Case report
Ενδιαφέρουσα περίπτωση

Restless legs syndrome mimicking S1 radiculopathy

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A case of a chronic idiopathic form of a severe type of Restless Legs Syndrome (RLS), which developed during pregnancy and persisted after this, misdiagnosed for 34 years as radiculopathy S1, is reported. In spite of the thorough clinical and laboratory investigation, in addition to constant changes of the therapeutic approach, the diagnosis of S1 radiculopathy could not be confirmed, resulting in a chronic clinical course; the latter was characterized by relapses and remissions not attributed or linked in any way to the treatment (various types of). In fact, it was due to a routine workup in a sleep clinic, where the patient was referred because of a coincident chronic insomnia (Restless Legs Syndrome is a known and important cause of insomnia/chronic insomnia), which resulted in a proper diagnosis and treatment of this case. With the use of Restless Legs Syndrome appropriate treatment (Pramipexole 0.18 mg taken at bedtime, a dopaminergic agent and Level A recommended drug for Restless Legs Syndrome) an excellent response and immediate elimination of symptoms was achieved. Restless Legs Syndrome may present with a variety of symptoms (with the most prominent shortly being reported with the acronym URGE: Urge to move the legs usually associated with unpleasant leg sensations, Rest induces symptoms, Getting active brings relief, Evening and night deteriorate symptoms); given the fact that Restless Legs Syndrome presents with a great variety and heterogeneity of symptoms (mostly pain, dysesthesia and paresthesia), which may occur in several other diseases (the so called "RLS mimics"), proper diagnosis of Restless Legs Syndrome usually fails. Restless Legs Syndrome misinterpreted as S1 radiculopathy, to the best of our knowledge, has not been reported yet in the literature. Here, case history, clinical course and common RLS mimics are presented. Different forms of Restless Legs Syndrome manifestations, which are commonly –as in this case– misinterpreted due to their mimicking several pathological conditions, Restless Legs Syndrome prevalence on general population according to various large epidemiological studies and pathogenic hypotheses on the issue of Restless Legs Syndrome are discussed. Finally, by presenting another possible "RLS-mimic" our aim is to highlight the common misdiagnosis of Restless Legs Syndrome, which can mimic a variety of disorders, some of which are very common, such as an S1 radiculopathy, thus raising concern among doctors of various specialties addressed to by Restless Legs Syndrome sufferers, on the importance of proper diagnosis of the syndrome.

Key words: Restless legs syndrome, misdiagnosis, S1 radiculopathy.

Introduction

Restless legs syndrome (RLS) is a common disorder and its prevalence has been underestimated in the past; population-based studies estimate it to be between 3–10%.[1–3] RLS, which is either idiopathic or secondary to renal failure, pregnancy or iron deficiency and is more frequent in women,[1,2] according to the current diagnostic criteria, is defined by four key features,[2] shortly reported also with the acronym URGE;[4,5] U: urge to move the legs usually associated with unpleasant leg sensations, R: rest induces symptoms, G: getting active brings relief, E: evening and night deteriorate symptoms. RLS is often under-diagnosed due to misdiagnosis of several other pathologic conditions, such as musculoskeletal/connective tissue diseases, movement disorders, peripheral vascular disease, depression, respiratory disorders, etc.[1,3] Here, we present a woman suffering from RLS (chronic form), misdiagnosed as S1 radiculopathy for 34 years.

Case history

A 56 year old Caucasian female, at the age of 22 during her first pregnancy, first complained of numbness, tingling and dull pain localized to the lower back, at the lumbar-sacral junction, bilaterally; these symptoms were projecting from the posterior thigh and leg to the soles of the feet, bilaterally. The symptoms together with an irresistible urge to move the legs used to occur at rest and mostly in the evening and/or at bedtime; thus, prolonged immobilization as when travelling or watching a movie was intolerable, and symptoms were relieved only by moving/stretching her legs and her back and/or by walking. Her sleep was also severely affected due to difficulty falling asleep. After delivery, there was a brief period of remission, but soon the symptoms reappeared. At that time her primary care physician, during a routine clinical examination, suspected an S1 radiculopathy and prescribed non-steroidal anti-inflammatory (NSAID) together with muscle relaxant drugs; there was no improvement. Following that, and in the next years, the patient performed repeated clinical (mainly orthopedic) and non-clinical investigations: imaging (CT/MRI) (figure 1), blood tests (standard including also ferrum/ferritin, thyroid function, Vit. B_{12}/folic acid, and standard rheumatic assessment), which were all normal. Despite the absence of clear clinical and/or non-clinical evidence, and based mostly on the symptoms referred by the patient, chronic relapsing-remitting S1 radiculopathy diagnosis was made and the patient underwent several therapeutic approaches comprising NSAID, steroidal drugs, tricyclic antidepressants and physiotherapy, without any benefit. Brief periods of remission (maximum of a few months), were not related to therapies.

We saw the patient at the age of 56 (in 2012) due to her chronic symptomatology, which has been in-

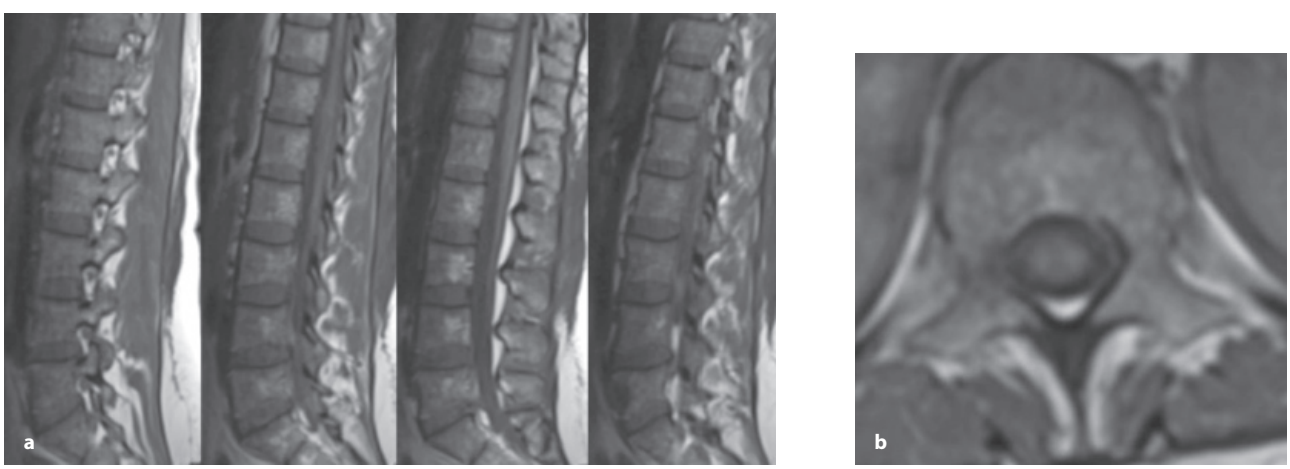

Figure 1. (a) Sequence of 4 normal sagittal sections of the lumbar-sacral part, (b) Normal S1 transverse section.

variant since the age of 22 and was burdening her activities of daily living, primarily her social life and her sleep. Neurological examination was normal; no sensory symptoms or deficits were noted, Lasègue sign was negative bilaterally, muscle strength was normal and deep tendon reflexes (both knee and ankle) were brisk bilaterally. An electrophysiological study, including motor conduction velocity of the peroneal and tibial nerve and sensory conduction velocity of the sural nerve bilaterally, was normal. Finally, because of her chronic insomnia (more than an hour needed for falling to sleep), the patient underwent a sleep workup; RLS criteria[4] were met, while with an RLS severity score of 23/40 (severe type). Pramipexole (a dopaminergic agent and Level A recommended drug for RLS5) 0.18 mg at bedtime was started, with an excellent response: all symptoms disappeared since the first night.

Discussion

In our patient, RLS onset occurred during pregnancy, a well-known risk factor for transient RLS,[6] and thereafter –except from a few symptom-free periods of time– she continued to suffer. There is recent evidence which supports the hypothesis that the transient pregnancy RLS form is a significant risk factor for the development of a future chronic idiopathic RLS form.[7] Moreover, the patient complained for chronic insomnia. Insomnia and disturbed sleep are among the most common associated features of RLS.[2] The pathogenesis of the syndrome remains unclear but the excellent response to levodopa and dopaminergic agonists offers a strong evidence for the role of a dopaminergic system in RLS pathogenesis;[1,2] in fact, our patient responded perfectly to the dopaminergic therapy; the immediate response of low-dose dopaminergic therapy is included among the supportive RLS diagnostic criteria.[2]

RLS is a common but still under-diagnosed disorder with a negative impact on quality of life.[1–3] In a large epidemiological multicenter study among primary care centers in USA and four different western countries, which comprised 23.052 patients, primary care physicians correctly recognized this disorder in only 7.7 and 13.6% of cases (mild and severe RLS respectively).[1] Another vast population study among primary care physicians in 6 western European countries comprising 10.564 patients, performed several years after the introduction of the existing RLS diagnostic criteria which have added further specificity and sensitivity to RLS diagnosis and increased the disease-awareness, revealed that despite repeated consultations for over one year regarding several symptoms –including those related to RLS– diagnosis was give only to 9% of the patients.[3] The previously mentioned data are mostly due to the vast symptomatology of RLS (i.e., pain, dysesthesia, paresthesia), which may "mimic" other pathologies, mainly back pain, joints and circulation diseases, myalgia, anxiety/depression, while arthritis and neuropathy are less frequently reported.[1,8] That is why RLS sufferers frequently consult phlebologists/vascular surgeons, rheumatologists and cardiologists, rather than neurologists or sleep experts (mainly in the US).[1] However, no reports of RLS misdiagnosed as S1 radiculopathy exist in the literature, while among the secondary forms of RLS, sporadic cases of RLS following myelopathy, spinal cord lesions or lumbosacral radiculopathy are reported.[9,10] Moreover, proper diagnosis of RLS becomes even more difficult in cases of co-morbid back pain, lumbar disc diseases or radiculopathy:[8] RLS prevalence in the context of lumbar radiculopathy has been reported to be up to 68%.[11] On the other hand "over-diagnosis" of RLS, i.e. in common conditions such as cramps or local leg pathology, which fulfill the RLS diagnostic criteria, may further complicate the RLS diagnostic issue.[12]

In summary, RLS diagnosis is difficult and at times fairly complicated. However, symptomatology compatible with back pain and/or radiculopathy, but with atypical features (i.e., normal neurological examination, circadian distribution of the phenomenology, unresponsiveness to painkillers/physiotherapy, amelioration of the symptoms following movement and co-morbid disturbed sleep – especially insomnia) should include RLS in the differential diagnosis.

Σύνδρομο ανήσυχων άκρων διαγνωσμένο ως ριζοπάθεια Ι1

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Στο παρόν άρθρο (παρουσίαση περιστατικού) γίνεται η περιγραφή μιας περίπτωσης γυναίκας 56 ετών πάσχουσας από σύνδρομο ανήσυχων άκρων (Restless Legs Syndrome, RLS) χρόνιας ιδιοπαθούς μορφής, το οποίο παρουσιάστηκε μετά από την εγκυμοσύνη, ενώ είχε λανθασμένα διαγνωσθεί ως ριζοπάθεια Ι1 για 34 χρόνια. Το σύνδρομο ανήσυχων άκρων είναι μια συχνή νευρολογική κινητική διαταραχή του ύπνου, η οποία χαρακτηρίζεται από μια πλειάδα συμπτωμάτων: κυρίαρχα συμπτώματα αναφέρονται η ανάγκη για κίνηση των άκρων που συχνά συνοδεύεται από δυσάρεστο αίσθημα στα άκρα, η επίταση των συμπτωμάτων με την ξεκούραση, η ανακούφιση με την κινητοποίηση, και η επιδείνωση κατά τις απογευματινές και νυχτερινές ώρες. Όλα τα παραπάνω συμπτώματα, μη όντας ειδικά για τη συγκεκριμένη νόσο και επειδή πολύ συχνά ομοιάζουν με συμπτώματα άλλων κοινών παθήσεων, συχνά στην καθημερινή πράξη αντιμετωπίζονται από διαφορετικές ειδικότητες ιατρών (π.χ. γενικοί ιατροί, παθολόγοι, ορθοπεδικοί, κ.λπ.) ως συμπτώματα άλλων παθήσεων. Αυτός είναι και ο σκοπός του παρόντος άρθρου, δηλαδή η ανάδειξη του γεγονότος ότι η νόσος ανήσυχων άκρων (RLS) –καίτοι ένα σύνδρομο που απαντάται συχνά στον γενικό πληθυσμό (σε ποσοστό 3–10%)– πολύ συχνά είτε υποδιαγιγνώσκεται είτε του αποδίδεται λανθασμένη διάγνωση (όπως εν προκειμένω η ριζοπάθεια). Στη βιβλιογραφία δεν υπάρχουν αναφορές σχετικά με λανθασμένη διάγνωση RLS ως ριζοπάθεια Ι1, ως εκ τούτου το παρόν είναι το πρώτο περιστατικό. Παρουσιάζεται το περιστατικό με λεπτομερή αναφορά στο ιστορικό, στην κλινική εικόνα, στη διαφορική διάγνωση, καθώς και στη θεραπευτική αντιμετώπισή του. Συγκεκριμένα, παρά τον συστηματικό κλινικό και εργαστηριακό έλεγχο στον οποίο υπεβλήθη η ασθενής αλλά και τις συνεχείς αλλαγές της φαρμακευτικής αγωγής, η διάγνωση και αντιμετώπιση ως ριζοπάθεια Ι1 δεν επιβεβαιώθηκε, και η κλινική πορεία του συνδρόμου ανήσυχων άκρων –με εξάρσεις και υφέσεις ανεξάρτητες της όποιας θεραπείας– συνεχίστηκε επί μακρόν. Ένας ενδελεχής και συστηματικός έλεγχος σε ιατρείο ύπνου, στο οποίο η ασθενής παραπέμφθηκε λόγω χρόνιας συνοδού αϋπνίας, έθεσε τη σωστή διάγνωση βαρείας μορφής συνδρόμου ανήσυχων άκρων, καθώς και την ενδεδειγμένη θεραπεία, με την οποία επετεύχθη άριστη ανταπόκριση και πλήρης υποχώρηση των συμπτωμάτων ήδη από την έναρξή της. Συμπερασματικά, διερευνώνται η πολυμορφία στην εμφάνιση των συμπτωμάτων του συνδρόμου (τα οποία συχνά, όπως και στην περίπτωση που παρουσιάζεται στο παρόν άρθρο, μιμούνται άλλες παθήσεις, με αποτέλεσμα τη λανθασμένη διάγνωση και θεραπευτική αντιμετώπιση), η επίπτωση στον γενικό πληθυσμό –όπως προκύπτει από μεγάλες επιδημιολογικές μελέτες–, καθώς και οι αιτιοπαθογενετικές υποθέσεις που έχουν γίνει σχετικά με το εν λόγω σύνδρομο. Επισημαίνεται η ανάγκη ευαισθητοποίησης και εκπαίδευσης των ιατρών διαφόρων ειδικοτήτων, στους οποίους συχνά απευθύνονται οι ασθενείς με RLS, όσον αφορά στην ύπαρξη και τη σωστή διάγνωσή του.

Λέξεις ευρετηρίου: Σύνδρομο ανήσυχων άκρων, λανθασμένη διάγνωση, ριζοπάθεια Ι1.

References

1. Hening W, Walters AS, Allen RP et al. Impact, diagnosis and treatment of Restless legs syndrome (RLS) in a primary care population: the REST (RLS epidemiology, symptoms, and treatment) primary care study. *Sleep Med* 2004, 5:237–246
2. Allen RP, Picchietti D, Hening WA, Trenkwalder C, Walters AS, Montplaisir J. Restless legs syndrome: diagnostic criteria, special considerations, and epidemiology. A report from the Restless legs syndrome diagnosis and epidemiology workshop at the National Institute of Health. *Sleep Med* 2003, 4:101–119
3. Allen RP, Stillman P, Myers AJ. Physician-diagnosed restless legs syndrome in a large sample of primary medical care patients in western Europe: Prevalence and characteristics. *Sleep Med,* 2010:31–37
4. Hening W, Trenkwalder C. Restless legs syndrome. In: Schapira A et al (eds) *Movement Disorders,* Saunders Elsevier, Philadelphia, 2009:587–621
5. Garcia-Borreguero D, Ferini-Strambi L, Kohnen R et al. European guidelines on management of restless legs syndrome: report of a joint task force by the Euro- pean Federation of Neurological Societies, the European Neurological Society and the European Sleep Research Society. *Eur J Neurol* 2012, 19:1385–1396
6. Manconi M, Govoni V, De Vito A, Economou NT et al. Restless legs syndrome and pregnancy. *Neurology,* 2004:1065–1095
7. Cesnik E, Casetta I, Turri M et al. Transient RLS during pregnancy is a risk factor for the chronic idiopathic form. *Neurology* 2010, 75:2117–2120
8. Benes H, Walters AS, Allen RP et al. Definition of restless legs syndrome, how to diagnose it, and how to differentiate it from RLS mimics. *Mov Disord* 2007, 22(Suppl 18):S401–S408
9. Hartmann M, Pfister R, Pfadenhauer K. Restless legs syndrome associated with spinal cord lesions. *J Neurol Neurosurg Psychiatry* 1999, 66:688–689
10. Walters AS, Wagner M, Hening WA. Periodic limb movement as the initial manifestation of RLS triggered by lumbosacral radiculopathy. *Sleep* 1996, 19:825–826
11. Kocabicak E, Terzi M, Akpinar K et al. Restless leg syndrome and sleep quality in lumbar radiculopathy patients. *Behav Neurol* 2014, 2014:245–358
12. Henning WA, Allen RP, Washburn M et al. The four diagnostic criteria for Restless Legs Syndrome are unable to exclude confounding conditions (mimics). *Sleep Med* 2009, 9:976–981

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