

Tourette Syndrome: A Neurologic Disease That Can Mimic Allergy

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ABSTRACT

Tourette syndrome is a hereditary neurologic disorder that usually occurs in childhood. The diagnosis is based on the clinical history of multiple motor and vocal tics. Tics often are confused as being symptoms of other diseases, including allergy. This article reviews the characteristics of Tourette syndrome, including the nature of the tics, associated conditions, etiology, and management. Distinguishing Tourette syndrome from allergy is important, since the treatment for the two entities is vastly different.

INTRODUCTION

NEUROLOGIC AND BEHAVIORAL DISORDERS can have signs and symptoms that are similar to the signs and symptoms of allergy. One of these, respiratory tic, also called tic cough, habit cough, or psychogenic cough, has been reviewed in this journal by Walker⁽¹⁾ and by Mansmann.⁽²⁾ We believe it is important to review for both the pediatrician and the allergist another of these conditions. Tourette syndrome (TS) is a relatively common hereditary neurologic disorder that has its onset in childhood. During its course, multiple motor and vocal tics occur and can resemble behaviors usually associated with allergy. Sniffing, snorting, throat clearing, coughing, and nose wiping can be nagging and distracting symptoms that are unattractive to parents and peers and can interfere with family and school functioning. Often, lesions on the hands or forearms and a rash around the mouth are assumed by parents and physicians to be manifestations of allergies when actually they represent compulsive picking of the skin and stereotyped licking seen in TS. Children with TS have an increased incidence of attention deficit disorder with or without hyperactivity, obsessive compulsive disorder, and conduct disorder.⁽³⁾ An unproven theory is that these behavioral symptoms are attributable to food or environmental allergies, thus prompting a referral to an allergist. Failure to recognize the association of these signs, symptoms, and behaviors can result in misdiagnosis and even implementation of inappropriate allergy therapy.

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CASE REPORT

A 5½-year-old white male child was referred to an allergist in July 1986 because of constant nasal congestion. He had been noted to have an "allergic salute" as well as dark circles under his eyes (allergic shiners). During the spring of 1986, he began making sniffing noises, which progressed to snorting sounds. The snorting had increased in frequency and at times occurred every 5 minutes. The frequency increased when he was upset and decreased when he was preoccupied or playing. The children in the neighborhood had begun making fun of him, and his parents were concerned about the reaction of his peers when he started school in the fall. There was no history of frequent sneezing, cough, epistaxis, nose picking, mouth breathing, snoring, or eye rubbing. He did have a history of frequent eye blinking at 3½ years that resolved after 8 months. Family history was positive for hayfever and asthma in paternal relatives and for a recurrent sinus condition in the mother.

Physical examination revealed a well-developed, well-nourished child with wide patent nares who was snorting every 20 seconds. He was not a mouth breather and did not rub his nose. There was no transverse nasal crease. The nasal mucosa was slightly pale. The rest of the physical examination was normal. A nasal smear showed a few eosinophils on one occasion and none on another. Skin testing by prick and intradermal methods was negative to epidermoids, dust mite, mold spores, spring, summer, and fall pollens, and limited foods (milk, wheat, peanut, soybean, egg white, chicken, chocolate). He was then referred for a pediatric neurology evaluation.

Additional history obtained at the time of the pediatric neurology evaluation revealed that he would often repeat words and phrases that he had just said. He also had had frequent throat clearing at 4½ years that had disappeared after several months. Every night when preparing for bed, he insisted that each activity be performed in a certain order and would become very upset if there was any change in this routine. There was no history suggestive of other obsessive or compulsive tendencies. The paternal grandmother had a history of frequent eye blinking and stuttering, and two paternal aunts had a history of "rocking-type movements" of the upper body during childhood. The diagnosis of TS was made, and he was started on haloperidol, resulting in a marked reduction in the frequency of snorting. However, 3 months later when in the first grade, he was noted to be fidgety and easily distracted. His attention span was short, and he was often unable to complete his work. Treatment with methylphenidate did not improve his ability to concentrate, and the attention deficit disorder has continued to be more disabling than the tics.

HISTORY

Tics are abrupt, brief, involuntary, coordinated, repetitious movements or vocalizations that are stereotyped and serve no apparent purpose. They are a common disturbance in childhood, occurring in up to 24% of children.⁽⁴⁾ Tic disorders probably represent a continuum, with transient simple tic disorder being the mildest condition. In this disorder, the tics are single and persist for less than a year. When a single tic persists for more than a year, the disorder is classified as a chronic simple tic disorder. Next along the continuum is chronic motor tic disorder, characterized by multiple motor tics that persist for more than 1 year. When vocal tics are present in addition to multiple motor tics, the disorder is known as Tourette syndrome.

In 1885, George Gilles de la Tourette described 9 patients who had the disorder that later became known as TS.⁽⁵⁾ At that time, the disorder was believed to be rare; however, as physician and public awareness of TS has increased, cases with milder symptomatology are being recognized. It is currently estimated that the prevalence of TS is at least 5 per 1,000, or over 1 million people in the United States.⁽⁶⁾

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TABLE 1. DIAGNOSTIC CRITERIA OF TOURETTE SYNDROME

Both multiple motor and one or more vocal tics have been present at some point during the illness, although not necessarily concurrently.
Tics occur many times a day (usually in bouts), nearly every day or intermittently throughout a period of more than 1 year.
The anatomic location, number, frequency, complexity, and severity of the tics change over time.
Onset prior to age 21.
Occurrence not exclusively during psychoactive substance intoxication or known central nervous system disease, such as Huntington's chorea and postviral encephalitis.

Adapted from ref. 7.

TABLE 2. TICS THAT MIMIC ALLERGY SYMPTOMS

Throat clearing	Eye blinking
Sniffing	Grunting
Coughing	Noisy breathing
Snorting	Nose wiping
Facial grimacing	Nose twitching

DIAGNOSIS

The diagnostic criteria for TS according to DSM-III-R⁽⁷⁾ are noted in Table 1.

In a study of 200 patients, Erenberg et al.⁽⁸⁾ found the mean age of onset to be 6.3 years, with 90% having symptoms before age 10. At onset, 50% of patients have a single tic, whereas the other 50% have more than one tic.⁽⁶⁾ The initial tics are more often motor tics than vocal tics and usually involve the face. Later, tics may involve the neck, shoulders, and upper extremities and, less commonly the torso, and lower extremities. Motor tics generally are divided into simple tics that are a brief contraction of a limited number of muscle groups and complex tics that are coordinated contraction of several muscle groups, resembling mannerisms. Common simple motor tics include eye blinking, facial grimacing, lip movements, nose twitching, head jerking, tongue protrusion, and shoulder shrugging. Examples of complex motor tics include hitting or touching self or others, jumping, smelling hands or objects, skipping, and finger snapping. Copropraxia, which is an involuntary, socially unacceptable, obscene gesture, is another example of a complex motor tic and occurs in approximately 12% of patients at some time during the course of the disorder.^(6,9)

Vocal tics are quite variable and include noises produced by the throat as well as shouting of syllables, words, or phrases. Common vocal tics are throat clearing, grunting, squealing, sniffing, coughing, screaming, and snorting. Barking, humming, stammering, and stuttering occur less frequently. Echolalia, repetition of the last word or phrase of another person, and palilalia, repetition of one's own last word or phrase, are other vocal tics that occur in approximately 17% of patients.⁽⁶⁾ Coprolalia, the involuntary use of obscenities, was thought initially to be necessary to make the diagnoses of TS. More recent studies have shown the incidence to be less than 35%,^(6,9) and one study in children reported it to be as low as 8%.⁽⁸⁾ Several of these motor and vocal tics could be confused with symptoms of allergy. Common tics that mimic allergy are listed in Table 2.

The tics in TS typically wax and wane, with exacerbations of tics during periods of stress and improvement when the child is involved in enjoyable activities. Another characteristic feature of TS is that tics change over time, with new tics developing as previous tics disappear. Often, a tic

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may disappear for weeks to months and then later reappear. One of the most characteristic features of tics is their suppressibility by conscious effort of the patient. Suppression of the tics creates a feeling of pressure, and a point is finally reached at which the patient has to exhibit the tics. Once the tics are expressed, the patient experiences a feeling of relief. Obviously, a young child may not be able to describe these feelings associated with suppression and expression of tics. Another feature of tics is their occurrence during all stages of sleep. Polygraphic sleep studies in TS patients have demonstrated the presence of both motor and vocal tics similar to those observed during wakefulness. Other sleep disturbances include an increased percentage of stage 3 and 4 sleep, an increased number of awakenings, enuresis, and somnambulism.^(10, 11)

ASSOCIATED CONDITIONS

There are several conditions that are associated with TS, including obsessive compulsive disorder, attention deficit disorder, learning disabilities, and conduct disorder. The exact incidence of obsessive compulsive disorder is not known, although it has been reported to occur in as many as 68% of patients.⁽¹²⁾ One of the difficulties in determining the incidence of obsessive compulsive disorder is differentiating complex tics from compulsive behavior. Frankel et al.⁽¹³⁾ found that obsessive compulsive behavior in TS patients older than 18 years was characterized by fear of contamination and repetitive checking and arranging, whereas in patients younger than 18, the behaviors related to impulse control. Among TS patients, there is a sex difference in the expression of obsessive compulsive disorder, with a higher incidence in females.⁽¹⁴⁾

Attention deficit disorder and learning problems occur in a higher frequency in TS patients than in the general population. In a study of 200 pediatric and adolescent patients with TS, over 50% had learning disabilities or attention deficit disorder with or without hyperactivity. The reason for the association of these conditions with TS is unknown. Learning and behavioral problems occurred as frequently in children with mild motor and vocal tics as they did in those with more severe tics. It was noted also that behavioral and learning problems often preceded the onset of tics and that these problems were more disabling than the tics.⁽⁸⁾

There is evidence that there is an increased incidence of conduct disorder in children with TS. In a large study, Comings and Comings⁽¹⁵⁾ found that 35% of TS patients had behaviors that fulfilled the criteria of conduct disorder as defined by DSM-III-R.⁽⁷⁾ These behaviors include lying, stealing, starting fires, vandalism, fighting, shouting, and cruelty to animals. TS patients with attention deficit disorder are much more likely to have conduct disorder than are those without attention deficit disorder.^(6, 15) Steffl⁽¹⁶⁾ reported that the traditional forms of psychotherapy generally are not helpful and that medication often does not ameliorate the behavioral problems.

EPIDEMIOLOGY

TS occurs about three times more frequently in males than in females. It has been reported in all races, with the highest frequency in Caucasians.⁽⁶⁾ Some studies have noted an increased incidence in people of Eastern European and Ashkenazi Jewish background,^(17, 18) although other studies have not documented this increased incidence.^(8, 12) The apparent increased incidence in these groups may actually be a result of ascertainment bias.

GENETICS

During the past decade, there has been increasing evidence that TS and other tic syndromes have a genetic origin. Gilles de la Tourette,⁽⁵⁾ in his initial report, noted the familial nature of

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the disorder. Many studies have reported that TS, chronic motor tics, and other tic disorders tend to cluster in families.⁽¹⁹⁻²²⁾ Pauls and Leckman⁽¹⁴⁾ examined the mode of transmission of TS by performing segregation analysis in 30 nuclear families and concluded that TS is a highly penetrant, autosomal dominant trait with variable expressivity. Current research is directed toward genetic linkage studies and identification of a marker for the TS locus.⁽²²⁾

ETIOLOGY

The exact nature of the biochemical abnormalities in TS remains unknown, although many studies have focused on dopamine and its metabolites. A dopaminergic hypothesis was suggested by improvement in symptoms with such drugs as haloperidol, which are dopamine receptor blocking agents,⁽²³⁾ and by exacerbation of symptoms with stimulants that increase the release of dopamine.⁽²⁴⁾ Measurements of cerebrospinal fluid metabolites of dopamine have shown conflicting results, although most often the levels are decreased, suggesting that there is dopamine postsynaptic receptor hypersensitivity rather than increased turnover of dopamine.⁽²⁵⁾ Recently, there has been interest in the endogenous opioid system and its role in the pathogenesis of TS.⁽²⁶⁾ Using immunocytochemical techniques in postmortem brains, Haber et al.⁽²⁷⁾ demonstrated a decrease in dynorphin, an endogenous opioid, in the basal ganglia area of a TS patient compared to neurologically normal controls. It has been postulated that malfunction of the endogenous opioid system could result in hypersensitivity of postsynaptic dopaminergic receptors.⁽²⁸⁾ Further research is needed to better understand the neurochemical abnormalities in TS.

Although allergies and TS can occur in the same patient, there is no evidence that allergies are an etiologic factor in TS. Comings and Comings⁽²⁹⁾ studied 247 TS patients and found that there was no significant difference in the frequency of various allergies in TS patients and in controls. A suggested increase in the frequency of skin allergies was thought most likely to be related to obsessive picking of the skin.

TREATMENT

There is no cure for TS, and the objective of treatment is to alleviate the symptoms. Abuzzahab and Anderson⁽³⁰⁾ reviewed the literature and found that over 580 various kinds of treatment have been tried for TS. Included in the list of therapies are sedatives, anticonvulsants, antidepressants, curare, acupuncture, thalamotomy, shock therapy, lobotomy, hypnosis, and many others. Obviously, most types of therapy have been unsuccessful, but because of the waxing and waning frequency of tics, a spontaneous improvement often has been interpreted incorrectly as being a response to therapy.

The initial therapy of TS should be to identify sources of stress in the child's environment and attempt to decrease the stress. Any events or conditions that exacerbate tics should be identified and eliminated if possible. The involuntary nature of tics should be emphasized, so that the child is not punished for symptoms that he or she is not able to control. Parents should be educated to ignore tics as much as possible, since focusing on them actually may increase the frequency of tics. Pharmacotherapy is reserved for those children whose symptoms impair their psychosocial or educational functioning.

Haloperidol, a butyrophenone, has been used since 1961 and was the first medication that was found to be truly effective in TS. Studies have shown that between 78 and 91% of patients have improvement in their tics with treatment with haloperidol.⁽⁶⁾ Most side effects of haloperidol are dose-related, so that the smallest dose that is effective is used. The most common side effects are lethargy, personality changes, and weight gain, with higher doses resulting in anticholinergic symptoms and cognitive impairment. School avoidance and social phobias have resulted in some TS patients treated with haloperidol.⁽³¹⁾

Clonidine, which is an alpha-adrenergic agonist, has been reported to be successful in reducing tics in some clinical trials,^(32,33) although in others, it has had no effect.^(34,35) Some patients treated with clonidine show an improvement in behavioral problems with little improvement in tics.⁽³²⁾ Improvement with clonidine may not occur until the medication has been taken for several months. Adverse effects include sedation, lightheadedness, hypotension, and impaired cognition, although at low doses these are minimal.

One of the newer drugs that has been shown to be effective is pimozide, a diphenylbutylpiperidine that blocks central dopamine receptors. It appears to be similar in effectiveness to haloperidol but has fewer adverse effects.⁽⁶⁾ High doses of pimozide have been associated with adverse cardiac effects; therefore, monitoring with electrocardiograms is recommended.⁽³⁶⁾ Other drugs that have been effective in decreasing symptoms include fluphenazine and other phenothiazines.⁽⁶⁾ There is evidence also that naloxone, which reverses the effects of opioids, may have a role in treatment of TS.⁽³⁷⁾

PROGNOSIS

In the initial report of TS, the disorder was described as being lifelong.⁽⁵⁾ More recent studies, however, have shown that some patients experience marked improvement after several years.^(38,39) Erenberg et al.⁽⁴⁰⁾ reported a follow-up study of TS patients ranging in age from 15 to 25 years. In 73% of the patients, the tics had decreased markedly or almost disappeared, with the median age at improvement being 16 years. Many patients had associated learning and behavioral problems but felt they were coping well with these problems. The reason that patients often show improvement in late adolescence and early adulthood is unknown. These data suggest that the physician may be optimistic when discussing the natural history of TS with patients and parents.

DISCUSSION

TS is a genetic neurologic disorder characterized by motor and vocal tics. There is no laboratory test to confirm the diagnosis, which is based on the clinical symptoms and course. Because the tics often mimic symptoms of other diseases, including allergy, the diagnosis may be difficult. Physicians who evaluate a child referred for allergic symptoms should take a careful history with attention to other tics, such as head shaking, shoulder shrugging, and echolalia, that would not be consistent with allergic symptoms. Other important history would include associated conditions, such as attention deficit disorder, learning problems, conduct disorder, or obsessive compulsive tendencies, as well as any family history of tics or associated disorders. Because the tics may interfere with social and educational functioning, it is important to make the correct diagnosis. Although there is no cure for TS, medications can alleviate the symptoms, making it easier for the child to function at school and at home.

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