Primary dystonia misinterpreted as Parkinson disease

Video case presentation and practical clues

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Summary

Diagnosing dystonia can be challenging and depends on the recognition of subtle clinical signs. Due to clinical heterogeneity, variable age at presentation, and overlapping features with other disorders, dystonia is under-recognized. The presence of dystonic tremor is often a reason for misdiagnosis. We report an illustrative case of a patient with *DYT1* dystonia who was originally misdiagnosed with Parkinson disease. Careful physical examination and history-taking can reveal dystonia and prompt appropriate diagnostic studies, which, in turn, can lead to potentially life-changing treatment. Our report illustrates typical challenges in the recognition and diagnosis of dystonia, and serves to increase clinicians' awareness of this disabling, but treatable, condition.

Dystonia is a movement disorder characterized by sustained muscle contractions frequently causing twisting repetitive movements and abnormal postures.¹ It can present at any age with a variety of clinical features that may overlap with other movement disorders. Not surprisingly, patients with dystonia are commonly misdiagnosed.² Dystonic tremor is a substantial source of erroneous diagnosis of Parkinson disease (PD) and essential tremor (ET).²⁻⁴ We report an illustrative case of a patient with *DYT1* dystonia who was originally misdiagnosed with PD.

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Presence of head tremor argues against the diagnosis of PD and raises a consideration of ET or dystonia.

Case report

A 46-year-old man with a 5-year history of tremor and diagnosis of PD was referred to the movement disorders clinic. His initial symptom was left (dominant) hand tremor at rest and with action, followed by a head tremor. He had no family history of any movement disorder. Brain MRI was normal. Treatment with trihexyphenidyl, propranolol, and primidone was not helpful. Pramipexole and ropinirole resulted in suboptimal symptom control and excessive sedation. Carbidopa/levodopa provided some improvement. Examination showed slight rotation of his head to the left and tilt to the right, slight hypertrophy of right sternocleidomastoid muscle, and irregular head tremor that changed direction, frequency, and amplitude with changing of head position. Holding his chin with his hand temporarily decreased the tremor (video 1). He had a slight intermittent resting tremor of his left thumb (video 2) and a low-amplitude fast tremor in outstretched arms that worsened with hand inversion and fine movements (not shown on the video). Handwriting induced dystonic posturing with left arm extension, elbow elevation, wrist hyperextension, and an irregular tremor (video 3). The patient reported that he had this “writer’s cramp” since age 18. No rigidity, bradykinesia, nor postural instability was noted (video 3). Search for the etiology of his dystonia revealed a *GAG946* deletion in the *DYT1* gene. Botulinum toxin injections in the cervical muscles, along with carbidopa/levodopa and propranolol, improved tremor control but the patient remained relatively disabled. Deep brain stimulation (DBS) surgery was performed, resulting in complete resolution of his head tremor and improvement of his hand tremor and posturing (video 4). Although the most common DBS target for dystonia is the globus pallidus, the target in this patient was the subthalamic nuclei (STN) due to participation in a clinical trial, investigating STN DBS for dystonia.

Video

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DISCUSSION

Several unusual features of this patient’s dystonia led to initial misdiagnosis. First, parkinsonian tremor is a true resting tremor seen when the extremity is completely supported against gravity.⁵ In contrast, the hand tremor in our patient was position-specific, worse with handwriting, and satisfied criteria of dystonic tremor, which is a focal tremor in the body part affected by dystonia, postural and kinetic; irregular amplitude and variable frequencies, not seen during complete rest, frequently reduced by gestures antagonists (sensory cues) (table).⁵ His head tremor was typical for dystonic tremor: increasing amplitude and frequency in certain directions, sensory cue (touching chin temporarily decreased tremor), and partial null point (certain position almost or completely resolved tremor) (table, video 1). This patient had minimal dystonic posturing in his neck, but had a disabling head tremor. Presence of head tremor argues against the diagnosis of PD and raises a consideration of ET or dystonia. Disproportion between subtle posturing and severe tremor in the same part of the body is not unusual in dystonia,³ especially in the cervical region, where the tremor can be a predominant feature.

Second, his left hand dystonia was task-specific and not initially noted. The patient himself did not recognize the relationship between his longstanding “writer’s cramp” and the head tremor, and his first neurologist did not observe it. As a result, the onset of his symptoms was considered to be age 39, not age 18, when the “writer’s cramp” started. This emphasizes the importance of observing handwriting in patients with dystonia and atypical tremor (figure). *DYT1* dystonia usually manifests before the third decade,⁶ and genetic testing is indicated if

Table Comparison of tremor characteristics in dystonia, ET, and PD

Tremor characteristics	Dystonia	PD	ET
Common description of tremor	Irregular, "jerky," task-specific	"Pill-rolling," resting	Action, intention, kinetic
Frequency	Varies, can change depending on the position of the affected part of the body	4–6 Hz	5–10 Hz
Direction	Varies, can change depending on the position of the affected part of the body	Combination of pronation-supination and flexion-extension giving rotatory appearance	Flexion-extension
Limb tremor	Asymmetric	Asymmetric	Usually symmetric
Influencing factors			
Rest	Position-dependent	Increases	Decreases
Action	Increases frequently in task-specific manner	Decreases	Increases
Writing	Might increase	Decreases	Increases
Walking	Might increase in head and trunk	Increases	Decreases
Postural tremor	Position-dependent	Re-emergent	Without latency
Kinetic tremor	Frequently present	Rare	Present
Tremor in other parts of the body			
Jaw	±	+	–
Head	±	–	±
Voice	±	–	±
Null point: a point of cessation of tremor usually in the position of maximum pull of the affected part of the body	Frequently present	Absent	Absent
Geste antagoniste (sensory trick or cue): a maneuver that can temporarily improve dystonic postures, spasms, and tremors	Usually present, especially with cervical dystonia and dystonic tremor	Absent	Absent
Associated features	Abnormal posturing (e.g., writer's cramp, torticollis, foot inversion), unusual gait, hypertrophy of affected muscles	Rigidity, bradykinesia, postural instability, other motor and nonmotor symptoms of PD	Sometimes balance impairment
Response to treatment			
Dopamine replacement therapy	±	±	–
	Minimal to moderate, not in all cases	Good, except for subtypes with medication-resistant tremor	Usually none
Anticholinergic	+	++	–
β-blockers	±	+	++
Primidone	–	–	+
Botulinum toxin	+	–	±
Abbreviations: ET = essential tremor; PD = Parkinson disease.			

The diagnosis of dystonia is primarily clinical and is heavily dependent upon the physician's awareness of the condition and recognition of subtle clinical signs.

onset of symptoms is before age 26 or the patient with late onset has an affected relative with early-onset dystonia.^{7,8} After the actual age at onset was determined in our patient, it became evident that he met criteria for *DYT1* testing.

Third, as seen in some types of dystonia, our patient had a positive response to levodopa. The mutant *DYT1* gene encodes an ATP binding protein, torsin, which is expressed most intensely in the dopaminergic neurons of the substantia nigra and striatum, causing alterations in dopaminergic transmission.⁷ This may explain the partial responsiveness to levodopa in patients with *DYT1* dystonia.

Finally, this patient did not have any rigidity or bradykinesia, necessary for diagnosis of PD. According to UK Brain Bank criteria, bradykinesia is an obligatory feature of PD.⁹ Strict application of these criteria could have prevented the misdiagnosis.⁴ The diagnosis of dystonia is primarily clinical and is heavily dependent upon the physician's awareness of the condition and recognition of subtle clinical signs. Due to clinical heterogeneity and overlapping features with other disorders, dystonia is under-recognized and frequently misdiagnosed.² Tremor may be a predominant feature of dystonia and can be confused with ET or PD. However, careful history-taking and observation of handwriting may reveal dystonia, resulting in the correct diagnosis. Misdiagnosis of dystonia for PD has considerable social, prognostic, and

Figure Comparison of handwriting and spiral drawing in dystonia, Parkinson disease, and essential tremor

(A) Dystonia. Spiral demonstrates action tremor that is irregular (not all lines on the spiral have tremor). Handwriting is clumsy, "jerky," "edgy," and occasionally, but not with every word, demonstrates tremor. (B) Parkinson disease. Spiral is smaller with no tremor. Handwriting with no tremor but obvious micrographia with decrement: size of the letters is small and becomes smaller toward the end of the sentence. (C) Essential tremor. Regular tremor throughout the entire spiral—action tremor. Tremor with handwriting making it illegible, worse at the beginning of the first letter of the sentence, representing intention tremor—worsening tremor toward the target, in this case paper.

therapeutic implications. Our case illustrates typical challenges in the recognition and diagnosis of dystonia, and serves to increase clinicians' awareness of this disabling, but sometimes treatable, condition.

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