Clinical Characteristics of Tourette Syndrome with and without "Generalized Tics" and Coprolalia

"全般性チック"とコプロラリアからみたトゥレット症候群の臨床特徴について

金生由紀子

Background and Objects

Tourette syndrome (TS) is defined as a type of tic disorder characterized by multiple motor tics and one or more vocal tics present for more than one year.[3, 29]

Gilles de la Tourette (1885)[8] described this syndrome in detail, and mentioned that the triad of severe involuntary movement afflicting the entire body expressed as "jumping," coprolalia and echolalia constituted the main characteristics of this syndrome. Recently, the description of characteristic tic symptoms in the diagnostic criteria for TS have changed gradually. In DSM-Ⅲ,[1] the essential features of TS are "presence of recurrent, involuntary, repetitive, rapid, purposeless motor movements affecting multiple muscle groups" and "multiple vocal tics," and in DSM-Ⅲ-R[2] and DSM-Ⅳ,[3] "both multiple motor and one or more vocal tics have been present at some time during the illness, although not necessarily concurrently."

Complex vocal tics such as coprolalia and echolalia were not necessarily included as the essential features in these recent criteria, and patients with only one kind of simple vocal tic and multiple motor tics can be diagnosed as having TS after DSM-Ⅲ-R. The rate of coprolalia is estimated at 60% in DSM-Ⅲ, one-third in DSM-Ⅲ-R, and less

than 10% in DSM-Ⅳ. This decrease in rates of coprolalia seems to reflect directly changes in the diagnostic criteria.

Concerning motor tics, locations of body of tics are not stipulated in DSM criteria, and even two or more kinds of motor tics involving only the face such as blinking and opening mouth, etc. can be identified as multiple.

With this expansion of the diagnostic criteria, it seems that patients with milder symptoms have been included within TS. Although this expansion of the diagnostic criteria will be beneficial to researchers, especially for those dealing with uncommon disorders such as TS, it can be disadvantageous to clinicians in making prognosis and planning treatment.[5)]

Therefore, in order to select severe cases requiring intensive treatment, we proposed here the category of "generalized tics," [14)] focusing on the severity of tic symptoms. We defined it as complex motor tics that are more forceful than comparable voluntary movements, extend over the whole body involving such movements as sudden jumping, hopping and skipping, and that continue over an extended period of time with fluctuation in locations, frequency and intensity. Concurrence of typical simple motor tics in the face such as blinking confirms that these movements are a kind of tic symptoms, and

"generalized tics" can be judged regardless of the presence or absence of vocal tics. The definition of this category is based only on symptomatology of severe motor tics without taking into account of impairment of psychological, social, occupational functioning as defined in DSM-Ⅳ. In light of this category, we reviewed the data of the patients with infantile autism and tics. Eventually we could extract patients rated severe with both tic symptoms and social impairment. Thus, we concluded that "generalized tics" are corresponding to a group of severe cases of Tourette's disorder and chronic motor or vocal tic disorder of DSM-Ⅲ-R in infantile autism.

Obsessive-compulsive disorder (OCD) and attention deficit hyperactivity disorder (ADHD) are commonly associated with TS.[6, 26] Genetic relationships between TS and these disorders have recently come to the attention of researchers, and especially, studies on genetic continuity between TS and OCD have been suggested.[15, 21] We think it important to examine which tic symptoms have strong relationships with obsessive-compulsive symptoms (OCS) and/or hyperactivity, in order to explore the nature of TS.

Coprolalia, as well as copropraxia and echophenomena, was reported to be associated with aggression, hostility and obsessionality.[22] In an FDG-PET study, coprolalia, as

well as obsessions and compulsions, impulsivity, self-injurious behavior (SIB), echophenomena and depression, was reported to be associated with significant increases in metabolic activity in the orbitofrontal cortices.[4] It seems to be necessary to examine clinically whether coprolalia is related with these features.

Prevalence of coprolalia was reported to be more frequent in adolescence than in adulthood, and close relationship between coprolalia and severity of tics was suggested. [9] It was also reported that coprolalia had no predictive value in determining severity of tics in adulthood and adult dysfunction. [9] We think it necessary to examine relationship between coprolalia and global severity of TS.

Relationship between tic symptoms and associated features was examined through in-depth analysis of cumulative data of a large clinical population from many aspects, especially in the United States and Britain. In Japan, unfortunately, most TS studies are rather limited in the number of subjects and in the scope of investigation. There is a study on the clinical symptoms of 100 patients at only one pediatric neurological clinic. The study concludes that the prevalence of coprolalia in Japan is considerably lower than overseas.[20]

Contrary to this are studies of TS patients receiving

psychiatric treatment in Japan.[17, 24, 25] Though limited in the number of subjects in these studies, these have described that the prevalence of coprolalia, obsessive-compulsive symptoms (OCS), and complication of hyperkinetic syndrome is relatively high and close to the rates reported previously by researchers overseas.

In the present study, first, we described clinical characteristics of 64 TS patients at Tokyo University Hospital's outpatient clinic of neuropsychiatry and examined their symptomatology, comparing with previous studies on TS in Western countries and in Japan. Second, we examined whether severity of TS is different between TS patients with and without "generalized tics." Third, we examined whether severity of TS is different between TS patients with and without coproralia and whether coprolalia has strong relationships with OCS and SIB. Finally, we examined whether severity of TS and associated features are different between TS patients with and without a combination of "generalized tics" and coprolalia.

Subjects and Methods

Sixty-four subjects without severe mental retardation and with enough information on clinical characteristics were selected from TS patients who visited our outpatient clinic from 1974 to 1993 and who met criteria for

Tourette's disorder of DSM-III-R.[2] The subjects consisted of 55 males (85.9%) and 9 females (14.1%). The mean age at entry to the present study was 17.4 years (SD: 7.2). For the 55 patients who visited our clinic twice or more, the mean duration of treatment at our clinic was 54.2 months (range: 1 to 216).

Data on tic symptoms, courses of their development, complications, developmental histories, treatment, severity and outcome, etc. were collected through a systematic chart review of all the subjects. These data were judged after consultation of two psychiatrists (Y.K. and M.O.).

DSM-Ⅲ-R criteria were used for psychiatric diagnoses.

Tic symptoms were investigated at onset, on their first visit to our clinic, at the time of the first appearance of "full syndrome," at entry to the present study and during lifetime. For the purpose of this study, we defined the first appearance of "full syndrome" as the time when over two kinds of motor tics and at least one kind of vocal tic had appeared for the first time, though not necessarily concurrently.

"Generalized tics" were diagnosed, when tics were not only multiple motor tics but also complex motor tics extending throughout the body and continuing over an

extended period of time. Coproralia was defined as involuntary, socially unacceptable and/or obscene sounds, words, phrases, or sentences.[26] We carefully distinguished coprolalia from common cursing words in terms of nature of articulation and deviation from conversation.[19]

As for complications, the symptoms related to OCD and self-injurious behavior (SIB) were surveyed at onset of tic symptoms, first visit, entry to the present study and during lifetime. When patients had compulsion or obsession, they were identified as having OCS. OCS were classified with reference to the Japanese translation of the symptom checklist of Yale-Brown Obsessive-Compulsive Scale (Y-BOCS).[11, 12] It was reported that this Japanese version of Y-BOCS proved to excel in interrater reliability and internal consistensy. [16] ADHD-related symptoms were investigated at onset of tic symptoms, upon entry to the present study, and during lifetime. Also documented were maladjustment behaviors such as school refusal.

Although treatment at our clinic consists mainly of pharmacotherapy, psychotherapy, and family therapy, pharmacotherapy including the maximum dose of haloperidol was examined throughout the duration of this particular study.

For the evaluation of severity, we used the Shapiro Tourette Syndrome Severity Scale (STSSS)[26] which we

translated into Japanese. STSSS consists of five rating items: (1) tics noticeable to others, (2) tics elicit comments or curiosity, (3) patient considered odd or bizarre, (4) tics interfere with functioning, (5) incapacitated, homebound, or hospitalized. The global severity rating of STSSS is comprised of seven grades, ranging from 0 (none) to 6 (very severe). In our evaluation of severity, we included an estimate of the subjects' clinical records on their first visit, at the severest stage at our clinic and at entry to the present study. Our Japanese version is not yet put to the test sufficiency as regards its reliability and validity.

As another index of severity, we referred to each subject's history regarding hospitalization for treatment of TS.

For 55 patients who visited our clinic twice or more, outcome was classified based on the result of examination at entry to this study. Completion of treatment was determined when subjects had either remitted completely or when there was remarkable improvement of tic symptoms and complications. Continuance of treatment was determined because tic symptoms and/or complications did not ameliorate.

Because we were able to interview 39 of the total 64 patients more than once, most of whom we ourselves treated,

we carried out semi-structured interviews with those patients and parents. Our interviews focused on the characteristics of the tic symptoms, courses of their development, complications, developmental histories, etc., as much as possible. We comprehensively analyzed all information available to us on clinical characteristics of the subjects, comparing them by "generalized tics", coprolalia and their combination. In principle, we analyzed data on all the 64 subjects. However, for comparative analysis of records at first visit and data at follow-up, the 9 subjects who visited our clinic once were of course excluded.

For statistical analysis, we used t-test, χ^2-test including Yates' correction or Fisher's exact test, and McNemar test. Both significant difference ($p<0.05$) and trends ($p<0.1$) were reported.

Results

1. Description of subjects

1) Tic symptoms and courses of their development

Table 1 shows tic symptoms and the courses of development.

The mean age of onset was 6.9 years (SD: 2.7). Tic symptoms at onset were: motor tics in 48 subjects (75%), vocal tics in 25 (39.1%). Nine subjects (14.1%) exhibited

Table-1 Courses of Tic Symptoms

	(1) Onset	(2)"Full syndrome"	(3)First visit	(4)Entry to the study	During lifetime	Onset age of each tic symptom[a)]	Statistics[b)]
Age[a)]	6.9±2.7	10.1±3.1	13.5±5.8	17.4±7.2	17.4±7.2		
Motor tics	48(75%)	53(82.8%)	57(89.1%)	45(70.3%)	64(100%)		*, **, ns
Simple	45(70.3%)	49(76.6%)	52(81.3%)	38(59.4%)	63(98.4%)	7.8±3.7	ns, *, ns
Complex	11(17.2%)	35(54.7%)	40(62.5%)	22(34.4%)	57(89.1%)	9.8±3.3	***, ***, +
"Generalized tics"	(-)	(-)	16(25%)	10(15.6%)	41(64.1%)		(-), *, (-)
Face	35(54.7%)	(-)	38(59.4%)	25(39.1%)	61(95.3%)		ns, *, ns
Legs	3(4.7%)	(-)	9(14.1%)	6(9.4%)	37(57.8%)		ns, ns, ns
Vocal tics	25(39.1%)	59(92.2%)	53(82.8%)	39(60.9%)	64(100%)		***, ***, *
Simple	24(37.5%)	52(81.3%)	51(79.7%)	37(57.8%)	63(98.4%)	9.1±3.1	***, **, *
Complex	5(7.8%)	14(21.9%)	21(32.8%)	11(17.2%)	40(62.5%)	11.4±4.5	***, *, ns
Coprolalia	3(4.7%)	(-)	16(25%)	11(17.2%)	32(50%)		***, +, *

a): (mean±SD) yr. b): (1) VS (3), (3) VS (4), (1) VS (4) by Macnemar test, +: p<0.1, *: p<0.05, **: p<0.01, ***: p<0.005, df=1

both motor and vocal tics. The most common location of motor tics was in the face, recorded in 35 subjects (54.7%).

The mean age at the first appearance of "full syndrome" was 10.1 years (SD: 3.1). Tic symptoms at the first appearance of "full syndrome" were motor tics in 53 (82.8%) and vocal tics in 59 (92.2%).

The mean age at the subjects' first visit to our clinic was 13.5 years (SD: 5.8). Tic symptoms observed at that time were motor tics in 57 (89.1%) and vocal tics in 53 (82.8%). Complex motor tics and simple and complex vocal tics were significantly more frequent on their first visit to our clinic than at onset. "Generalized tics" were found in 16 (25%). Coprolalia was found in 16 (25%), which was significantly more frequent than at onset.

Tic symptoms at entry to the present study were motor tics in 45 (70.3%) of the subjects and vocal tics in 39 (60.9%). Complex motor tics and simple and complex vocal tics were significantly less frequent at the time of entry than on their first visit to our clinic. However, simple vocal tics were significantly more frequent at the time of entry to the study than at onset. At entry, "generalized tics" were found in 10 (15.6%), and coprolalia in 11 (17.2%) of the subjects.

Regarding the onset age of each tic symptom, simple motor tics appeared earliest at the mean age of 7.8 years (SD: 3.7) in 59 subjects, and complex vocal tics latest at the mean age of 11.4 years (SD: 4.5) in 36 subjects.

During lifetime, "generalized tics" were found in 41 (64.1%), copropraxia in 7 (10.9%), and echopraxia in 2 (3.1%). Coprolalia was observed in 32 (50%), echolalia in 11 (17.2%), and palilalia in 12 (18.8%). Twenty-three (35.9%) demonstrated both "generalized tics" and coprolalia.

2) Complications, developmental history, and past history

Symptoms related to OCD during lifetime, OCS was found in 40 subjects (62.5%), compulsion in 36 (56.3%), and obsession in 19 (29.7%). OCS was noted in 7 (10.9%) at the onset of tic symptoms, in 24 (37.5%) at their first visit to our clinic, and in 15 (23.4%) at the time of entry to our study. When all of OCS cases were classified according to Y-BOCS, it was found that "cleaning/washing" was the most common compulsion observed in 14 (21.9%), followed by "checking" in 12 (18.8%). "Aggressive" and "contamination" were the most common obsession and found in 7 (10.9%).

Regarding the symptoms related to ADHD during lifetime, impulsiveness and aggressiveness were found in 31 (48.4%), hyperactivity in 20 (31.3%), and clumsiness in 17 (26.6%). Eleven (17.2%) were diagnosed with ADHD complications.

Other symptoms documented were school refusal in 23 (35.9%), SIB in 13 (20.3%), etc. The most common SIB was slapping or poking of one's own eyes. This behavior was observed in 6 out of 13. Twelve out of the 13 with SIB also displayed symptoms of compulsion.

Regarding developmental histories and past histories, perinatal problems were found in 20 (31.3%), sleep disturbances in 17 (26.6%), head trauma in infancy in 17 (26.6%), convulsion in 15 (23.4%), and enuresis in 9 (14.1%).

3) Treatment

Fifty-two (94.5%) out of the 55 who visited our clinic twice or more received pharmacotherapy. The most common drug administered to the subjects while they were receiving care at our clinic was haloperidol (HPD). This drug was given to 42 (76.4%). The second was pimozide (PZD) for 32 (58.2%). Other drugs administered included: antianxiety drugs for 28 (50.9%); anticonvulsants for 13 (23.6%); neuroleptics except HPD and PZD for 10 (18.2%); antidepressants for 9 (16.4%); and stimulants for 3 (5.5%).

The most common drug administered at the time of entry to the present study was HPD for 26 (47.3%) of the subjects, followed by antianxiety drugs for 14 (25.5%), PZD for 8 (14.5%), anticonvulsants for 7 (12.7%). The mean

Table-2 Evaluation of Severity by Shapiro Tourette Syndrome Severity Scale (STSSS)

	First visit	Severest stage	Entry to the study
0 (none)	1 (1.6%)	0 (0%)	11 (17.2%)
1 (very mild)	2 (3.1%)	0 (0%)	11 (17.2%)
2 (mild)	2 (3.1%)	1 (1.6%)	10(15.6%)
3 (moderate)	25 (39.1%)	22 (34.4%)	17(26.6%)
4 (marked)	30 (46.9%)	28 (43.8%)	9 (14.1%)
5 (severe)	4 (6.3%)	13 (20.3%)	6 (9.4%)
6 (very severe)	0 (0 %)	0 (0%)	0 (0 %)

maximum dose of HPD was 4.6 mg/day (range: 0.75 to 27).

4) Severity and outcome

The global severity ratings of STSSS (Table 2) on the first visit to our clinic revealed that 4 (marked) was scored by 30 subjects, accounting for the largest 46.9% of the total 64 subjects. This was followed by 3 (moderate) for 25 (39.1%). At the severest stage while under observation at our clinic, 4 (marked) was also scored by plurality of 28 (43.8%), followed by 3 (moderate) with 22 (34.4%), and 5 (severe) with 13 (20.3%). At entry to the present study, 17 subjects (26.6%) were rated at 3 (moderate). Those rated at 0 (none) and 1 (very mild) equally numbered 11 (17.2%).

Eight (12.5%) had records of being admitted to psychiatric hospital as severe cases.

Regarding outcome for 55 patients at entry to the present study, completion of treatment was for 16 (29.1%), continuance of treatment for 15 (27.3%), drop-outs for 13 (23.6%), reference to other hospitals for 7 (12.7%), and admission to other psychiatric hospitals for 4 (7.3%).

2. Comparison between patients with and without "generalized tics"

Table 3 shows a comparison between 41 subjects with

Table-3 Comparisons between Patients with and without "Generalized Tics"

	GT group	NGT group	Statistics
Number and Gender (M:F)	41 (34: 7)	23 (21: 2)	
Age [a]	18.1±7.6	16.3±6.4	
Age at onset [a]	6.9±3.0	6.9±2.1	
Age at the first visit [a]	13.6±5.3	13.4±6.8	
Tic symptoms at the first visit			
Complex motor tics	30 (73.2%)	10 (43.5%)	χ^2=5.543, df=1, p=0.0186
Complex vocal tics	17 (41.5%)	4 (17.4%)	χ^2=2.858, df=1, p=0.0909 [b]
Topology of motor tics			
Legs	34 (82.9%)	3 (13.0%)	χ^2=26.708, df=1, p=0.0000 [b]
Trunk	35 (85.4%)	4 (17.4%)	χ^2=25.817, df=1, p=0.0000 [b]
Tic symptoms at entry to the study			
Complex vocal tics	10 (24.4%)	1 (4.3%)	χ^2=2.869, df=1, p=0.0903 [b]
Coprolalia	10 (24.4%)	1 (4.3%)	χ^2=2.869, df=1, p=0.0903 [b]
Tic symptoms during lifetime			
Complex motor tics	41 (100%)	16 (70.0%)	Fisher's exact test, p=0.0004
Complex vocal tics	29 (70.7%)	11 (47.8%)	χ^2=3.298, df=1, p=0.0693
Coprolalia	23 (56.1%)	9 (39.1%)	
Echolalia	10 (24.4%)	1 (4.3%)	
Palilalia	9 (22.0%)	3 (13.0%)	
"Ordering/arranging"	7 (17.1%)	0 (0%)	Fisher's exact test, p=0.0362
5 (severe) on STSSS			
At first visit	4 (9.8%)	0 (0%)	
At severest stage	13 (31.7%)	0 (0%)	χ^2=11.101, df=3, p=0.0112
At entry to the study	6 (14.6%)	0 (0%)	
History of hospital admission	7 (17.1%)	1 (4.3%)	

[a]: (mean±SD) yr. [b]: Yates' correction

"generalized tics" (GT) and 23 without "generalized tics" (NGT).

On their first visit, complex motor tics were significantly more frequently present in the GT group than in the NGT group. There was a trend for the patients in the GT group to develop complex vocal tics more frequently than the NGT group. Although the prevalence rate of motor tics in the face was about 60% in both groups, naturally, the prevalence rate of motor tics in the legs and trunk was significantly higher in the GT group than in the NGT group.

At entry to the study, there was a trend for the patients in the GT group to develop complex vocal tics and coprolalia more frequently than the NGT group.

During lifetime, there was a trend for the GT group to have complex vocal tics including coprolalia, echolalia and palilalia than the NGT group.

About 60% of the subjects in either of the two groups showed OCS during lifetime. "Ordering/arranging" compulsion was significantly more frequent in the GT group than in the NGT group.

Evaluation on STSSS at the severest stage at our clinic was significantly severer in the GT group than in the NGT group. All subjects rated at 5 (severe) belonged to the GT group.

Out of 8 subjects with a history of admission to psychiatric hospital, all except one belonged to GT group.

3. Comparison between patients with and without coprolalia

Table 4 shows a comparison between 32 subjects with "definite" coprolalia (COP) and 30 without coprolalia (NCOP). Two with "probable" coprolalia were excluded.

On their first visit, simple vocal tics were significantly more frequently observed in the NCOP group than in the COP group. Complex vocal tics, including not only coprolalia but also involuntary phonation of various words and sentences, were significantly more frequent in the COP group than in the NCOP group.

At entry to the study, complex vocal tics were present only in the COP group, with a significant difference between groups.

During lifetime, copropraxia was found only in the COP group. There was a trend for the patients in the COP group to develop echolalia at a higher rate than the NCOP group.

About 60% of the subjects in both groups showed OCS during lifetime. "Cleaning/washing" compulsion occurred significantly more frequently in the COP group than in the NCOP group. "Checking" compulsion was significantly more frequently recognized in the NCOP group than in the COP group. There was a trend for the patients in the COP group

Table-4 Comparisons between Patients with and without Coprolalia

	COP group	NCOP group	Statistics
Number and Gender (M: F)	32 (29: 3)	30 (25: 5)	
Age [a)]	18.4±7.3	16.4±7.2	
Age at onset [a)]	6.7±2.3	7.2±3.1	
Age at the first visit [a)]	14±6.8	14±4.7	
Tic symptoms at the first visit			
Simple vocal tics	22 (68.8%)	28 (93.3%)	χ^2=4.523, df=1, p=0.0334
Complex vocal tics	17 (53.1%)	4 (13.3%)	χ^2=9.241, df=1, p=0.0024
Tic symptoms at entry to the study			
Complex vocal tics	11 (34.3%)	0 (0%)	Fisher's exact test, p=0.0004
Tic symptoms during lifetime			
Complex motor tics	28 (87.5%)	27 (90%)	
"Generalized tics"	23 (71.9%)	17 (56.7%)	
Copropraxia	7 (21.9%)	0 (0%)	Fisher's exact test, p=0.0068
Complex vocal tics	32 (100%)	6 (20%)	χ^2=41.768, df=1, p=0.0000
Echolalia	9 (28.1%)	2 (6.7%)	χ^2=3.526, df=1, p=0.0604 [c)]
Palilalia	9 (28.1%)	3 (10%)	
"Cleaning/washing"	10 (31.3%)	3 (10%)	Fisher's exact test, p=0.0400
"Checking"	2 (6.3%)	10 (33.3%)	Fisher's exact test, p=0.0070
SIB during lifetime	10 (31.3%)	3 (10%)	χ^2=3.034, df=1, p=0.0815 [c)]
Max. dose of HPD [b)]	6.0±6.0	2.7±2.0	t=2.386, p=0.0219
5 (severe) on STSSS			
At first visit	4 (9.8%)	0 (0%)	χ^2=14.480, df=5, p=0.0128
At severest stage	10 (31.3%)	3 (10%)	χ^2=9.186, df=2, p=0.0101
At entry to the study	6 (14.6%)	0 (0%)	χ^2=13.634, df=5, p=0.0221

[a)]: (mean±SD) yr. [b)]: (mean±SD) mg/day [c)]: Yates' correction

to develop self-injurious behavior (SIB) during lifetime at a higher rate than the NCOP group. Out of 13 patients with SIB, all except one in the COP group had compulsion.

Although over 60% of both groups of patients received haloperidol (HPD), the mean maximum dose of HPD was significantly higher for the COP group than for the NCOP group.

Evaluation of severity on the STSSS was significantly severer in the COP group than in the NCOP group, on their first visit, at the severest stage and at entry to the study.

4. Comparison between patients with and without a combination of "generalized tics" and coprolalia

The subjects were divided into the four groups -- the GT/COP group (23 with both "generalized tics" and coprolalia), the GT/NCOP group (17 with only "generalized tics"), the NGT/COP group (9 with only coprolalia) and the NGT/NCOP group (13 without "generalized tics" and coprolalia). Tables 5-A, B, and C show a comparison among these four groups.

The onset age of complex vocal tics in the NGT/COP group was the lowest among the three groups.

At entry to the study, there was a significant difference in the incidence of complex vocal tics among

Table-5-A Comparisons between Patients with and without a Combination of "Generalized Tics" and Coprolalia

	1. GT/COP	2. GT/NCOP	3. NGT/COP	4. NGT/NCOP	Statistics
Number and Gender (M:F)	23 (20: 3)	17 (13: 4)	9 (9: 0)	13 (12: 1)	
Age [a)]	18.8±7.3	17±8.3	17.4±7.7	15.6±5.8	
Age at onset [a)]	6.7±2.5	7.2±3.6	6.8±1.7	7.1±2.4	
Onset age of complex vocal tics [a)]	12.1±4.9	12.3±3.2	9.6±3.9	(-)	
Age at the first visit [a)]	14±5.7	13.4±4.7	13±9.4	13.8±5.0	
Tic symptoms at the first visit					
Complex motor tics	18 (72.3%)	11 (64.7%)	4 (44.4%)	6 (46.2%)	p=0.0005 (1.VS 4.), p=0.0025 (2.VS 4.)
Complex vocal tics	14 (60.9%)	3 (17.6%)	3 (33.3%)	1 (7.7%)	χ^2=13.461, df=3, p=0.004
Tic symptoms at entry to the study					
Complex motor tics	12 (52.2%)	5 (29.4%)	1 (11.1%)	4 (30.8%)	p=0.0383 (1.VS 3.)
Complex vocal tics	10 (43.5%)	0 (0%)	1 (11.1%)	0 (0%)	χ^2=20.217, df=3, p=0.0002
Tic symptoms during lifetime					
Complex vocal tics	23 (100%)	5 (29.4%)	9 (100%)	1 (7.7%)	χ^2=43.233, df=3, p=0.0000
Echolalia	8 (34.8%)	2 (11.8%)	1 (11.1%)	0 (0%)	χ^2=8.068, df=3, p=0.047
Palilalia	7 (30.4%)	2 (11.8%)	2 (22.2%)	1 (7.7%)	

a): (mean±SD) yr.

Table-5-B Comparisons between Patients with and without a Combination of "Generalized Tics" and Coprolalia

	1. GT/COP	2. GT/NCOP	3. NGT/COP	4. NGT/NCOP	Statistics
At entry to the study					
ADHD	2 (8.7%)	1 (5.9%)	4 (44.4%)	1 (7.7%)	χ^2=9.389, df=3, p=0.0245
Hyperactivity	3 (13.0%)	2 (11.8%)	5 (55.6%)	1 (7.7%)	χ^2=10.481, df=3, p=0.0149
Impulsiveness and aggresiveness	9 (39.1%)	2 (11.8%)	7 (77.8%)	2 (15.4%)	χ^2=16.260, df=3, p=0.0010
During lifetime					
ADHD	3 (13.0%)	3 (17.6%)	4 (44.4%)	3 (23.1%)	χ^2=6.577, df=3, p=0.087
Hyperactivity	7 (30.4%)	6 (35.3%)	5 (55.6%)	1 (7.7%)	
Impulsiveness and aggresiveness	9 (39.1%)	9 (52.9%)	7 (77.8%)	5 (38.5%)	
Clumsiness	2 (8.7%)	5 (29.4%)	6 (66.7%)	3 (23.1%)	χ^2=11.531, df=3, p=0.009
"Checking"	2 (8.7%)	6 (35.3%)	0 (0%)	4 (30.8%)	χ^2=7.686, df=3, p=0.053
"Cleaning/washing"	6 (26.1%)	2 (11.8%)	4 (44.4%)	1(7.7%)	
Max. dose of HPD [b)]	6.2±6.5	3.7±2.5	6.2±4.1	1.9±1.1	p=0.0123 (3. VS 4.)
Neuroleptics except HPD and PZD	3 (13.0%)	2 (11.8%)	4 (44.4%)	1 (7.7%)	χ^2=6.419, df=3, p=0.093
Anticonvulsants	7 (30.4%)	3 (17.6%)	3 (33.3%)	0 (0%)	χ^2=20.190, df=3, p=0.003

[b)]: (mean±SD) mg/day

Table-5-C Comparisons between Patients with and without a Combination of "Generalized Tics" and Coprolalia

	1. GT/COP	2. GT/NCOP	3. NGT/COP	4. NGT/NCOP	Statistics
Severity on STSSS at first visit [c)]					χ^2=9.343, df=4, p=0.0531 (1. VS 4.)
3 (moderate)	6 (26.1%)	8 (47.1%)	1 (11.1%)	10 (76.9%)	
4 (marked)	12 (52.2%)	8 (47.1%)	6 (66.7%)	3 (23.1%)	
5 (severe)	4 (17.4%)	0 (0%)	0 (0%)	0 (0%)	
Severity on STSSS at severest stage					χ^2=11.999, df=2, p=0.0025 (1. VS 4.),
3 (moderate)	4 (17.4%)	7 (41.2%)	2 (22.2%)	9 (69.2%)	χ^2=5.926, df=2, p=0.0517 (1. VS 3.)
4 (marked)	9 (39.1%)	7 (41.2%)	7 (77.8%)	4 (30.8%)	
5 (severe)	10 (43.5%)	3 (17.6%)	0 (0%)	0 (0%)	
Severity on STSSS at entry to the study [c)]					χ^2=13.136, df=5, p=0.0221 (1. VS 4.)
3 (moderate)	4 (17.4%)	6 (35.3%)	1 (11.1%)	6 (46.2%)	
4 (marked)	5 (21.8%)	1 (5.9%)	3 (33.3%)	0 (0%)	
5 (severe)	5 (21.8%)	1 (5.9%)	0 (0%)	0 (0%)	

[c)]: From 0 (none) to 2 (mild) were omitted.

the four groups.

During lifetime, there was a significant difference in the incidence of echolalia among the four groups. Echolalia was significantly more frequent in the GT/COP group than in the NGT/NCOP group. Palilalia was most frequent in the GT/COP group (30.4%), although there was no significant difference in the occurrence rate among the four groups.

Hyperactivity, impulsiveness and aggressiveness, and ADHD complication were found most frequently in the NGT/COP group, both at entry to the study and during lifetime. There was a significant difference in the occurrence of clumsiness among the four groups, and clumsiness was found significantly more frequently in the NGT/COP group than in the GT/COP group. "Cleaning/washing" compulsion occurred most frequently in the NGT/COP group (44.4%), though with no significant difference.

Although over 80% of four groups of patients were on pharmacotherapy, the mean maximum dose of HPD was lowest for the NGT/NCOP group and significantly lower for the NGT/NCOP group than for the NGT/COP group. The NGT/COP group received neuroleptics except HPD and pimozide(PZD) and anticonvulsants more frequently than other three groups.

There were significant differences in severity on

STSSS among the four groups, on their first visit, at the severest stage and at entry to the study. On the first visit, there was a trend for the GT/COP group to be rated as severer than the NGT/NCOP group. At the severest stage and at entry to the study, evaluation of severity on the STSSS was significantly severer in the GT/COP group than in the NGT/NCOP group.

Discussion

We could obtain precise information on clinical characteristics of 64 TS patients, and compared them with previous studies and analyzed them in association with "generalized tics" and coprolalia.

First, the age and tic symptoms of onset were very similar to those in the previous reports.[17, 20, 24, 26] Most of the tic symptoms during lifetime, including copropraxia, echolalia, and palilalia, were very similar to those of the 666 patients reported by Shapiro, et al.[26] The prevalence of coprolalia in this study (50%) was higher than that of the study by Shapiro et al. (32%).[26]

Compared with other Japanese studies on TS, the prevalence of coprolalia in this study was much higher than that of the study conducted at one pediatric neurological clinic (4%)[20] ; and yet similar to that of the studies on patients which included adolescent and

adult as subjects at other psychiatric hospitals (41.2%,[24] 43%[18]).

It has been indicated by some that sociocultural factors and specialty of reporting centers influence coprolalia strongly.[19, 27, 28] This could perhaps be part of the reason for the difference in findings of the prevalence of coprolalia between this study and the study by Shapiro et al.[26]

Coprolalia tends to develop during and after puberty when various mental and behavioral disorders including both tic symptoms and other related symptoms such as OCS develop. A recent study in the U.S.A. indicated that the prevalence of coprolalia is lower in patients at a pediatric neurological clinic than what was previously reported.[10] The ages of patients and patient hospital visiting behaviors related to a variety of symptoms may explain the difference in the prevalence of coprolalia between this study and the aforementioned study at the pediatric neurological clinic.[28]

Second, there was a trend for TS patients with "generalized tics" (the GT group) to have multiple complex vocal tics more frequently than TS patients without "generalized tics," although we defined "generalized tics" as forceful complex tics extending over the whole body rapidly with or without vocal tics. TS patients with

"generalized tics" seemed to be identified as severe in terms of vocal tics as well as motor tics.

Furthermore, on the STSSS, which is a scale for the evaluation of the severity of tic symptoms and social impairments, all of the patients rated at 5 (severe) had "generalized tics." Most of the patients with a history of admission to psychiatric hospitals had "generalized tics". Although we defined "generalized tics" on the basis of symptomatology of severe motor tics, TS patients with "generalized tics" were severe in terms of both tic symptoms and social impairment. Therefore, "generalized tics" seemed to be a useful index of severity that should also be used in selecting the patients requiring intensive treatment for TS in TS patients without developmental disorders as well as in autistic patients.

Third, coprolalia and copropraxia seemed to have a common mechanism as coprophenomena, since all of the patients with copropraxia had also coprolalia.

With regard to OCS, TS patients with coprolalia (the COP group) had "cleaning/washing" compulsion significantly more frequently than TS patients without coprolalia (the NCOP group). It is reported that this type of compulsion was more frequent in OCD patients without TS than OCD patients with TS,[7, 13] suggesting subtypes of OCD in terms

of tics. Therefore, this type of compulsion, which is not "tic-like," seems to be the core symptom of "typical OCD" which can be equivalent to traditional obsessive compulsive neurosis. As TS patients with coprolalia had this type of compulsion significantly more frequently, they seem to have stronger affinity to "typical OCD" than TS patients without coprolalia.

In this study, there was a trend for TS patients with coprolalia to have SIB more frequently than TS patients without coprolalia. It has been reported that the forms of SIB of TS were similar to SIB of mental retardation.[21] However, as 12 out of 13 with SIB were found to have compulsion in this study, a strong relationship between SIB and OCS in TS was made clear. SIB of TS may be different from those of mental retardation in terms of psychopathological mechanism. Namely, more frequent coincidence of SIB and compulsion in TS patients with coprolalia may suggest that SIB of TS had obsessive-compulsive trait and impulsiveness to break taboo actually, although the patients are afraid of carrying it out, as is the case of coprolalia.

Fourth, examining clinical characteristics of TS in terms of a combination of "generalized tics" and coprolalia, TS patients with both "generalized tics" and coprolalia (the GT/COP group) showed multiple complex vocal tics most

frequently, especially with significantly more frequent echolalia. On the STSSS, TS patients with both "generalized tics" and coprolalia were rated as the severest, on their first visit, at the severest stage and at entry to the study. At entry to the study, SIB was found only in this group. Therefore, TS patients with both "generalized tics" and coprolalia were included under the severest group with respect to both tic symptoms themselves and social impairments. TS patients having neither "generalized tics" nor coprolalia were identified to be the patients belonging to the mildest group on all aspects such as tic symptoms, complications, pharmacotherapy and evaluation on the STSSS.

We found that TS patients with only coprolalia (the NGT/COP group) developed complex vocal tics including coprolalia in an earlier stage and concomitantly had ADHD more frequently. TS patients with only coprolalia also showed "cleaning/washing" compulsion most frequently. Coprolalia without "generalized tics" seemed to imply a subtype of TS that often showed symptoms related to ADHD and OCS and required multiple pharmacotherapy for both TS itself and the associated symptoms.

Lastly, in TS patients with and without "generalized tics" and coprolalia, severity and relationship with

obsessionality and impulsiveness were different. These differences in terms of "generalized tics" and coprolalia may suggest biological heterogeneity of TS. Therefore, consideration of these differences seems to be necessary in future research to explore the nature of TS and to develop new treatments of TS.

Conclusion

We described clinical characteristics of 64 TS patients (55 males and 9 females; mean age: 17.4 years, SD: 7.2) at Tokyo University's outpatient clinic of neuropsychiatry through systematic chart review and examined whether there are differences in clinical characteristics between TS patients with and without "generalized tics" and coprolalia.

Tic symptoms and courses of their development were similar to those in the previous reports. However, the prevalence of coprolalia in this study was 50%. This was much higher than that of a representative study in Japan conducted at one pediatric neurological clinic. Our findings indicated that the incidence of coprolalia in TS patients under psychiatric treatment in Japan is as high as Western countries.

TS patients with "generalized tics" tended to show multiple complex vocal tics more frequently and to become

severer with respect to both tic symptoms and social impairments than TS patients without "generalize tics."

TS patients with coprolalia tended to show higher rates of copropraxia, "cleaning/washing" compulsion and SIB than TS patients without coprolalia. Thus, it was confirmed that coprolalia is related with both obessionality and impulsiveness.

TS patients with both "generalized tics" and coprolalia showed complex tics most frequently and came under the severest group in terms of both tic symptoms and social impairment. TS patients having neither of these two morbidities were classified as the mildest group in all aspects. TS patients with only coprolalia often showed symptoms related to ADHD and OCS.

References

1. American Psychiatric Association. Diagnostic and Statistical Manual of Mental Disorders, Third edition. APA, Washington, DC, 1980.
2. American Psychiatric Association. Diagnostic and Statistical Manual of Mental Disorders, Third edition-revised. APA, Washington, DC, 1987.
3. American Psychiatric Association. Diagnostic and Statistical Manual of Mental Disorders, Forth edition. APA, Washington, DC, 1994.
4. Braun AR, Randolph C, Stoetter B, Mohr E, Cox C, Vladar K, Sexton R, Carson RE, Herscovitch P, Chase TN. The functional neuroanatomy of Tourette's syndrome: an FDG-PET study. II: Relationships between regional cerebral metabolism and associated behavioral and cognitive features of the illness. Neuropsychopharmacology, 1995; 13: 151-168.
5. Cantwell DP, Rutter M. Classification: Conceptual issues and substantive findings. In: Rutter, M, Taylor, E, Hersov, L (eds.), Child and adolescent psychiatry: Modern approaches, third edition. Blackwell scientific publications, London, 1994: 3-21.
6. Comings DE, Comings BG. Tourette's syndrome and attention deficit disorder. In: Cohen DJ, Bruun RD,

Leckman JF (eds.), Tourette's syndrome & tic disorders. John Wiely & Sons, Inc., New York, 1988; 119-135.

7. George MS, Trimble MR, Ring HA, Sallee FR, Robertson MM. Obsessions in obsessive-compulsive disorder with and without Gilles de la Tourette's syndrome. Am J Psychiatry 1993; 150: 93-97.
8. Gilles de la Tourette G. Etude sur une affection nerveuse caracterisee par de l'incoordination motrice accompagnee d'echolalie et de coprolalie. Arch Neurol 1885; 9: 19-42, 158-200.
9. Goetz CG, Tanner CM, Stebbins GT, Leipzig G, Carr WC. Adult tics in Gilles de la Tourette's syndrome: Description and risk factors. Neurology 1992; 42: 784-788.
10. Goldenberg JN, Brown SB, Weiner WJ. Coprolalia in young patients with Gilles de la Tourette's syndrome. Movement Disorders 1994; 9: 622-625.
11. Goodman WK, Price LH, Rasmussen SA, Mazure C, Fleishmann RL, Hill CL, Heninger GR, Charney DS. The Yale-Brown Obsessive Compulsive Scale (Y-BOCS). Part I: Development, use, and reliability. Arch Gen Psychiatry 1989; 46: 1006-1011.
12. Goodman WK, Price LH, Rasmussen SA, Mazure C, Delgado P, Heninger GR, Charney DS. The Yale-Brown Obsessive

Compulsive Scale (Y-BOCS). Part Ⅱ: Validity. Arch Gen Psychiatry 1989; 46: 1012-1016.

13. Holzer JC, Goodman WK, McDougle CJ, Baer L, Boyarsky BK, Leckman JF, Price LH. Obsessive-compulsive disorder with and without a chronic tic disorder. A comparison of symptoms in 70 patients. Br J Psychiatry 1994; 164: 469-473.
14. Kano Y, Ohta M, and Nagai Y. Generalized tics developing in patients with infantile autism. Seishin-igaku 1989; 31: 1261-1268 (in Japanese).
15. Leonard HL, Swedo SE, Rapaport JL, Kenneth CR, Topol D, Lee S, Rettew D. Tourette syndrome and obsessive-compulsive disorder. In: Chase TN, Friedhoff AJ, Cohen DJ (eds.), Advance in Neurology, Vol.58 Tourette syndrome: Genetics, neurobiology, and treatment. Raven Press, New York, 1992; 83-93.
16. Nakajima T, Nakamura M, Taga C, Yamagami S, Kiriike N, Nagata T, Saitoh M, Kinoshita T, Okajima Y, Hanada M, Tazoe H, Yamaguchi K. Reliability and validity of the Japanese version of the Yale-Brown Obsessive-Compulsive Scale. Psychiatry and Clinical Neurosciences 1995; 49: 121-126.
17. Nomoto F, Yashiro R, Takahashi S, Miya M, Shiihara Y, Yamaoka M, Ogino T. Gilles de la Tourette syndrome: Clinical study of ten cases. Seishin-igaku 1984; 26:

929-935 (in Japanese).

18. Nomoto F, Takahashi R. A study of the etiology in Gilles de la Tourette's syndrome: Comparison between the symptoms and symptom-like behaviors in normal childhood. Seishin-igaku 1988; 30: 1081-1088 (in Japanese).

19. Nomoto F. Peculiarity of coprolalia in Japan. Seishin-igaku 1988; 30: 1305-1309 (in Japanese).

20. Nomura Y, Segawa M. Tourette syndrome in oriental children: Clinical and pathophysiological consideration. In: Friedhoff AJ, Chase TN (eds.) Advances in Neurology Vol.35 Gilles de la Tourette syndrome. Raven Press, New York, 1982; 277-280.

21. Pauls DL, Raymond CL, Stevenson JM, Leckman JF. A family study of Gilles de la Tourette syndrome. Am J Hum Genet 1991; 48: 154-163.

22. Robertson MM, Trimble MR, Lees AJ. The psychopathology of the Gilles de la Tourette syndrome. A phenomenological analysis. Br J Psychiatry 1988; 152: 383-390.

23. Robertson MM. Self-injurious behavior and Tourette syndrome. In: Chase TN, Friedhoff AJ, Cohen DJ (eds.), Advance in Neurology, Vol.58 Tourette syndrome: Genetics, neurobiology, and treatment. Raven Press, New York, 1992; 105-114.

24. Saitoh M. Psychiatric aspects of Gilles de la Tourette syndrome: (1) On the symptomatology. Seishin-igaku 1988; 30: 35-43 (in Japanese).

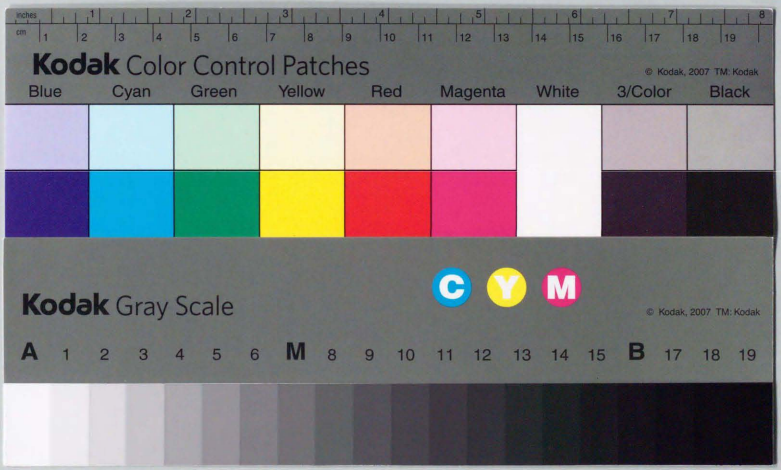
25. Saitoh M. Psychiatric aspects of Gilles de la Tourette syndrome: (2) On the organic factors. Seishin-igaku 1988; 30: 529-535 (in Japanese).

26. Shapiro AK, Shapiro ES, Young JG, Feinberg TE. Gilles de la Tourette Syndrome, Second edition. Raven Press, New York, 1988.

27. Singer C: Coprolalia and other coprophenomena. Neurologic Clinics of North America 1997; 15: 299-308.

28. Staley D, Wand R, Shady G. Tourette disorder: A cross-cultural review. Comprehensive Psychiatry 1997; 38: 6-16.

29. World Health Organization. The ICD-10 classification of mental and behavioral disorders: Clinical description guidelines. World Health Organization, Geneva, 1990.


inches
cm
Kodak Color Control Patches
© Kodak, 2007 TM: Kodak
Blue
Cyan
Green
Yellow
Red
Magenta
White
3/Color
Black
Kodak Gray Scale
C
Y
M
© Kodak, 2007 TM: Kodak
A 1 2 3 4 5 6 M 8 9 10 11 12 13 14 15 B 17 18 19