Findings that shed new light on the possible pathogenesis of a disease or an adverse effect

Sensory trick with metoclopramide-associated tardive tremor

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Summary

Tardive tremor is a 3–5 Hz bilateral resting and action tremor, associated with the use of dopamine receptor blocking drugs, accompanied by other tardive movement disorders and responsive to tetrabenazine or clozapine. We describe a case of a sensory trick associated with tardive tremor which raises important points about semiology and management. First, the presence of a sensory trick with tardive limb tremor suggests that the disorder may be a form of dystonia. Second, further study of osteopathic manipulative therapy for treatment of dystonia or tardive tremor is supported by a symptomatic response observed in our case.

BACKGROUND

Metoclopramide is a widely used antiemetic and promotility agent. It is the non-antipsychotic most commonly responsible for tardive movement disorders, presumably due to non-selective blockade of dopamine type 2 receptors in the striatum.¹ Tardive tremor is a 3–5 Hz bilateral resting and action tremor, associated with the use of dopamine receptor blocking drugs, accompanied by other tardive movement disorders and responsive to tetrabenazine or clozapine.^{2–3} The following case raised two important points. First, the presence of a sensory trick with tardive limb tremor suggests that the disorder may be a form of dystonia. Second, further study of osteopathic manipulative therapy for treatment of dystonia or tardive tremor is supported by a symptomatic response observed in our case.

CASE PRESENTATION

A 74-year-old man presented with a 4-month history of gradually worsening tremor and involuntary facial movements, which began upon discontinuation of metoclopramide. He had over 20 years' exposure to metoclopramide for gastric ulcer disease. Tremor was exacerbated during socially engaging activities. The patient could ameliorate the tremor by applying pressure with his own hand to the back of his neck. He was legally blind due to macular degeneration and had a history of chronic back pain. On being examined, he had a persistent asymmetric bilateral rest and action tremor, with irregular rate. It did not have directional features, such as amelioration or exacerbation with pronation or supination. Rest tremor showed no delay to re-emergence with sustained posture. Blepharospasm and orofacial dyskinesias, but no other dystonic postures, were present. Tone was normal without bradykinesia (video 1). Gait was antalgic due to low back pain. Tremor did not respond to metoprolol, amantadine, baclofen, chlordiazepoxide or lorazepam.

INVESTIGATIONS

MRI of the brain showed moderate global atrophy of the brain, without evidence of mid-brain atrophy or

significant white matter disease. MRI of the cervical spine showed moderate stenosis of the lower cervical spinal canal without cord deformity or increased cord signal.

DIFFERENTIAL DIAGNOSIS

Atypical parkinsonian disorders such as progressive supranuclear palsy can present with action tremor of the limbs accompanied by dystonic features such as blepharospasm. While the patient had difficulty generating saccades due to poor vision, he did not have a progressive disorder, did not develop postural instability and did not have exacerbation of symptoms with the dopamine-depleting agent tetrabenazine. A conversion disorder is possible; however, this would usually be characterised by sudden onset, evolution of new symptoms over time and accompanied by psychosocial stressors. Spinal myoclonus would also be considered, given concern about the cervical region. Tardive dystonia (blepharospasm), orofacial dyskinesia and tremor were best supported given remission with tetrabenazine and exacerbation with effective dose reduction of the drug (increased volume of distribution due to weight gain).

TREATMENT

Blepharospasm remitted with tetrabenazine 75 mg per day (video 2). The patient endorsed significant

Video 1 Patient had blepharospasm, orofacial dyskinesia and resting and action tremor.

Video 2 Patient on 75 mg of tetrabenazine before osteopathic manipulative therapy.

improvement of his tremor when he applied manual pressure to the posterior neck or wore a cervical collar. A single session of osteopathic manipulative therapy, using muscle energy technique, was employed to treat somatic dysfunction (misalignment) of the cervical spine (video 3). This resulted in resolution of his limb tremor for a period of approximately 10 min. Further titration of tetrabenazine to 150 mg per day abolished the tremor (video 4).

OUTCOME AND FOLLOW-UP

The patient was seen again in follow-up 1 year later. He had undergone a lumbar discectomy and fusion in the interim. Blepharospasm and tremor were beginning to re-emerge. No further sensory trick or improvement with osteopathic manipulative therapy could be demonstrated. Since the patient had gained 20 pounds, tetrabenazine was increased to 187.5 mg per day in order to address a presumed increase in volume of distribution. Tremor was again abolished.

DISCUSSION

Dystonic limb tremor may occur in association with other forms of idiopathic adult-onset dystonia (or in isolation), and can have both resting and postural-kinetic features.⁴ Recent data suggest that dystonic limb tremor is

Video 3 Shows tremor transiently improved after osteopathic manipulative therapy.

Video 4 Tremor virtually resolved on 150 mg tetrabenazine.

under-recognised and frequently misdiagnosed,⁵ including individuals enrolled in Parkinson disease clinical trials who had dopamine transporter scans without evidence of dopaminergic deficit. Key distinguishing features include short latency of re-emergence (after moving the upper limb from a resting to sustained unsupported posture), lack of bradykinesia and accompanying forms of dystonia (such as blepharospasm in our patient).⁶

A sensory trick is a form of tactile stimulation which leads to transient improvements in posture or spasm amplitude in cervical or other forms of dystonia.⁷ Our patient described a sensory trick (amelioration of tremor by tactile stimulation of the posterior neck), which suggests that tardive limb tremor may represent a form of dystonic limb tremor. Idiopathic forms of dystonia are associated with abnormal sensorimotor integration, as evidenced by abnormal short interval intracortical inhibition with repetitive transcranial magnetic stimulation.⁸ Given the cervical location of the sensory trick, we chose to explore response to an osteopathic technique designed to restore sensorimotor integration in that region. Muscle energy is an active stretching technique designed to lengthen hypertonic muscles to restore motion in a dysfunctional joint.⁹ There are at least two lines of evidence to suggest that interventions acting at the muscle spindle level (such as muscle energy), could influence sensorimotor integration in dystonia. First, proprioceptive training improves sensorimotor organisation and objective piano performance in pianists with task-specific hand dystonia.¹⁰ Second, intramuscular botulinum toxin injections lead to normalisation of intracortical inhibition in patients with dystonia.¹¹

To our knowledge, sensory tricks have not been previously reported with tardive or dystonic limb tremor, and osteopathic manipulative therapy has not been rigorously studied in cervical or other forms of dystonia. Our patient's transient response to a single session resembled that to his sensory trick. These observations raise questions as to whether treatment at the muscle spindle level (through muscle energy or other non-medical therapies) could be worthy of study as a potential adjunct treatment for dystonic or tardive tremor associated with a sensory trick.

Tardive tremor is very infrequently reported in the literature, and therefore may be under recognised. Prospective acquisition of comprehensive case data is needed to clarify predisposing factors, semiology and how best to manage (or prevent) it.

Learning points

- ▶ Chronic dosing of dopamine receptor blocking antiemetics or antipsychotics requires that patients be warned about, and monitored for, tardive movement disorders.
- ▶ Bilateral resting and action tremor, when accompanied by other tardive movement disorders, should lead to consideration of tardive tremor in the differential diagnosis.
- ▶ In order to clarify a potential dystonic nature of the tremor, patients with unusual presentations of limb tremor should be asked about the presence of a sensory trick.

Competing interests None.

Patient consent Obtained.

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