baclofen via lumbar puncture had no effect on symptoms. Clinical interrogation revealed frequent awakenings during sleep caused by spasms. Furthermore, the spasms tended to occur when the patient was lying down in the evening or night or when fishing (when he bent back the backrest of his wheelchair). He had no disabling spasms during the morning. These features led us to perform nocturnal polysomnography (PSG), which revealed a high index of periodic limb movements (PLMs) and related arousals (56 events/h and 15/h, respectively) (Fig. 2). Sleep was fragmented because of the PLMs and organized during 5 cycles as follows: N3 55 min (15.6% of total sleep time), rapid eye movement (REM) 102 min (28.7%) and N1-N2 198 min (55.7%). Sleep efficiency was estimated at 79.7%; wake after sleep onset (WASO) was measured as 89 min. The sleep disturbance index [3], calculated as SDI = WASO/(WASO + TST), where TST is the total sleep time in minutes, was 0.2. The higher the SDI, the more the sleep is disturbed. This equation has no normal or cutoff values and serves as a marker of treatment efficacy for quality of sleep. The apnea-hypopnea index was 9.1/h, with no time spent below 90% of oxygen saturation. Our patient did not complain of any symptoms of sleep apnea. Heart rate and encephalographic activity were not altered during PLMs.

Pramipexole 0.09 mg (half a tablet of the lower dosage) was initiated for the first night, then increased to 0.18 mg as recommended by international guidelines for treating PLM [4]. Perceived nocturnal movements significantly decreased thereafter. At the control PSG (9 months later), the PLM index had decreased by half, and related arousals decreased to 2 events/h (Fig. 3). Sleep architecture was not significantly modified. The SDI was decreased by half (Fig. 3). Of note, of the two recorded periods of PLMs, the first occurred during N2-N3 sleep and the second during REM sleep. Finally, we were able to decrease the ITB dosage, to 375 μg/day, without recurrence of spasticity or any other complaint.

PLMs were previously described in SCI patients [5–8], more frequently than in non-neurological conditions [7], but this is the first report of these movements as a differential for spasticity and what is thought to be flexor spasms in clinically complete paraplegia treated with ITB pump.

This case raises two points of discussion.

First, in some cases, as described here, spasms remain present and disabling despite ITB treatment. The present strategy combined clinical evaluation with standard radiography and nuclear imaging to rule out all known and common diagnoses related to spasticity and device dysfunction and were previously published by another French team [9,10]. This situation represents a diagnostic and therapeutic challenge because we tend to increase the doses of ITB up to potentially harmful levels or consider a surgical revision of the device, when no malfunction is found [9]. Knowing this reality, as specialized PRM physicians, we have to keep in mind differentials for what is thought to be spasticity and

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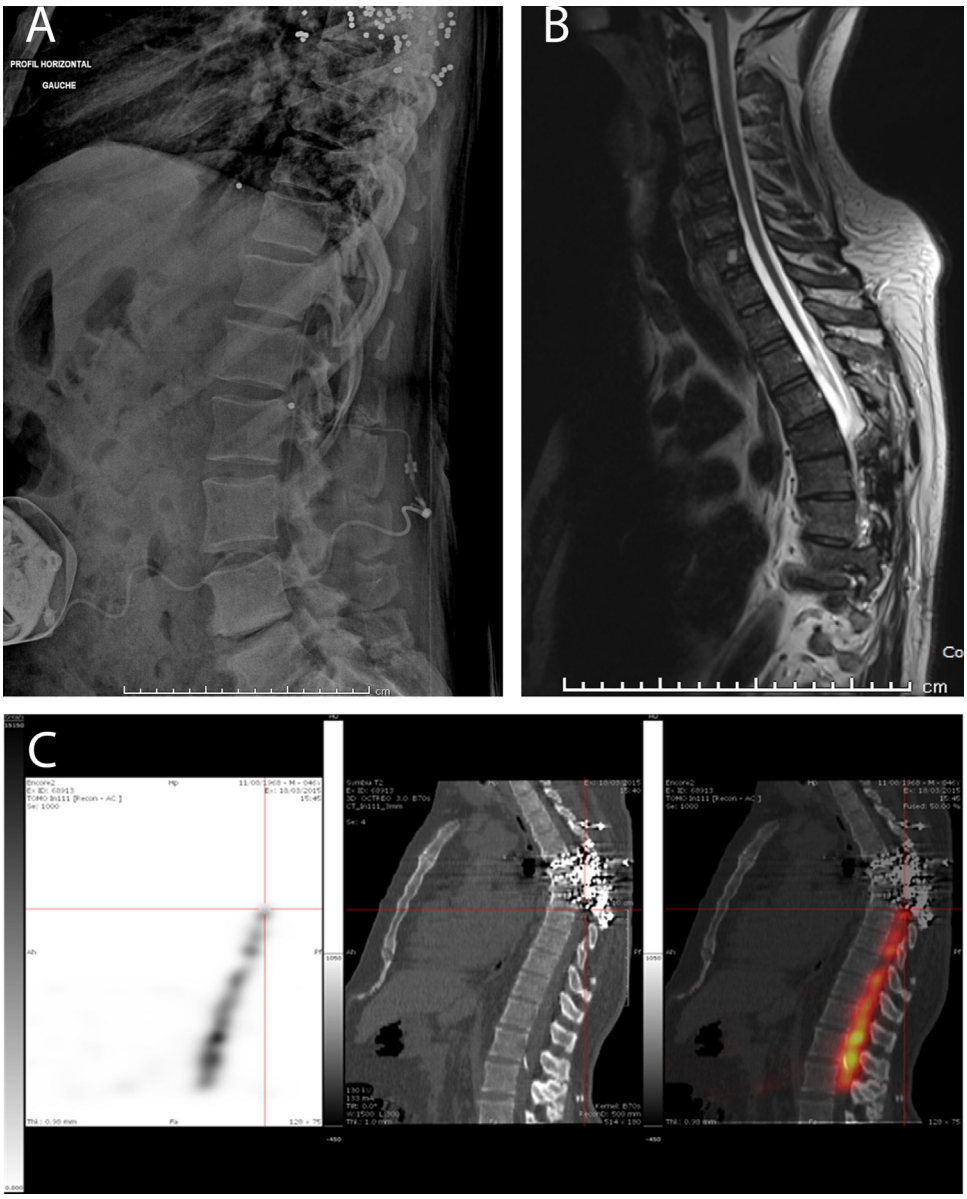


**Fig. 1.** A. Abdominal X-ray. The pump is in the anterior abdominal position, and the catheter enters the subdural space between L1-L2. The top extremity of the catheter is in the Th11 position. No disconnection of the device is seen on this radiograph. B. MRI of the spine in medial sagittal plane. FLAIR imaging shows an intramedullar hyperintense signal at Th3 and Th4 vertebrae, evocative of a syringomelic cyst. The lesional atrophy is visible at Th5-6, with metal artifacts due to gunshot residue below Th6. C. Tomoscintigraphy coupled with CT performed 96 h after $^{[111In]}$-DTPA injection revealing indium activity in the subarachnoid space but sudden interruption of $^{[111In]}$-DTPA at the thoracic level without activity above the lead shot. $^{[111In]}$-DTPA: indium-111 diethylenetriamine pentaacetic acid; FLAIR: fluid-attenuated inversion recovery.

flexor spasms and for which early non-invasive explorations could prevent from risky strategies. The nocturnal predominance of the movement disorders in our patient was evocative of PLMs. PLMs are often associated with restless legs syndrome, whose criteria can easily be searched by a thorough clinical interrogation [11]. These features are considered before prescribing a PSG to identify PLMs [12]. PLMs are alternate flexion movements, occurring during sleep or sometimes when in the supine position in neurological patients [13]. They are clearly distinct from other sleep-related motor behaviours and scored on PSG if they occur in a series of 4 consecutive movements lasting 0.5 to 10 s, separated by intervals of 4 to 90 s [12]. A PLM index $>5$ events/h is a debated cutoff for the diagnosis of PLM disorder. In our experience, we usually define PLM disorder with indices of $\geq 15$ events/h to avoid misinterpretation with spontaneous flexor spasms that can be associated and occur during the day or night. Pramipexole is a dopamine agonist that specifically targets D3 receptors and is recommended as the first-line treatment for PLM and restless legs syndrome [4]. In our case, a low dose of pramipexole (maximal dosage for restless legs syndrome is 0.54 mg) allowed for significantly decreased abnormal movements of the lower limbs and lowering the doses of ITB by a 3-fold ratio, without recurrence of spasticity.

Second, our case adds more evidence to the hypothesis of a spinal origin of PLMs, in a central pattern generator. Data from animal studies are scarce. In SCI rats, PLMs were also significantly more frequent than in control animals but only recorded during non-REM sleep [14]. A previous study in humans raised this hypothesis, although the data were minimal and methodology not appropriate: PSG was performed 3 months after trauma, only 4 of 20 patients had PLMs, and not all had a grade A paraplegia on the AIS [15]. The observation and study of complete SCI provide good

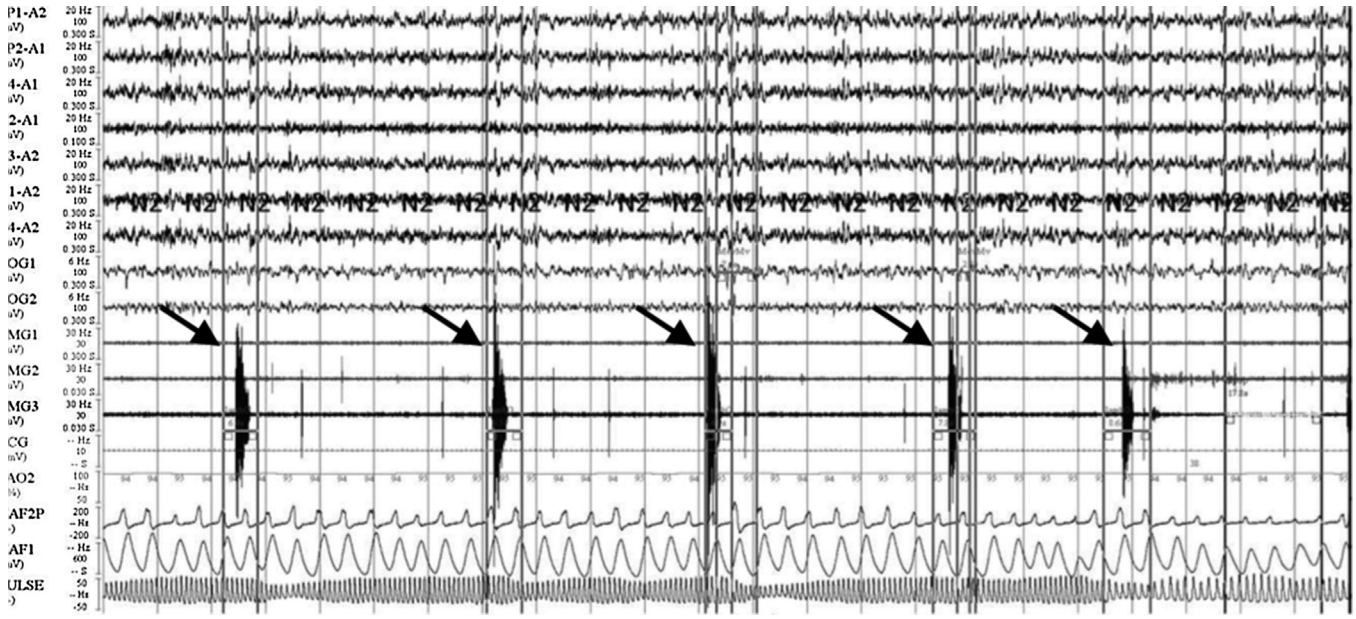


**Fig. 2.** Four-minute polysomnographic recording during N2 sleep, before treatment with pramipexole. Repetitive, rhythmic, brief contractions of the *tibialis anterior* muscles (arrows) favored frequent periodic limb movements. PLM index was 56.1 events/h of sleep and related arousals 14.6/h. PLM: periodic limb movements.

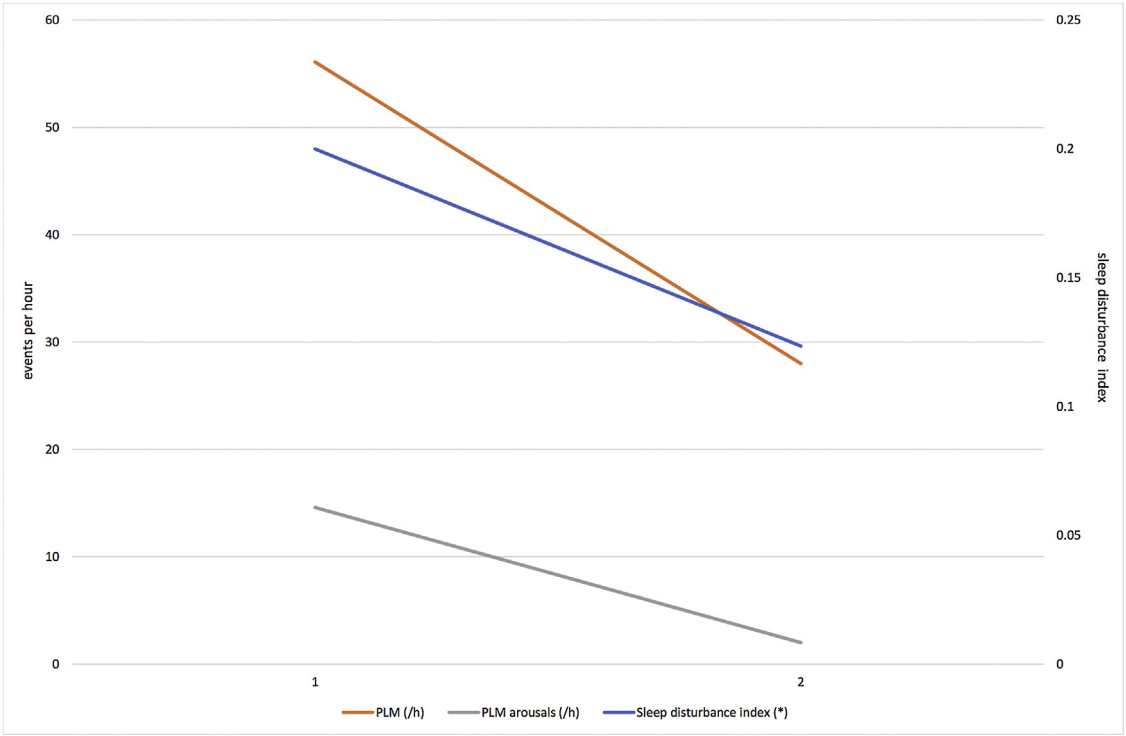


**Fig. 3.** Pre-post pramipexole comparison of PLM index (orange line), PLM-related arousals (grey line) and sleep disturbance index (blue line). PLM index and related arousals are expressed as events per hour, reported on the left axis. Sleep disturbance index was defined as wake after sleep onset (WASO) calculated as WASO/[total sleep time + WASO] [3] and reported on the right axis. PLM: periodic limb movements.

evidence for this hypothesis. Cohort reports have described other patients with complete traumatic SCI experiencing PLMs not suppressed during REM sleep [5,16]. These two studies demonstrated an automation of lower-limb movements of spinal origin, after disconnection from supra-spinal control. More recently, Salminen et al. reported the case of a clinically complete SCI with nocturnal PLMs associated with obstructive sleep apnea [8]: the treatment of sleep-disordered breathing significantly affected related cortical arousals but not the recorded activity of tibialis anterior muscles. This too favours a mechanism independent of supra-spinal control [8]. Furthermore, the lack of efficacy of GABAergic drugs on PLMs, as demonstrated with oral baclofen [3], reinforced by the efficacy of dopaminergic drugs, supports the hypothesis of PLMs as a motor disorder distinct from spasticity. Hence, PLMs should be considered different from positive signs of upper motor-neuron syndrome (e.g., spastic hypertonia, flexor spasm, dystonia, propriospinal spasm), with different anatomical and pharmacological substrates.

In conclusion, PLMs and spasms can have a very similar clinical presentation and are associated because they both result from the automation of two different spinal mechanisms. The nocturnal predominance of abnormal limb movements, along with the lack of efficacy of GABA drugs are highly evocative of PLMs in this situation. With these features, one has to think of this differential diagnosis from spasticity, which can easily be diagnosed with PSG and treated with dopamine agonists before surgical revision of an ITB device or an increase in ITB doses.

## Disclosure of interest

The authors decare that they have no competing interest.

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