

Clinical Characteristics of 15 Patients With Tardive Dystonia

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Clinical characteristics of 15 consecutively referred patients with tardive dystonia are reported. The onset of tardive dystonia occurred in all age groups and in both sexes, with some preponderance in men. There was considerable overlap with tardive dyskinesia and tardive akathisia. Six subjects reported past acute dystonia, and four had histories of essential tremor, suggesting a vulnerability to the development of dystonia.

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Tardive dystonia is a rare disorder with a reported prevalence of 1%–2% in chronic hospitalized psychiatric patients (1) and 1% in chronically medicated schizophrenic outpatients (2). Studies of its clinical characteristics have been few and have involved small numbers of subjects (3), with the exception of a report of 42 cases by Burke et al. (4) and a later report of 67 cases by Kang et al. (5) that included some of the cases previously reported by Burke et al.

The Kang et al. study raised some important issues that deserve independent replication. Contrary to earlier reports (3), which suggested that tardive dystonia was more likely to occur in young men, these authors reported a lack of predilection for any particular age group or sex. They found no relation between the duration of exposure to neuroleptic drugs and the sex of the subjects or their age at the onset of dystonia. Patients who were younger at onset were, nevertheless, more likely to have a generalized dystonia. There was frequent overlap with tardive dyskinesia and tardive akathisia. Subjects with concomitant oral-buccal-lingual dyskinesia did not differ, however, from those without it on any of the variables examined.

This article reports a study that examined the same issues in a series of 15 consecutively referred patients with tardive dystonia.

METHOD

Between 1987 and 1990, 15 patients consecutively referred to a movement disorders clinic met the following predetermined operational criteria for tardive dystonia (adapted from Kang et al. [5]): 1) the

presence of dystonia (sustained, involuntary muscular contractions frequently causing twisting and repetitive movements or abnormal postures) for more than 1 month; 2) if other movements (e.g., dyskinesia, akathisia) were also present, the dystonia was the most prominent disturbance; 3) the dystonia developed during or within 3 months of discontinuation of treatment with dopamine antagonists; 4) other known causes of secondary dystonia had been ruled out; and 5) there was no family history of dystonia. I made a detailed assessment of each patient, and the diagnosis of tardive dystonia was confirmed by a neurologist. Information was obtained from the patients, their medical records, and key informants, and an item was rated as positive if two of the three sources agreed that it was present.

The following information was obtained: sociodemographic data; psychiatric diagnoses; medication-related data, including age at first neuroleptic treatment, duration of neuroleptic use prior to onset of movement disorder, total neuroleptic load in chlorpromazine equivalents (with use of the empirical data provided by Davis [6]) and whether drug use was continuous or intermittent (drug-free periods of more than 3 months); past history, including serious head injury, perinatal injury, epilepsy, severe extrapyramidal side effects, acute drug-induced dystonia, essential tremor, stuttering, akathisia, and ECT; family history of dystonia, Parkinson's disease, dementia, and major psychiatric disorders; and movement-related data, including age at onset of movement disorder, first muscle group involved, muscle groups currently involved, and ratings on the Abnormal Involuntary Movement Scale (AIMS) (7) and the Rating Scale for Akathisia (8).

RESULTS

Clinical characteristics of the patients are presented in table 1. Nine (60.0%) of the patients were men. The mean age of the group was 39.7 years (SD=10.0), and the mean age at onset of tardive dystonia was 35.7 years (SD=9.0). Eleven (73.3%) of the patients had a diagnosis of a schizophrenic disorder, three (20.0%) had bipolar disorder, and one (6.7%) had generalized anxiety disorder. They had first been treated with neuroleptic drugs at a mean age of 22.8 years (SD=5.9), thereby having a mean exposure to neuroleptics of 13.1 years (SD=9.5, range=0.7–27.2) before developing tardive dystonia. The approximate mean neuroleptic load was 1.24 kg (SD=1.2) of chlorpromazine equivalents. Eight (53.3%) of the subjects had received neuroleptics

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TABLE 1. Clinical Characteristics of 15 Patients With Tardive Dystonia

Patient	Age at Onset (years)	Sex	Primary Diagnosis ^a	Duration of Exposure to Neuroleptics (years) ^b	Muscle Groups Affected				Associated Disorders			
									Tardive Dyskinesia (AIMS score) ^c	Akathisia (Rating Scale for Akathisia score) ^d	Past History	
					Cranial	Cervical	Trunk	Arms			Acute Dystonia	Essential Tremor
1	33	M	Bipolar disorder	3.0	Yes	Yes	Yes	Yes	0	0	No	Yes
2	35	M	Schizophrenia	16.0	Yes	Yes	No	Yes	2	2	No	No
3	50	M	Schizophrenia	24.0	Yes	Yes	No	Yes	1	2	No	No
4	45	F	Schizophrenia	27.2	No	Yes	No	No	3	0	No	No
5	26	M	Schizophrenia	7.0	No	Yes	Yes	Yes	2	0	No	Yes
6	47	M	Anxiety disorder	3.0	Yes	No	No	No	2	2	No	Yes
7	27	M	Schizophrenia	9.0	Yes	Yes	Yes	Yes	2	0	No	No
8	27	M	Schizophrenia	7.0	Yes	Yes	Yes	Yes	2	0	No	Yes
9	34	F	Bipolar disorder	12.0	Yes	No	No	No	2	0	Yes	No
10	39	F	Bipolar disorder	20.0	Yes	Yes	No	No	3	3	Yes	No
11	22	M	Schizophrenia	0.7	Yes	Yes	Yes	No	2	0	Yes	No
12	44	M	Schizophrenia	20.0	No	Yes	No	No	2	0	Yes	No
13	44	F	Schizophrenia	20.1	Yes	No	No	No	3	3	No	No
14	25	F	Schizophrenia	5.0	Yes	No	No	No	2	3	Yes	No
15	38	F	Schizophrenia	19.0	Yes	No	No	No	1	0	Yes	No

^aAccording to DSM-III-R.

^bPrior to onset of dystonia.

^cGlobal severity scores=0-4: none, minimal, mild, moderate, severe.

^dGlobal scores=0-5: absent, questionable, mild, moderate, marked, severe.

continuously, and the rest had had at least one 3-month drug-free period. High-potency drugs had been used in only six cases (40.0%).

There was no past history of serious head injury or epilepsy, and only one subject had a history of birth trauma. Neuroleptic-induced extrapyramidal side effects had been common in the past; they were severe at the time of initiation of medication in eight (53.3%) of the patients, and acute akathisia occurred in five (33.3%). Six (40.0%) of the subjects had developed acute dystonia soon after initiation of neuroleptics, and there was a prompt response to anticholinergic medication in each case. Four (26.7%) of the subjects had histories of essential tremor and two (13.3%) of stuttering prior to the initiation of treatment with neuroleptics. There were no family histories of movement disorders and dementia.

The muscle groups most severely involved were cervical in 10 (66.7%) of the patients and cranial in five (33.3%). Cranial muscles were additionally involved in another seven patients (46.7%), while the trunk and upper limbs were involved in five (33.3%) and six (40%), respectively. The lower limbs were not involved in these subjects. No subject, therefore, met the criteria for generalized dystonia (9). The first muscle group affected was cranial in eight patients (53.3%), cervical in six (40.0%), and upper limb in one (6.7%). In addition to the dystonia, nine (60.0%) of the subjects were rated on the AIMS as having mild tardive dyskinesia and three (20.0%) as having moderately severe tardive dyskinesia. Six (40.0%) had diagnoses of associated tar-

dive akathisia, three mild and three moderate according to the Akathisia Rating Scale. Three (20.0%) of the subjects had considerable muscular rigidity as a side effect of neuroleptics.

The age and sex distribution of the group suggested that tardive dystonia is not a disorder of young men exclusively. The cumulative frequency of tardive dystonia increased linearly with age, suggesting a lack of predilection for any age group. Age at onset was poorly correlated with global AIMS score (Pearson's $r=0.10$, $N=15$, $p=0.70$, two-tailed), suggesting that the overlap with tardive dyskinesia was also independent of age. Younger subjects, however, had a shorter exposure to neuroleptics (the correlation between age at onset and duration of neuroleptic use was 0.70 , $N=15$, $p=0.003$). The male and female subjects did not differ significantly in age at onset (male subjects, mean=34.5 years, $SD=10.2$; female subjects, mean=37.5, $SD=7.3$; $U=22.5$, $p=0.64$, Mann-Whitney test). The female subjects had a more circumscribed dystonia; five of the six women and three of the nine men had a focal cranial or cervical dystonia, but the comparison did not reach statistical significance (for sex versus one or more than one muscle group involved, $p=0.08$, Fisher's exact two-tailed test; odds ratio=10.0). All subjects with involvement of the trunk ($N=5$), suggesting a more widespread dystonia, were young men (mean age=27.0 years, range=22-33). While the difference between the sexes in the severity of tardive dyskinesia was not significant, it is noteworthy that all three of the subjects with moderately severe ratings on the AIMS were female.

DISCUSSION

This study supports the data of Kang et al. (5), which suggest that the onset of tardive dystonia can occur in all age groups and that there is a linear increase of cumulative incidence with increasing age. The data suggest, however, that the disorder may present differently in the young and the old. More widespread dystonia was seen in the young, although it was not "generalized," for which involvement of leg muscles is considered necessary (9). Tardive dystonia occurred in both men and women, with a slight overall preponderance for men in this series, as in the published literature (1-5). The men were not younger at onset than the women, unlike the findings reported by Kang et al. (5).

Tardive dystonia had a considerable overlap with tardive dyskinesia and tardive akathisia, and the age at onset did not seem to affect the likelihood of this. The more severe associated tardive dyskinesia tended to occur in women, but the small numbers make this finding tentative. The overlap of tardive dystonia with tardive dyskinesia raises the question whether tardive dystonia should be considered a subsyndrome of tardive dyskinesia or a separate syndrome, but the present study was not designed to address this issue.

The nature of the movement disorder in tardive dystonia is essentially indistinguishable from that of idiopathic dystonia, although some minor differences have been previously noted (5). It is the history of neuroleptic exposure, the overlap with tardive dyskinesia and tardive akathisia, and the reported improvement of some patients with the withdrawal of neuroleptics that distinguish tardive dystonia. In idiopathic dystonia, patients with earlier onset are more likely to develop a generalized disorder, as compared to patients with adult onset, who usually have focal dystonias (9). A similar age-related manifestation was seen in these tardive dystonia subjects. The absence of any subject with onset before the age of 15 may explain the lack of generalized dystonia in this group. Thus, an important question is, Were these subjects constitutionally vulnerable to the development of dystonia, with the neuroleptics perhaps facilitating the expression of the vulner-

ability? This question cannot be answered with the data presented in this article, but there are some findings that warrant further examination of this issue: 1) a past history of acute dystonia in 40.0% of the subjects, suggesting a particular pattern of response, and 2) a past history of essential tremor in 26.7% of the subjects. An association between essential tremor and idiopathic dystonia has been reported (10). Tremor is seen frequently in patients with dystonia and in their relatives, and some patients with tremor have signs of dystonia. There is some evidence of a shared pathophysiology between some cases of essential tremor and dystonia. In addition, patients with an earlier onset of tardive dystonia have a shorter exposure to neuroleptics. The issues of vulnerability and the role of neuroleptics in causing tardive dystonia can only be settled by large epidemiological studies.

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