Case Presentation
A 28-year-old, right-handed male presented with abnormal jerky movements of the head, neck, and upper extremities since age thirteen. These movements were made worse by stress, and became particularly aggravated by writing with his left hand. Further questioning elicited that the jerks were decreased by alcohol intake, not suppressed by conscious effort, and not preceded by an urge to carry out the movement. The patient reported symptoms of obsessive-compulsive disorder, depression, social anxiety, and difficulty sleeping and was previously diagnosed with TS when the movements began. Questioning regarding family history revealed the presence of a similar movement disorder in his father.

Neurological examination revealed intermittent, variable, high frequency myoclonic jerks of the head, neck, and upper extremities. His head tended to turn and tilt to the left. He tended to hold his left hand in a dystonic posture, particularly when walking. He had intermittent facial myoclonus and the rest of the cranial nerves were normal. He was somewhat poorly coordinated with tandem gait but toe tapping was adequately done. Finger movements were somewhat clumsy for a person of his age and myoclonus interfered with fine motor coordination. Romberg test was negative and Babinski reflex was absent and there were no signs of ataxia. Muscle tone, strength, and bulk were normal. Sensations and reflexes were normal.

On the basis of these findings, genetic testing for Myoclonus-dystonia (M-D) was carried out by PCR amplification and sequencing of the SGCE gene. The patient was found to be heterozygous for a nonsense mutation in exon 3 of the SGCE gene (c.304C>T), a mutation that has been clearly documented as causative for M-D. The patient was counseled on the hereditary nature of this disorder. Symptomatic treatment with sodium valproate 250 mg two times daily and clonazepam 0.5 mg two times daily was initiated. He did not find these medications to be effective for his myoclonus and dystonia, but found that the clonazepam did improve his sleeping. Sodium valproate was tapered off and he was continued on clonazepam to help with sleeping. The patient was counseled on available symptomatic treatments and chose to initiate the antidepressant paroxetine to help with symptoms of myoclonus and dystonia, as well as depression.

Discussion
M-D is a rare movement disorder characterized by a combination of myoclonic jerks, usually in the arms and axial muscles, and mild dystonia, in the head and upper extremities. Diagnostic criteria for M-D includes onset before 20 years of age, myoclonus predominating in the upper body, positive family history for M-D with paternal transmission, normal brain MRI, and exclusion of additional neurological features such as cerebellar ataxia, spasticity, and dementia. Elevated rates of psychiatric disturbances, including obsessive-compulsive disorder, depression, social anxiety, and panic disorders, have been reported in patients with M-D. Patients with M-D often have a drastic reduction of myoclonus in response to alcohol ingestion.
however, cases have been identified in families of various regions including Europe, South America, North America, and Asia.\(^2\)

M-D is an autosomal dominant disorder with reduced penetrance attributed to maternal imprinting.\(^4,5\) Maternal inheritance has a penetrance of 10–15%, while paternal inheritance results in full penetrance.\(^4,5\) The SGCE gene was identified in 1997 and linked to M-D in 2001.\(^6\) Gene testing in 25 patients diagnosed clinically with definite or probable M-D showed that mutations in the SGCE gene are present in 36% of patients with M-D.\(^1\) The SGCE gene encodes \(\varepsilon\)-sarcoglycan protein, a transmembrane protein that is believed to help link the cytoskeleton to the extracellular matrix. Genetic mutations in the D2 dopamine receptor gene (DRD2) and TOR1A gene have been identified in patients with M-D, however, it is unclear whether these mutations contribute to disease phenotype as mutations in the SGCE gene were also identified in these patients.\(^7–9\) Genetic mutations in the DTY15 gene locus were identified in a Canadian family with M-D in the absence of mutations in SGCE, indicating that mutations in DYT15 gene locus alone are sufficient to cause M-D.\(^10,11\) Spontaneous cases of M-D have also been reported.\(^12\) Although management of M-D is not greatly changed based on the results of genetic testing, genetic testing is useful to confirm a diagnosis of M-D, allow for genetic counseling, and to provide insight into the clinical spectrum of M-D, as M-D patients with mutations in the SGCE gene are more likely to experience psychiatric impairments (obsessive-compulsive disorder, depression, and social anxiety) and mild impairment of executive cognitive function.\(^3\)

The pathophysiology of M-D is not well understood. M-D is believed to be of a subcortical origin due to the absence of cortical correlates of myoclonic jerks.\(^2\) It has been proposed that the M-D phenotype occurs due to increased synchronization of neuronal activity in the basal ganglia network.\(^13\)

There are several features that can be used clinically to differentiate M-D from TS. Myoclonic jerks are lightning-like movements involving the head, neck and upper limbs, they cannot be consciously suppressed, are often made worse by certain actions (e.g. writing with the left hand in this case), can interfere with voluntary movement, and are reduced by alcohol intake. Conversely, tics seen in Tourette syndrome (TS) can be suppressed with conscious effort, are preceded by an urge to tic, do not interfere with voluntary movement, and are not reduced by alcohol intake (Figure 1).\(^14\) Tourette syndrome symptomology also differs from M-D in that verbal tics are present, symptoms tend to remit by adulthood, and there is a complex inheritance pattern. In M-D verbal tics are absent, symptoms continue into adulthood, and inheritance is autosomal dominant with reduced penetrance (Figure 1).\(^14\) Features that favoured a clinical diagnosis of M-D in this case were the nature of the movements (fast jerks

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**Figure 1. Differential and common features of Myoclonus-dystonia and Tourette syndrome.**
involving head and upper extremities, made worse by and interfered with writing with non-dominant hand, and reduced by alcohol intake), absence of verbal tics, positive family history for a similar movement disorder with paternal transmission, and symptoms continuing into adulthood.

Conditions that include myoclonus as a major component may be considered in the differential diagnosis of M-D, but certain characteristics of the myoclonus are usually different and additional neurological manifestations may be present. For example progressive myoclonus epilepsy may present with myoclonus as a prominent clinical feature, however, this is usually accompanied by grand mal seizures.2 Myoclonus may be a prominent feature of other primary dystonias, including DYT1,16,17 and dopa-responsive dystonia18,19 in rare cases. Vitamin E deficiency has also been reported to cause myoclonus and dystonia, though it is usually accompanied by ataxia.20 It is important to rule out vitamin E deficiency, as this is easily treatable.

A variety of symptomatic treatments have been tried for M-D with limited success. There are case reports of benzodiazepines, anticholinergic drugs, neuroleptics (tetrabenazine and haloperidol) and serotonergic agents (tryptophan, paroxetine, and venlafaxine) occasionally improving both myoclonus and dystonia.2,21,22 There are case reports of antiepileptic drugs, such as sodium valproate, levetiracetam, barbiturates, primidone, piracetam, carbamazepine, and gabapentin, improving myoclonus.2 Deep brain stimulation of the internal globus pallidus has been shown to be safe and effective at improving myoclonus and dystonia in a small number of refractory patients.23–25 A number of therapies used for M-D, including the anticonvulsant drugs levetiracetam and topiramate, can cause depression. We did not pursue these therapies as they could potentially worsen our patient’s depression. Instead we chose to initiate the anti-depressant paroxetine to help with symptoms of myoclonus and dystonia, as well as depression.

Conclusion

This is a case of M-D diagnosed as Tourette syndrome for 15 years that illustrates the importance of revisiting an initial diagnosis with the aid of genetic testing. This is similar to a recent case in which M-D was misdiagnosed as Tourette syndrome26, indicating that, although M-D is rare, it must be considered in patients with early onset myoclonus and dystonia, especially in cases with a positive family history.

References