

# Clinical Reasoning: A 13-year-old boy presenting with dystonia, myoclonus, and anxiety

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## SECTION 1

A 13-year-old, right-handed boy was referred for movement and speech abnormalities. His mother reports his voice becoming soft and choppy at 8 years of age. Over the past year, he developed head jerking to the right while using his right hand. The patient denied a premonitory urge or ability to suppress these movements. They had become so disabling that he had to eat and write with his left hand. He has no other medical problems, other than a pectus excavatum. His family history is notable for his father being diagnosed with Tourette syndrome as a teen. His father continues to have episodic head jerking to the left at times. The patient's general examination was

notable for an anxious teenager with marfanoid features including pectus excavatum and long limbs. The patient's neurologic examination revealed strained, choppy speech, which was present while speaking but not while singing. He had involuntary forced head turn to the right with right tilt and right upper extremity sustained twisting posturing when trying to use his right hand. He had right upper extremity fast jerking movements with attempts to use his right arm. His deep tendon reflexes were brisk, with crossed adductors. The remainder of his neurologic examination was normal.

### Question for consideration:

1. What type of movement is being described in the history?

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## SECTION 2

Although his father had been diagnosed with Tourette syndrome, the patient's movements were neither suppressible nor preceded by an urge, which are the hallmarks of tics. The strained choppy voice was consistent with spasmodic dysphonia, a form of laryngeal dystonia. His forced head turn to the right and twisting posturing was consistent with cervical dystonia and limb dystonia, respectively. The jerking

movements of his arm suggested a dystonic tremor vs myoclonus. On his initial examination it was difficult to differentiate between these 2 involuntary movements.

### Questions for consideration:

1. What is the definition of dystonia?
2. What is the differential diagnosis for dystonia with onset in childhood or early adolescence?
3. What diagnostic tests would you order?

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### SECTION 3

Dystonia in childhood has been defined as a movement disorder with involuntary sustained or intermittent muscle contractions which cause twisting and repetitive movements, abnormal postures, or both.<sup>1</sup>

A broad differential diagnosis must be considered in the evaluation of childhood or adolescent onset dystonia, including primary dystonias, dystonia plus syndromes, secondary dystonias, and hereditary degenerative disorders.<sup>2,3</sup> Primary dystonias do not have other neurologic or systemic findings. The most common primary dystonia is DYT-1 dystonia, which is typically characterized by childhood onset limb dystonia often with subsequent generalization.<sup>2,3</sup> It is an autosomal dominant disease with a penetrance rate of 30%–40% which is caused by a GAG deletion in the *TOR1A* gene. Dystonia plus syndromes include additional neurologic findings such as parkinsonism and myoclonus.<sup>4</sup> Two dystonia plus syndromes are dopa-responsive dystonia (DYT 5) and myoclonus dystonia (DYT 11). Dopa-responsive dystonia (DYT 5) typically presents in midchildhood with gait dystonia. There is diurnal variation in symptoms in 75% of patients.<sup>2</sup> Other possible associated features include parkinsonism and hyperreflexia.<sup>2,3</sup> A key feature of this condition is a dramatic and sustained response to levodopa.<sup>2,3</sup> It is caused by a mutation in the GTP-cyclohydrolase-I gene. The presence of myoclonus in association with dystonia is characteristic of myoclonus dystonia (DYT 11).<sup>2,3</sup> Secondary and hereditary degenerative dystonias typically present with other neurologic and systemic signs and symptoms in addition to dystonia. Secondary dystonia is due to an acquired or exogenous cause including drug exposures, toxins, infections, and focal CNS lesions.<sup>3</sup> Important historical information includes drug or toxin exposure, perinatal injury, en-

cephalitis, or head trauma. A focal structural lesion may present with hemidystonia. Hereditary degenerative disorders which have dystonia as a feature are genetic disorders including Huntington disease, Wilson disease, and pantothenate kinase-associated neurodegeneration.<sup>2</sup> These are often associated with other signs including cognitive impairment, seizures, oculomotor dysfunction, retinal abnormalities, neuropathy, spasticity, as well as liver dysfunction and skeletal abnormalities.

Our patient presented with dystonia, a dystonic tremor vs myoclonus, and marfanoid features. In addition, on further examination of the patient's father, his findings were more consistent with myoclonus rather than tics. His father also reported that his head jerking resolved with alcohol use. This suggests the most likely diagnosis was either a primary dystonia or a dystonia plus syndrome. The patient's abnormal movements were unilateral, so a focal etiology was considered. Given the presence of marfanoid features, abnormal vessels leading to a basal ganglia stroke was considered. Marfanoid features are not associated with a primary dystonia or dystonia plus syndrome. The following laboratory testing was normal: complete blood count, complete metabolic panel, copper, ceruloplasmin, zinc, thyroid function testing, and ferritin. He had MRI of the brain and magnetic resonance angiography (MRA) of the head and neck, which showed no evidence of stroke or abnormal vessels to suggest his presentation was related to his marfanoid habitus. He had a normal ophthalmologic examination with no evidence of Kayser-Fleischer rings or retinal detachment. DYT-1 genetic testing was pending.

#### Question for consideration:

1. Would you treat the patient while awaiting genetic testing results? If so, with what?

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#### SECTION 4

It is recommended that patients with early onset dystonia without an alternative diagnosis undergo a levodopa trial.<sup>4</sup> Although our patient's presentation was not typical for dopa-responsive dystonia, he was treated with levodopa while additional genetic testing was pending. There was no clinical response to

levodopa, making that an unlikely diagnosis. DYT-1 testing was negative. On repeat examination, his abnormal movements appeared to be consistent with myoclonus in addition to a dystonic tremor.

#### Question for consideration:

1. What additional diagnostic testing would you send at this time?

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## SECTION 5

Given the constellation of dystonia, myoclonus, anxiety, and his father's history, the patient was evaluated for myoclonus dystonia. Epsilon sarcoglycan gene (*SGCE*) testing revealed a known mutation and a diagnosis of myoclonus dystonia syndrome was made. Our patient was treated with trihexyphenidyl, which resulted in significant improvement of his myoclonus and dystonia. He was able to eat and write with his right hand and was remarkably less anxious.

**DISCUSSION** Myoclonus dystonia is a rare disorder characterized by myoclonic jerks and dystonia. Presentation is typically in childhood or early adolescence.<sup>5</sup> The most common presenting symptom is myoclonus, but dystonia can be the initial presentation in 20%.<sup>5</sup> Myoclonus typically involves the arm and axial musculature and is responsive to alcohol. Dystonia is usually mild and most often manifests as cervical dystonia or writer's cramp. Psychiatric features are common and include depression, obsessive-compulsive behavior, panic attacks, and attention deficit hyperactivity disorder.<sup>2,5</sup> Severity of symptoms varies. Spontaneous resolution of limb dystonia and improvement of myoclonus occur in 20% and 5%, respectively.<sup>5</sup> Although spontaneous resolution can occur, myoclonus and dystonia can progress at any time during the disease course.<sup>5</sup>

Inheritance is autosomal dominant with reduced maternal inheritance due to maternal imprinting. Paternal inheritance always results in the disease whereas maternal inheritance has a penetrance of 10%–15%.<sup>2</sup> Mutations in the *SGCE* gene, which encodes the protein epsilon sarcoglycan, is located in chromosome region 7q21. Mutations in the *SGCE* gene are found in less than 40% of patients with the clinical phenotype.<sup>5</sup> There are reports of both sporadic cases as well as kindreds with *SGCE*-negative myoclonus dystonia. One notes a kindred presenting with autosomal dominant clinical features of myoclonus dystonia syndrome who was found to have GTP cyclohydrolase I deficiency, which is typically associated with dopa-responsive dystonia.<sup>6</sup> The pathophysiology of myoclonus dystonia is unknown.

Treatment of myoclonus dystonia is symptomatic. Anticholinergic drugs and benzodiazepines may improve dystonia and myoclonus.<sup>5</sup> Antiepileptic drugs including levetiracetam, piracetam, valproic acid, and zonisamide have improved myoclonus in some patients.<sup>5</sup> Levodopa has been shown in isolated cases to improve symptoms.<sup>7</sup> Botulinum toxin is an option to treat focal dystonia. Deep brain stimulation (DBS) of the globus pallidus interna (GPi) and ventral intermediate thalamic nucleus have been shown to improve symptoms in more than 70% of

patients with DBS-GPi, having fewer adverse effects.<sup>8,9</sup>

Diagnostic criteria for definite myoclonus dystonia have been proposed and include early onset (<20 years), myoclonus predominating in the upper body either isolated or associated with dystonia, positive family history with paternal transmission when due to *SGCE* mutation or deletion, exclusion of additional neurologic findings such as cerebellar ataxia, spasticity, and dementia, and a normal brain MRI.<sup>5,10</sup>

Myoclonus dystonia is a rare cause of dystonia in childhood but must be considered in the setting of early onset dystonia when myoclonus is present, especially in cases with potential paternal inheritance. Our patient meets the suggested criteria for the diagnosis of myoclonus dystonia as described above. *SGCE* testing in his father confirmed that his father also has a diagnosis of myoclonus dystonia, rather than the previous diagnosis of Tourette syndrome.

## AUTHOR CONTRIBUTIONS

Dr. Blackburn qualifies as an author for drafting and revising the manuscript for content including medical writing for content. Dr. Cirillo qualifies as an author for drafting and revising the manuscript for content including medical writing for content.

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