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Head Tremor and Restless Legs Syndrome: Is it within the Realm of Possibility to Classify as Clinical Entity? Diagnostic and Therapeutic Procedure with Coenzyme Q10 Support in a Case Report

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Abstract

The clinical case of a 72-year-old patient was examined in the movement disorders clinic of Albano Laziale with a head tremor. The patient was affected by several comorbidities: renal cell carcinoma (RCC) removal, splenectomy and left lung lobe removal for cancer (recent since the initial visit). Furthermore, a meningioma of the middle cranial fossa, causing visual disturbances, was diagnosed immediately thereafter. However, the reason for her referral to the clinic was the tremor involving mainly head and slightly and inconstantly the upper limbs that had existed for approximately 10 years. The patient was initially treated with gabapentin for Essential Tremor, with partial relief. Subsequently, a diagnosis of Restless Legs Syndrome (RLS) was made. Since the patient reported that the RLS symptoms were preceded by intense cramps, high-dose coenzyme Q10 (200 mg/day) was added to the therapy, with relief for both the cramps and the RLS. Subsequently dopaminergic therapy for complete remission of the RLS was added. This therapy was also effective on the head tremor and for limbs. Therefore, a Datscan was performed, which was negative for impairment of the dopaminergic receptor system. As a consequence, a co-pathology of dopamine-sensitive dystonic tremor of the head and RLS was evident, treatable with traditional therapies and the support of high-dose coenzyme Q10, as already noted in previous experiences.

Keywords: Coenzyme Q10; Essential tremor; Head Tremor Parkinson's disease; Restless leg syndrome

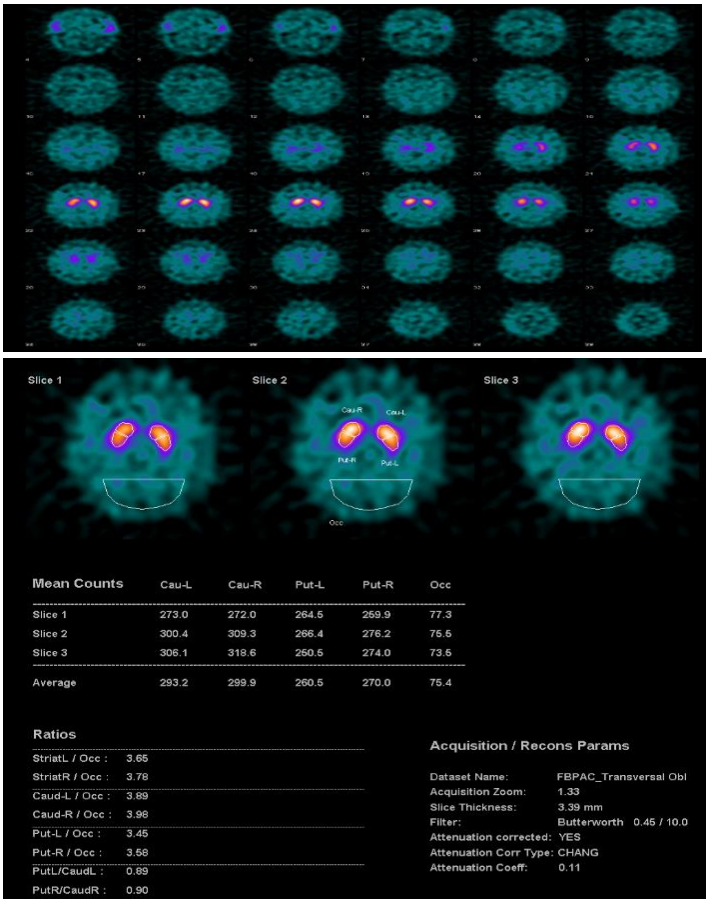
Introduction

In previous published papers we described some clinical cases of different Movement Diseases comorbidity affecting patients examined in the Movement Disorders clinic [1-3]. Movement disorders' comorbidities are known and classified in the literature, as is the case of coexisting Parkinson's disease and RLS, or Essential Tremor and RLS, Dystonia and RLS etc. [4-8]. Among different expression of tremor in neurological diseases Head Tremor (HT) represents a challenge in clinical practice as it is observed in most cases as a typical symptom of Essential Tremor (ET), but even in Parkinson's disease (PD) it can be a significant if not exclusive symptom, even if infrequent when isolated, compared to other typical and full-blown symptoms; moreover it is scarcely described in literature (8,9).However, in various clinical experiences in this Movement Disorders Clinic, head tremor has been frequently found and successfully treated with dopaminergic therapy both in subjects with positive Datscan, and in cases where there was no evidence of impairment of the nigro-striatal receptor system, but such therapy had been adopted for the indication of a coexisting RLS [1,3]. Moreover, recently clinical evidence about the relevant support of coenzyme Q10 (CoE Q10) for treatment of RLS has been highlighted (12). The therapeutic pharmacological tools known and used in RLS are mainly dopamine agonists. The therapeutic and preventive role of antioxidant molecules in

neurodegenerative diseases and movement disorders has been discussed in numerous studies, but are used anecdotally and empirically by specialists and physicians, not finding reference in guidelines; moreover, many physicians do not consider their usefulness reliable. This study debates several issues of clinical interest: in fact the clinical case in object showed a comorbidity of HT and RLS; moreover, the diagnosis of tremor was focused as a possible PD expression; finally, the antioxydant Coenzyme Q10 played an interesting role in the complex of therapeutic interventions with positive outcome on the patient described for RLS. The clinical presentation shows strong analogies with previously published ones, suggesting the possibility of adopting innovative criteria both in the diagnostic process and in the therapy of these clinical conditions.

Clinical Case Description

The patient is a 72-year-old woman at the time of her first access to the Movement Disorders clinic (July 2023), who was suffering from multiple oncological pathologies, with outcomes of left nephrectomy for chromophobe carcinoma and spleen removal (2022) and, approximately one month before the first access, lobar lung removal (2023) for moderately differentiated primary lung cancer. Moreover she had undergone surgery for lumbar stenosis with L4L5 radiculopathy and arthrodesis, and for hallux valgus in 2019, which resulted in a gait impairment. She underwent surgery for bilateral cataracts with gaze fogging in 2024. In the family history there was a familiarity with 'generic' tremor. At proximate pathological history, she suffered from mainly head tremor type 'no' from several years, at least 10, which improved while lying with the head resting on the pillow, and that was the reason for her access to the Movement Disorders clinic. A brain TC scan in November 2023 showed a meningioma with implantation base at the apex of the right petrous rock, causing inconstant diplopia, treated with cycles of stereotactic radio therapy with Cyberknife, subsequently assessed as stable by brain imaging. The medical history revealed from the beginning that the patient suffered from a disorder in her lower limbs during bedtime, consisting of the onset of annoying leg cramps, followed by paresthesias and the need to move her legs for relief, with difficulty falling asleep, to the point of having to get up, during the night. Also, during the hours she was able to sleep, she was affected by snoring. Blood tests showed normal iron metabolism, while obstructive syndrome (OSAS) was not assessed as significant in the scenario of oncological lung disease outcome. The neurological objective examination showed severe gait impairment caused by polyarticular disease, with the need for walking support, lack of signs of extrapyramidal type stiffness, mild high frequency postural tremor of the hands and the already described tremor of the head, particularly evident. The patient reported a partial relief of HT while resting on the pillow. The clinical picture was compatible with the coexistence of TE and RLS. RLS may have been partly due to lumbosacral stenosis; an electromyographic (EMG) examination performed in 2022 showed clear signs of chronic neurogenic distress in the L4L5 and L5S1 territories, with no signs of peripheral neuropathy.



Figures 1,2: *Show the I123-Ioflupane perfusion brain tomoscintigraphy in the patient described, responder to dopaminergic and CoEQ10 therapy for Head Tremor and RLS, with normal values and exclusion of PD diagnosis.*

Gabapentin therapy was initiated, which was also useful for the patient's reported neuroradicular algic symptoms and had an off-label application for tremor too, due to contra-indication for other drugs, such as beta blocker (not approved by the cardiologist and pneumologist) and benzodiazepines (BDZ), giving excessive drowsiness; the latter in particular was more pronounced following radiotherapy cycles. The patient achieved mild benefit; however, cramps persisted due to lumbosacral stenosis and RLS. Given the previous good results achieved on cramps with the use of CoEQ10, this was introduced in a first step, at a dosage of 200 mg\day; the patient reported a notable improvement in cramp symptoms, which preceded the onset of involuntary movements of the RLS. However, after some time, the urge to move the limbs in bed returned, even in the absence of cramps. Therefore nocturnal dopaminergic therapy was introduced, with the use of rotigotine

patch, firstly at a dosage of 2mg, then 4mg H12. It was unexpected to observe an improvement in both RLS disorder and tremor, particularly evident in the head, which was also reported by the patient. This discovery prompted a rethinking of the diagnosis of TE, and resulted in the request for 123-Ioflupane scintigraphy (Datscan) performed in February 2025. However, the test result did not show an impairment of the presynaptic dopaminergic system and was therefore negative for a diagnosis of PD. Dopaminergic therapy is still ongoing with benefit of symptoms, both RLS and HT; the patient also continued taking CoeQ10 which was reported as a benefit for cramps and RLS.

Discussion

The experience of specialists includes frequent occurrences of Movement Disorders' comorbidities, which are described and classified in the literature, as is the case of coexisting Parkinson's disease and RLS, or Essential Tremor and RLS, Dystonia and RLS etc [4- 9,13]. Clinical practice is often challenged by HT as it is believed to be a primary sign of ET. However, clinicians know that even PD can show it as a significant and sometimes exclusive symptom, although infrequent if isolated, compared to other typical symptoms, such resting tremor of hands [10-15]. Furthermore, some clinical studies published by this Author on tremor have demonstrated in some occasions on the one hand that the evidence of HT in RLS comorbidity corresponded to the diagnosis of PD, by means of clinical and instrumental data (2), on the other hand that the use of dopaminergic therapy for RLS in other subjects had showed a benefit on HT, even if the diagnosis of PD was not confirmed by the instrumental data (Datscan negative:1,3). RLS is a disabling disease as it compromises sleep-wake rhythms. It is associated to different conditions, such as peripheral neuropathies, most commonly diabetic neuropathy, lumbosacral stenosis, sideropenia. In many cases there is a correlation with affections interfering with the quality of sleep, such as obstructive sleep apnea syndrome (OSAS) [15-17]. On the other hand, it is not uncommon to record a family history with other movement disorders, such as Parkinson's disease (PD), Essential Tremor (ET), dystonic syndromes, or even the coexistence with one or more of these diseases. However, in many cases it is not possible to establish a genetic origin or a reliable alternative pathogenesis, but the disorder is idiopathic. The correlation with dopaminergic system able to explain the efficacy of LDopa agonists for treatment is still under investigation; on the other hand it is known that some variants of Dystonia are susceptible to treatment with dopaminergic therapy, like the Segawa Syndrome: these group of Dystonias, based on known genetic anomalies, are worsened by muscle effort and tension [18-20]. it is singular that in the experience of the outpatient clinic for Movement Disorders, several cases of association between HT and RLS have come to attention, among most of which showed no signs of impairment of the dopaminergic receptor system at the central level (Datscan within normal limit) but also good response of HT to dopaminergic therapy. This finding suggests the idea that the two diseases may share a common biomolecular pathogenic mechanism that may be interfered by dopamine and that the diagnosis of TE should be reviewed in many cases of HT\RLS comorbidity, establishing some analogy with Segawa syndromes. The data is also supported by common successful therapeutic procedures based on brain deep stimulation with regards to TE and RLS [21,22]. From this point of view, an element of additional interest is represented precisely by the effects found with the use of CoeQ10. CoEQ10 is a strong antioxidant, and has proven to be very effective in the experience of this Author for treatment of some patients affected by RLS related to diabetic neuropathy, so much so that in some cases it alone resulted effective on both cramps and motor disorder of RLS, without adding dopamine-agonists. It is known that this component plays a role in mitochondrial metabolism, therefore it has a positive effect in conditions such as iatrogenic myotoxic effects of statins or it is used as support for the functionality of the cardiac muscle. To some extent, mitochondrial disfunction can be a cofactor for the pathogenesis of the movement disorders under consideration, and the susceptibility of 'dystonic' tremor to dopaminergic therapy could be linked to mitochondrial metabolic mechanisms involving dopamine. From what has been described above, as a final consideration we should take in consideration that this kind of tremor\dystonia, with its 'linkage' to RLS could extend, albeit on a small scale, beyond the genetically known forms, similarly to the genetically indeterminate forms of idiopathic PD, and may be classified as a specific disease.Date/Time Report: 05/02/2025. Investigation performed pursuant to art. 4 of Legislative Decree 101/2020 Radiopharmaceutical: I123-Ioflupane (Datscan); Activity dose: 145 MBq. During the nuclear medical examination, the appropriateness of the request was verified. The scintigraphic study was performed using the SPECT technique approximately 3 hours after administration of the radiopharmaceutical; The analysis of the images, reconstructed trans-axially along planes parallel to the fronto-occipital line, was completed with semi-quantitative evaluation using ROIs. The scintigraphic study showed good concentration of the receptor tracer for the dopamine transporter in the striatum, whose morphology appears substantially regular. No significant asymmetries in the concentration of the receptor tracer were detectable in the caudate nuclei and putamen. The specific/nonspecific uptake ratio obtained by analysis with regions of interest shows normal values. Conclusions: The SPET study does not show impairment of the presynaptic dopaminergic system.

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