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Case Report

Focus on a Clinical Experience in the Diagnostic and Therapeutic Framing of Head Tremor Responsive to Dopaminergic Therapy

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Abstract

Head Tremor (HT) is a challenge for neurologists, as the therapy of this symptom is commonly supposed to be included within the treatment interventions for the pathology that causes it, usually with poor expectation of resolution, compared to other associated symptoms. The diagnostic pathway of HT is strictly linked to that of the suspected extrapyramidal disease, of which it can be the leading symptom, as occurs in the majority of cases for Essential Tremor (ET); in this pathology a combination with vocal or limbs' tremor is usual, otherwise in some cases it can be isolated; in literature, extrapyramidal syndromes associations have been described, commonly classified with various names, such as ET plus or Parkinson Plus, or Parkinson\ET.

Keywords: head tremor; tremor; dystonia; parkinson's disease; essential tremor; ldopa

Introduction

Head Tremor (HT) is a challenge for neurologists, as the therapy of this symptom is commonly supposed to be included within the treatment interventions for the pathology that causes it, usually with poor expectation of resolution, compared to other associated symptoms. The diagnostic pathway of HT is strictly linked to that of the suspected extrapyramidal disease, of which it can be the leading symptom, as occurs in the majority of cases for Essential Tremor (ET); in this pathology a combination with vocal or limbs' tremor is usual, otherwise in some cases it can be isolated; in literature, extrapyramidal syndromes associations have been described, commonly classified with various names, such as ET plus or Parkinson Plus, or Parkinson\ET. However, the specific therapy of HT is particularly important with respect to the relief requests of the affected patients, both due to social discomfort, but also to the functional complications (possible secondary gaze disturbances, arthropathies of the cervical spine, etc.). Few studies have been performed on the response of HT to dopaminergic therapy, with anecdotal observations. This study has examined some clinical cases in which a routine diagnosis of ET head tremor could be made at first approach, but whose diagnosis and treatment were subsequently redefined based on a more careful clinical-instrumental examination and response to pharmacotherapy.

Clinical Cases

This study was conducted retrospectively by previously considering a group of patients taken in charge in the outpatients' clinic of Movement Disorders of Albano Laziale (Rome), in whom there was a prominent HT. In most cases, head tremor was observed within the outpatients' clinic population's patients diagnosed as ET, with associated symptoms affecting the limbs, and treated with drugs for this indication, such as propranolol and, in case of contraindications, clonazepam and gabapentin, according to the best individual response and eventual contraindications. However, two clinical cases are described in this study with positive response to dopaminergic therapy of HT.

Case 1. A woman aged 59 yrs at the time of first examination affected by diabetes type 2 in oral medication, COPD, depressive syndrome, OSAS, Restless Leg Syndrome (RLS), and HT type 'no', which was initially slight and episodic. The clinical examination did not show extrapyramidal signs like limbs' resting tremor, plastic hypertone, hypomimia, gait disturbances or postural instability. A slight postural tremor of hand fingers was observed at antigravity position in the upper limbs. Since propranolol was contraindicated due to COPD and cardiopathy, and the patient resulted intolerant to clonazepam, gabapentin was introduced into the therapy at a dosage of 100 mg twice daily. At the same time, the patient began to complain of impellent nocturnal movements of the lower limbs while lying in bed, which forced her to get up and walk to get relief (Restless Leg Syndrome, RLS). However, an electromyography did not demonstrate the expected diabetic neuropathy, as it resulted normal; furthermore, the blood iron values were within the normal range. Therefore, a dopaminergic therapy was introduced using a nocturnal rotigotine patch (first 2 mg, then 4 mg), to promote patient compliance by reducing oral intake. The patient could not define whether the head tremor was influenced by the position (e.g., standing or with the head on the pillow) and the clinical observation in the outpatient clinic was doubtful in this regard. However, she noticed an improvement

after the introduction of the dopaminergic therapy, therefore we decided to extend the use of the patch 24 hours. A 123I-ioflupane SPECT DaTSCAN was carried out, which showed normal values. She mantained the dopaminergic therapy with higher dosages (up to 8 mg), with improvement of RLS. Tremor of head and handfingers were found to be improved on clinical examination. The DaTSCAN was repeated after 7 years resulting within normal limits.

Case 2. A woman aged 70 yrs at first examination (october 2018), affected by severe diffuse spinal discopathy and arthropathy, already operated on the lumbosacral tract for stenosis 4 years before and with documented signs of cervical spondylogenetic myelopathy, with balance and gait instability, severe gonarthrosis, depressive syndrome, bronchial asthma, cardiopathy, hypothyroidism, previous cholecystectomy and hysterectomy. She came to the clinical examination for depressive syndrome and difficulty in standing and walking, complaining also mild tremor of the hands when holding objects. Actually, at the clinical examination she showed gait impairment with motor uncertainty and a degree of slowing, which was attributed to osteoarticular pathology and depression; moreover, she showed head tremor type 'round or no', which was more noticeable than that of the hands, only slightly visible at the anti-gravity test, not at all at rest. a slight hypomimia and plastic hypertonicity of the upper limbs, without trochlea, were also appreciated. The patient could not report whether the HT, of which she did not seem to be sufficiently aware, varied with the position of the body. However, the objective examination showed an improvement when lying down. Brain magnetic resonance imaging showed diffuse vascular damage with leukoaraiosis Fazekas type 2. She was treated with dopaminergic therapy, which was prograssively incresed in dosages over time since she reported a motor improvement. Moreover, due to her serious family problems, antidepressant therapy was also adopted. A first DaTSCAN was carried out about 6 months after taking in charge (2019), which showed "a specific/non-specific radiotracer uptake ratio with values lower than normal with reduction of putamina visualization, mildly altered receptor imaging". The HT disappeared with the dopaminergic therapy, a fact that was more remarkable with respect to the improvement of standing and walking, strongly affected by the progression of the osteoarthritic pathology of the spine and knees. A second evaluation of DaTSCAN was carried out 4 years after taking in charge (2022) and showed "altered receptor brain imaging for reduced functional activity of the putamina, greater on the left".

Discussion

The clinical cases presented are not isolated. The knowledge in literature regarding the definition and treatment of HT argues marginally about the diagnostic difficulty, especially if the symptom is almost isolated or accompanied by other doubtful or not full-blown extrapyramidal signs. Some articles include this topic in the classifications of Essential Tremor Plus, or Parkinson's Disease Plus, or Cervical ET-Dystonia (1,2,3,4,5,6). However, in previous articles by this Author, clinical experiences on tremor and pharmacological therapy in extrapyramidal syndromes not simply classified as Parkinson's Disease have been described, both with single cases' reports and statistical retrospective studies (7,8). The patients' cases of this study have been part of the investigated populations' groups in previous papers to ascertain an overall perspective about the correlation between symptoms, brain instrumental and morphological data and the response to drugs, both in monotherapy and in polytherapy (7,8). The diagnosic tools to ascertain the diagnosis of PD with isolated HT can be surprising both with positive response to dopaminergic therapy or positive DatSCAN, which are rarely attempted in clinical routine practise in those cases (6).In the first case described, it is interesting to note that dopaminergic therapy was introduced afterwards the diagnosis and for the treatment of RLS, therefore obviously even though the DaTSCAN was normal. This coincidence allowed to observe, despite the non-apparent indication for HT, initially considered ET or dystonia, a significant response to therapy of HT, which was reported by the patient and detected during the objective clinical examination (the retrospective study is missing instrumental indicators, like the neurophysiological measurement of tremor, not included in routine practice). It is also interesting to note that the patient was monitored over time, and had a control DaTSCAN few years after, still not showing detectable damage of the dopaminergic receptor system. This could suggest in some cases a pathogenetic mechanism different or distinct from that of PD (but which can coexist in PD), and eventually shared with the RLS, which is coherent with cervical dystonia described in literature by some researchers. Moreover, it is also known that some forms of congenital\genetic dystonia respond to LDopa (9,10). Therefore, given the frequent familiarity for PD in patients described in literature with dystonic syndromes (9,10), it can be hypothesized that the incidence of cases, usually diagnosed as Essential head Tremor, which are indeed responsive to LDopa even with 'negative' DaTSCAN is in general underestimated and worthy of more extensive statistical studies.

In the second clinical case we are dealing with a more evident status of head tremor as the main indicator of PD, as also demonstrated by the DaTSCAN results, but whose differential diagnosis with respect to ET is made difficult by the scarcity of sure extrapyramidal symptoms or is confused by other comorbidities (gait impairment on an osteoarticular basis and prosthetic interventions, depressive syndrome due to objective socio-environmental factors, absence of typical tremor in the limbs). This leads to deem that HT is a non-rare and non-negligible symptom in PD, given that in this case it was decisive in the diagnosis of the pathology and in monitoring the pharmacological efficacy.

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