Medications and Tardive Dyskinesia

Numerous medications have been associated with chorea. The most common direct cause of drug-induced chorea is levodopa-induced dyskinesias in individuals with Parkinson's disease. Tardive dyskinesia is a late complication of treatment with dopamine receptor blocking agents, usually neuroleptic antipsychotics, and may have chorea as a prominent feature. Advancing age, female gender, and use of high potency antipsychotics are associated with an increased risk for this complication. While removal of the offending agent is critical to prevent worsening, symptoms persist in approximately two thirds of patients and treatment can be challenging.

Dystonia

Dystonia is a heterogenous class of movement disorders characterized by sustained muscle contractions that lead to twisting movements, abnormal postures, and repetitive movements. The classification of dystonia is challenging, having undergone numerous revisions over time, and is based on age of onset, distribution (focal versus generalized), association with neurological signs other than dystonia, and cause, if known. Mutations in at least 23 different genes are associated with dystonia. In general, the specific mutation does not reliably predict the phenotype. Childhood onset dystonia often has an underlying genetic cause, tends to generalize, and has a more severe course; while adult onset focal dystonia of the neck (e.g. cervical dystonia) tends to be non-progressive without a defined genetic cause.

Adult onset focal dystonias are by far the most common dystonias encountered clinically. Cervical dystonia is the most common dystonia, followed by focal dystonias involving the face and jaw muscles (blepharospasm, oromandibular dystonia or the combination); laryngeal and limb dystonias are rare. Adult onset limb dystonias are usually task-specific; dystonic contraction only occurs during specific voluntary actions (e.g., writer's cramp, musician's dystonia). This task specificity may be lost over time and occur even at rest. Focal adult onset limb dystonia that is not task specific can be the earliest manifestation of Parkinsonism and Parkinson's disease.

A mutation in the *TOR1A* gene is the most common cause of early onset generalized dystonia. DYT1 is an autosomal dominant disorder with reduced penetrance (30%). Onset is usually during childhood (10 to 15 years of age) with focal limb dystonia with action that rapidly generalizes often sparing the craniocervical muscles. It accounts for less than 50% of childhood onset dystonia in non-Jews and approximately 80% in children of Ashkenazi Jewish descent.

Dopa-responsive dystonia is a rare but important cause of childhood onset dystonia. It is inherited in autosomal dominant fashion with reduced penetrance (30%) with females more commonly affected than males. It is characterized by lower extremity dystonia, Parkinsonism, and diurnal variability with the symptoms worsening as the day progresses and improving with sleep. As the name suggests, it is exquisitely sensitive to levodopa therapy. The condition is often misdiagnosed and untreated; therefore, patients with childhood onset dystonia should have a trial of levodopa.

Myoclonus dystonia syndrome is an autosomal dominant disorder with alcohol responsive myoclonic jerks and dystonia. Dystonia is often focal with cervical dystonia and writer's cramp predominating. Onset is usually prior to the age of 20 years and psychiatric symptoms are common.

Rapid-onset dystonia Parkinsonism is a rare autosomal dominant condition with reduced penetrance that presents over hours or weeks with craniofacial and limb dystonia, dysarthria, bradykinesia, and postural instability. After initial progression the disorder stabilizes. The rapid onset and triggers, including emotional trauma or physical exertion, often result in it being misdiagnosed as a somatoform disorder.

Treatment of dystonia consists of a combination of oral medications and focused botulinum toxin injections. Oral medications include anticholinergics, benzodiazepines, and muscle relaxants. Deep brain stimulation has shown recent benefit in treating dystonia resulting from multiple causes.

Tics and Tourette's Syndrome

Tics are rapid, stereotyped, non-rhythmic movements or vocalizations. They can mimic many normal motor activities and movement disorders and occur on a background of otherwise normal activity and motor function. The key differentiating characteristics of tics are that they are associated with an irresistible urge or sensation that is temporarily relieved with performance of the tic. Tics are voluntarily suppressible but suppressing them results in increasing urge and rebound exacerbation of tics. Tics of childhood are extremely common and if transient, require no treatment.

Tourette's syndrome (TS) is a tic disorder, beginning in childhood with both motor and vocal tics persisting for more than one year. Approximately 50% of individuals with TS will also have features of obsessive compulsive disorder and/or attention deficit disorder. These other features are often more disabling than the tics themselves. In the majority of individuals there is partial or complete resolution of symptoms by adulthood. Treatment of tics and associated comorbidities should be reserved only for functionally disabling symptoms. A combination of behavioral approaches (comprehensive behavioral intervention for tics), oral medications, and botulinum toxin injections can be effective at minimizing the impact of symptoms. Extreme cases with persistence in adulthood may respond to deep brain stimulation.

CEREBELLAR ATAXIAS

The ataxias are a heterogeneous group of conditions reflecting impaired cerebellar function or impairment in cerebellar afferent and efferent pathways. Structural lesions due to abnormalities of brain development, stroke, tumor, infection, trauma, and inflammatory and demyelinating diseases can frequently affect cerebellar function and result in cerebellar symptoms and signs. Table 114-8 summarizes the differential diagnosis of the ataxic disorders divided by genetic and acquired causes.

Inherited/Genetic Ataxias

Progressive ataxia in coordination and gait disturbance are the cardinal features of the inherited ataxias. Autosomal dominant spinocerebellar ataxias (SCA) may present with a pure cerebellar syndrome or be associated with other extrapyramidal, pyramidal,