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Risk Factors and Demographics in Patients With Spasmodic Dysphonia

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Objectives: **Spasmodic dysphonia has been characterized as a functional, psychogenic, or movement disorder with no known etiology or cure. In the present study, risk factors associated with other movement disorders were evaluated in patients with spasmodic dysphonia.** ***Study Design:*** **Retrospective patient survey of 168 patients with a known diagnosis of spasmodic dysphonia who completed questionnaires at the time of interval botulinum toxin injection.** ***Methods:*** **Patients completed questionnaires on demographics, education level, work history, significant life events, medical, social, and family history. The results were compared with those of first-degree relatives as a control group with similar demographics. Data were analyzed using percentages calculated on the total number of responses and distribution of frequency of each. Statistical significance was estimated on *t* tests of χ^2 values.** ***Results:*** **In the series of 168 patients, there was a female predominance of 79%. Age range at onset was 13 to 71 years with an average of age of 45 years. Sixty-five percent of patients had previously had the measles or mumps compared with the national average of 15% in a similar age group (*P* = .0001). Thirty percent of patients directly associated onset of spasmodic dysphonia symptoms to an upper respiratory tract infection, and 21% to a major life stress. There was no significant incidence of any other medical or neurological condition or symptomatology. There was no family history of spasmodic dysphonia. Twenty-six percent of patients had an essential tremor compared with 4% of first-degree relatives (*P* = .0001), and 11% had associated writer's cramp compared with 2% of relatives (*P* = .02). Less than 1% of patients described a history of toxic exposure or electrical injury.** ***Conclusions:*** **The majority of patients with spasmodic dysphonia are girls and women. A significantly higher incidence of childhood viral illness was found in the patients with spasmodic dysphonia. Patients with spasmodic dysphonia had a significant incidence of both essential tremor and writer's cramp but no history of major illness or other neurological disorder. There appear to be no significant environmental or hereditary patterns in the etiology of spasmodic dysphonia. Stress or viral infection may induce the onset of symptoms of spasmodic dysphonia. Many features of the disorder are common to other movement disorders, and this knowledge may direct future research efforts.** ***Key Words:*** **Spasmodic dysphonia, dystonia, etiology, stress, viral infection.**

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INTRODUCTION

Dystonia is defined as a syndrome of sustained, uncontrolled muscle contractions resulting in abnormal, unintended actions.[1] Spasmodic dysphonia is considered to be one form of an idiopathic adult-onset dystonia that exhibits focal manifestations. Other focal dystonias with a presumed similar etiology include spasmodic torticollis, blepharospasm, writer's cramp, and trunk and foot dystonia.

The cause or origin of spasmodic dysphonia and other focal dystonias remains unknown. Historically, spasmodic dysphonia has been thought to be psychogenic or traumatic in origin.[2] Risk factors for certain types of nonfocal dystonia have been well delineated. These range from patterns of autosomal inheritance to acquired genetic mutations, trauma, stress, electrical injury, viral and psychiatric illness, heavy metal poisoning, hydrocephalus, degenerative cortical diseases, and endocrine disorders.[3–13] The purpose of the present study was to determine any possible association between known risk factors for other nonfocal dystonias and spasmodic dysphonia.

PATIENTS AND METHODS

One hundred sixty-eight consecutive patients presenting for botulinum toxin injections for spasmodic dysphonia completed a questionnaire (Appendix). In addition to a complete medical and social history, environmental, industrial, geographical, and educational data were obtained. First-degree relatives were chosen as control subjects. A complete history was obtained for 186 control subjects. Both patient and control subject shared similar geographic and environmental history. Geographical information was restricted to size and economy of place of birth and later sites. Subjects were asked about conditions affecting first- and second-degree relatives. In addition, information about individuals living in the same area was obtained where possible from the subjects'

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knowledge. Patients and control subjects were asked specifically about all published risk factors for dystonia. Data were analyzed by percentages calculated from the total number of responses and the distribution of frequency. Statistical significance was estimated on paired, two-tailed t tests of χ^2 values (Statview, version V.1, Abacus Concepts, Inc., Berkeley, CA).

Diagnosis of spasmodic dysphonia was first made by a physician and a speech pathologist based on criteria in widespread use and described in the literature.[14,15] Patients with segmental dystonias such as Meige's disease were excluded from the study and are not treated with botulinum toxin injection at the Hershey Medical Center (Hershey, PA). After a careful review and discussion with neurologists at our institution, we have not identified cases in which benefit was added through the use of magnetic resonance imaging; therefore, routine imaging of the head and neck in cases of spasmodic dysphonia was not performed in these patients.

RESULTS

Thirty-four male and 134 female patients were included in the study. Included in the control group were 89 male and 97 female relatives. Age range at onset of spasmodic dysphonia was 13 to 71 years with a mean age of 45 years. Mean age at the time of treatment was 56 years. Fifty-five percent were born and lived for an average of 19 years in a rural area with a population of less than 150,000 individuals, then moved to an industrial area with a population of more than 150,000. No relatives or individuals living in the same area as the patients with a diagnosis of spasmodic dysphonia were identified. The average patient had completed 2 years of college.

Sixty-five percent of patients had previously had the measles or mumps. This is statistically significantly different from the national average incidence of 17% under the age of 25 years during the period between 1958 and 1962 ($P = .0001$). Thirty percent of patients directly associated onset of spasmodic dysphonia to an upper respiratory tract infection, and 21% to a major life stress (confidence interval [CI], 15%–42%).

Eleven percent of patients had associated writer's cramp compared with 2% of individuals in the control group ($P = .02$). Associated features of other movement disorders were observed. Twenty-six percent of patients had an essential tremor of the upper extremities compared with 4% of first-degree relatives ($P = .0001$). Despite these findings, there was no significant incidence of any other major medical or neurological condition or symptomatology. All of the patients exhibited stable focal disease without segmental spread over a mean interval of 11 years. The incidence of peripheral vascular concurrent hypertension at 25% was similar to a 27% rate in the father and a 43% rate in the mother. One patient described a history of toxic exposure, and one an electrocution injury. There were no other cases of associated injury.

The Voice Handicap Index and Short-Form 36 surveys were administered to this same group of patients before and after treatment with botulinum toxin. Improvements in the patients' perception of their functional, physical, and emotional voice handicap were statistically significant. In addition, treatment improved their social functioning and their perception of their mental health.[16]

DISCUSSION

In the current study, a 79% female predominance in spasmodic dysphonia, as well as an association with childhood infectious disease, writer's cramp, and essential tremor, was identified. The average age was 56.7 years, and median age, 56 years. A strong connection with childhood viral illness was also noted with 65% of patients having had the measles or mumps. With respect to neurological findings, there was an association with upper-extremity essential tremor and, to a lesser degree, writer's cramp. In each patient, the manifestations of spasmodic dysphonia remained focal. Fifty-one percent of patients associated the onset of symptoms with an acute upper respiratory tract illness or a major life stress. However, this finding was well within confidence intervals of the expected frequency of such occurrences within the general population. There was no identifiable familial association with spasmodic dysphonia. Geographical history does not appear to be relevant to the etiology of spasmodic dysphonia.

There are a number of inherent biases in examining the patient population of a given practice area, including referral, age, and sex bias. By examining trends between similar studies, some of the biases may be ruled out. Onset of symptoms in the middle decades of life has been noted in studies of patients with spasmodic dysphonia, as well as those of other focal types of dystonia.[17,18] Another previously cited epidemiological finding is female predominance. This was noted initially by Izdebski et al.,[18] which they did not believe established "spastic dysphonia as a predominantly female disorder." This issue was reexamined by Adler et al.,[19] who reviewed their own data, as well as five other published reports, and concluded that female predominance is not a result of ascertainment bias. They were able to find only one report of a higher male ratio in spasmodic dysphonia.[19] In a review of more than 900 patients with primary laryngeal dystonia, Blitzer et al.[20] recorded a 63% female predominance. Therefore, the finding of female predominance is most likely an accurate cross-section of the population of patients with spasmodic dysphonia and is not related to ascertainment bias.

The reason for a predilection toward female sex in a disorder currently thought to be neurological in origin is unclear. The predominance of autoimmune diseases in female patients is thought by some authors to be a phenomenon of microchimerism.[21] This theory holds that persistent fetal cells in the mother's circulation after pregnancy may be responsible for the autoimmune phenomenon as a result of a mechanism similar to graft-versus-host disease. A precedent in neurological disorders exists in multiple sclerosis, which has features of other autoimmune disorders.[22] This theory does not explain disease occurrence in nonparous female patients; yet, the parallels are compelling and certainly warrant further investigation into this area.

Examination of geographical data may give information about possible environmental exposure during childhood that could potentially cause the disorder. Geographical data obtained indicates a rural prevalence during the developmental years and an industrial or large-city environment in adulthood. Most likely, this phenomenon is

more closely related to referral pattern bias, the south-central location of our treatment facility, and the overall trend of urban migration patterns in the United States. Incidence of toxic exposure leading to disease development is sporadic and does not appear to be associated with the development of spasmodic dysphonia because there was no incidence of spasmodic dysphonia in the control group, despite similar environmental exposure. This information may become useful in future studies as more becomes known about the effects of specific toxins.

An incidence of childhood measles and mumps infection of 65% in individuals with spasmodic dysphonia was discovered in the present study. Izdebski et al.[18] reported a 45% incidence of these illnesses and also noted that patients with spasmodic dysphonia typically contracted these illnesses later in life than control subjects. In the present study, age at onset of disease was not examined because objective medical records were not consistently available. Between 1958 and 1962, an average number of cases of measles per year of 503,282 was reported in the United States.[23] Reporting of mumps cases did not begin until 1968. In that year, 152,209 cases were recorded. Assuming that the vast majority of patients contracted the measles before the age of 25 years, this approximates an incidence of 15%.[24] The potential for latent viral diseases to cause neurological manifestations is well described in the case of chickenpox and herpes zoster. There are also reports in the literature of ataxia following measles, mumps, and rubella vaccine.[25]

An association of essential upper-extremity tremor with other types of dystonia has been noted in other studies but was found to be common in first-degree relatives as well.[14,26] The present study recorded similar results.

Marsden and Sheehy[27] were among the first to identify spasmodic dysphonia as a manifestation of adult-onset torsion dystonia. Greene et al.[28] found that symptoms in the majority of patients with onset after age 21 years remained focal, and only 15% to 30% eventually developed symptoms outside the initially involved segment. The authors also found a family history of dystonia of 3% or less. Therefore, our findings of no spread of disease and no familial association are correlated in other studies of dystonia.

Previous studies have suggested that radiographically significant basal ganglia or brainstem lesions can cause focal or segmental dystonia.[29,30] Lesions in the putamen, thalamus, and inferior olives have been associated with spasmodic dysphonia.[5,31] In a study of three patients with spasmodic dysphonia and a history of head trauma, Finitzo et al.[32] noted abnormal findings on magnetic resonance imaging in one patient, but abnormal brain electrical activity mapping in all three. Defazio et al.,[26] as well as the present study, noted no history of head trauma or radiographic lesions. However, they did note an association between trauma to an area of the body and later development of dystonic symptoms, as with cervical dystonia. Our patient population had no focal neurological findings or suggestive history that would have prompted neurological or radiological evaluation.

The association between psychological stress and spasmodic dysphonia may possibly be the most important but, at the same time, misleading clue as to its etiology. This connection has not been reported with other dystonias. In the present study, 21% of patients who had such a stress exhibited a strong correlation with the onset of dysphonia. Ginsberg et al.[33] also recognized this association. In a German study of 18 patients with spasmodic dysphonia, the authors noted a prevalence of stress within a 2-year period of symptom onset.[34] Standard psychometric testing failed to show deviation from standardized norms indicating no underlying psychopathology. Because the type of stress is individual and subjective, it is difficult to measure qualitatively or quantitatively. A review of the literature revealed no published reports of an association between *Diagnostic and Statistical Manual, Fourth Edition*, axis I disorders, such as major depressive disorders, brief reactive psychosis, or post-traumatic stress disorder, and spasmodic dysphonia. Although stress may play a role in the development of spasmodic dysphonia, it does not appear to be an independent risk factor.

One possible model for stress-related central disorders is attributable to the plasticity of the central nervous system. Dauer et al.[35] theorized that painful stimuli cause synaptic changes in the basal ganglia where they are received and processed, leading to the development of dystonia. A similar mechanism has been postulated in the pathogenesis of writer's cramp. Bara-Jimenez et al.[36] demonstrated abnormal finger representation in the somatosensory (S1) cortex of dystonic patients. This supposition followed animal studies in which repetitive peripheral sensory stimulation and movements induced plastic changes in the animals' S1 cortex[37]; the authors further postulated that this condition may potentially be treatable by reordering the S1 representational areas of the affected organ.[38]

CONCLUSION

We found a 79% female predominance in spasmodic dysphonia, as well as an association with writer's cramp and essential tremor. There was a strong correlation between psychological stress and onset of the disorder. In addition, there was a significantly higher incidence of measles and mumps in our patient population than in a similar age group in the general population. There was no familial or apparent environmental association in the development of spasmodic dysphonia. The incidence of illness and injury in patients with spasmodic dysphonia was well within confidence intervals of that of the general population.

The epidemiology of spasmodic dysphonia is similar in many respects to other dystonias. Although frequently associated with specific causes and events, ultimately, the etiology is most likely multifactorial. The future application of knowledge of other well-studied diseases may further our understanding of spasmodic dysphonia, as well as provide new directions for future research.

BIBLIOGRAPHY

1. Fahn S. The varied clinical expressions of dystonia. *Neurol Clin* 1984;2:541–554.
2. Heaver L. Spastic dysphonia: a psychosomatic voice disorder. In: Barbara DA, ed. *Psychological and Psychiatric Aspects*

of Speech and Hearing. Springfield, IL: Charles C. Thomas, 1960:250–253.
3. Ondo W. Lingual dystonia following electrical injury. *Mov Disord* 1997;12:253.
4. O'Brien CF. Involuntary movement disorders following lightning and electrical injuries. *Semin Neurol* 1995;15: 263–267.
5. Lee MS, Lee SB, Kim WC. Spasmodic dysphonia associated with a left ventrolateral putaminal lesion. *Neurology* 1996; 47:827–828.
6. Cheng JT, Liu A, Wasmuth J, et al. Clinical evidence of genetic anticipation in adult-onset idiopathic dystonia. *Neurology* 1996;47:215–219.
7. Baxter P, Forsyth R, Eyre J. Relapse and movement disorder after herpes simplex encephalitis [letter]. *J Child Neurol* 1997;12:283.
8. Montgomery EB Jr. Heavy metals and the etiology of Parkinson's disease and other movement disorders. *Toxicology* 1995;97:3–9.
9. Man CK, Zheng YH, Mak PK. *Science of Total Environment*. 1996;191:291–295.
10. Dragasevic N, Petkovic-Medved B, Svetel M, Filipovic SR, Kostic VS. Paroxysmal hemiballism and idiopathic hypoparathyroidism. *J Neurol* 1997;244:389–390.
11. Krauss JK, Regel JP, Droste DW. Movement disorders in adult hydrocephalus. *Mov Disord* 1997;12:53–60.
12. Yen DJ, Shan DE, Lu SR. Hyperthyroidism presenting as recurrent short paroxysmal kinesigenic dyskinesia. *Mov Disord* 1998;13:361–363.
13. Cassady SL, Adami H, Moran M, et al. Spontaneous dyskinesia in subjects with schizophrenia spectrum personality. *American Journal of Psychiatry* 1998;155:70–75.
14. Blitzer A, Brin MF. Spasmodic dysphonia: evaluation and management. In: Fried MP, ed. *The Larynx,* 2nd ed. St. Louis: Mosby, 1996:187–198.
15. Deems DA, Sataloff RT. Spasmodic dysphonia. In: Sataloff RT, ed. *Professional Voice,* 2nd ed. London: Singular Press, 1997:499–506.
16. Courey MS, Garrett CG, Billante CR, et al. Outcomes assessment following treatment of spasmodic dysphonia with botulinum toxin. *Ann Otol Rhinol Laryngol* 2000;109: 819–822.
17. Garcia Ruiz PJ, Sanchez del Rio M, Cenjor Espanol C, et al. Adduction spastic dysphonia: clinical and treatment [in Spanish]. *Rev Clin Esp* 1998;198:156–158.
18. Izdebski K, Dedo HH, Boles L. Spastic dysphonia: a patient profile of 200 cases. *Am J Otolaryngol* 1984;5:7–14.
19. Adler CH, Edwards BW, Fransberg SF. Female predominance in spasmodic dysphonia [Letter]. *J Neurol Neurosurg Psychiatry* 1997;63:688.
20. Blitzer A, Brin MF, Stewart CF. Botulinum toxin management of spasmodic dysphonia (laryngeal dystonia): a 12-year experience in more than 900 patients. *Laryngoscope* 1998;108:1435–1441.
21. Nelson JL, Lambert N, Medsger TA, et al. Persistent fetal and maternal microchimerism: a new etiology for autoimmune disease? *Arthritis Rheum* 1999;42(Suppl):S277.
22. McCombe PA, Chalk JB, Pender MP. Familial occurrence of multiple sclerosis with thyroid disease and systemic lupus erythematosus. *J Neurol Sci* 1990;97:163–171.
23. Impact of vaccines universally recommended for children: United States, 1900–1999—achievements in public health, 1900–1999. *MMWR* 1999;48:243–248.
24. U.S. Bureau of the Census. *Current Population Survey*. Washington, DC, 1960.
25. Plesner AM. Gait disturbances after measles, mumps, and rubella vaccine. *Lancet* 1995;345:316.
26. Defazio G, Berardelli A, Abbruzzese G, et al. Possible risk factors for primary adult onset dystonia: a case-control investigation by the Italian movement disorders study group. *J Neurol Neurosurg Psychiatry* 1998;64:25–32.
27. Marsden CD, Sheehy MP. Spastic dysphonia, Meige disease and torsion dystonia. *Neurology* 1982;32:1202–1203.
28. Greene P, Kang UJ, Fahn S. Spread of symptoms in idiopathic torsion dystonia. *Mov Disord* 1995;10:143–152.
29. Fletcher NA, Harding AE, Marsden CD. The relationship between trauma and idiopathic torsion dystonia. *J Neurol Neurosurg Psychiatry* 1991;54:713–717.
30. Burton LS, Jankovic J. Delayed-onset progressive movement disorders after static brain lesions. *Neurology* 1996;46: 68–74.
31. Yamamoto T, Yamashita M. Thalamo-olivary degeneration in a patient with laryngopharyngeal dystonia. *J Neurol Neurosurg Psychiatry* 1995;59:438–441.
32. Finitzo T, Pool KD, Freeman FJ, et al. Spasmodic dysphonia subsequent to head trauma. *Arch Otolaryngol Head Neck Surg* 1987;113:1107–1110.
33. Ginsberg BI, Wallack JJ, Strain JJ, Biller HF. Defining the psychiatric role in spastic dysphonia. *Gen Hosp Psychiatry* 1988;10:132–137.
34. Kiese-Himmel C, Sqirner P. Psychological factors in spasmodic dysphonia. *Laryngorhinootologie* 1996;75:397–402.
35. Dauer WT, Burke RE, Greene P, et al. Current concepts on the clinical features, etiology and management of idiopathic cervical dystonia. *Brain* 1998;121:547–560.
36. Bara-Jimenez W, Catalan MJ, Hallett M, Gerloff C. Abnormal somatosensory homunculus in dystonia of the hand. *Ann Neurol* 1998;44:828–831.
37. Xerri C, Coq JO, Merzenich MM, Sameshima K, Jenkins WM. Experience-induced plasticity of cutaneous maps in the primary somatosensory cortex of adult monkeys and rats. *J Physiol* 1996;90:277–287.
38. Byl NN, Merzenich MM, Jenkins WM. A primate genesis model of focal dystonia and repetitive strain injury, I: learning-induced dedifferentiation of the representation of the hand in the primary somatosensory cortex in adult monkeys. *Neurology* 1996;47:508–520.