

Brief Reports

Tic Exacerbation in Adults with Tourette Syndrome: A Case Series

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Abstract

Background: Tourette syndrome (TS) has been described as peaking in adolescence with subsequent regression. We report patients who were diagnosed with TS during childhood who experienced a latent period (significant reduction in or absence of tics) followed by tic re-emergence in adulthood.

Methods: We performed a retrospective chart review of outpatients over age 21 seen at the Yale neurology clinic between January 2012 and July 2016 who were diagnosed with childhood-onset tics, and who experienced a latent period of greater than 1 year followed by an exacerbation.

Results: Sixteen patients were identified. The mean latent period was 16 years. Ten patients (62.5%) identified an exacerbation trigger, most commonly changes in substance use (five patients). Seven patients (43.8%) reported worsening of tics since childhood. Six patients (37.5%) had received pharmacological intervention for tics as children, and 15 patients (93.8%) as adults. Six of 15 patients (40.0%) had an effective response from those pharmacological intervention(s).

Discussion: Our study demonstrates that the decline in symptoms as patients age may represent temporary improvement. The latent period lasted years in our patients, different from the more rapid waxing and waning in children. A change in substance use was an important trigger. Requests for pharmacological intervention were not necessarily correlated with worsening tic severity.

Keywords: Tics, Tourette syndrome

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Introduction

Tourette syndrome (TS) is a life-long disorder but it is characterized by childhood onset, with the most severe symptoms occurring between 8 and 12 years, usually followed by a linear decline in severity.¹ It has been shown in a number of follow-up studies of TS patients that by young adulthood one-third to one-half of patients have minimal to no tics.^{1–4} Many patients follow a less benign course and suffer from impairing tics that persist into adulthood. However, the average age at follow-up evaluation has generally not exceeded the late 20s, and is often even younger.^{1,5} Pappert et al.⁶ identified and videotaped 31 adult patients who had been videotaped for tics as children, and found that 90% of them still had tics. However, all of the patients were under 30 years of age. A recent questionnaire-based study investigating the time course of

tics included patients up to age 35, but also included children as young as 13, diluting the results of the adult group.⁷ We therefore have an incomplete understanding of the natural history of tics as patients progress through age categories, and do not know if young adults whose tics improve will experience recurrences or worsening later in life.

There is some indication from small case series and reports that tics do recur later in adult life in patients who had tics as children. The largest report to date that separately identified such patients is by Chouinard and Ford.⁸ They described nine patients who presented for tics as adults who retrospectively had mild tics as children but had not sought neurological care until adulthood. Their symptom-free hiatus spanned 25–63 years. Klawans and Barr⁹ reported four such cases in 1985; the patients had remission from tics before the age of 20 years,

then recurrence after 60 years old. Sandyk and Awerbuch¹⁰ reported one case of tic recurrence in a woman at the age of 50, after previous resolution in early adulthood. Owing to the scarcity of such reports in the literature, it remains difficult to know whether delayed recurrence of tics is a rare event or simply underreported.

In this exploratory chart review, we sought to identify adult patients in our movement disorders clinic who experienced tic recurrences after a latency period (period of significant reduction in or absence of tics), and to identify any patterns related to demographics, exacerbation triggers, or tic phenomenology that could inform our understanding of the waxing and waning of tics in adult patients.

Methods

In July 2016, one of the authors (D.R.) performed an electronic search of the electronic medical record (EPIC) at Yale to identify 1) outpatients 2) seen at the Yale Medical Group neurology clinic, 3) evaluated between January 2012 and July 2016, 4) diagnosed by a movement disorders neurologist 5) with tics or Tourette Syndrome. Sixty-five patients fulfilled these search criteria. Their medical charts were reviewed and those who had tics of childhood onset, had experienced a latent period of relative tic abatement (defined as the significant reduction in or absence of tics) of greater than one year, and were greater than 21 years of age at the time of the tic exacerbation, were included in the series. The ICD-9 codes for tics of organic origin: 333.3 and Tourette syndrome: 307.23 were used as EPIC search terms. Sixteen patients met all our inclusion criteria. The study was approved by the Yale institutional review board. Demographic and clinical data from the medical record was abstracted by trained staff (C.C.) using a data abstraction form designed for this study.

Results

Of the 16 patients identified, 12 (75.0%) were male and four (25.0%) were female, with an average age at the time of presentation to our clinic of 47 years old (Table 1). Sixteen (100%) of the patients had a diagnosis of TS. Fifteen of the 16 patients (93.8%) had comorbidities commonly associated with tic disorders (obsessive compulsive disorder [OCD], attention deficit disorder [ADD], autism spectrum disorder [ASD], anxiety, depression), and many patients demonstrated more than one of these comorbidities. Other neurological and psychiatric

comorbidities included migraine (one patient), multiple sclerosis (one), cervical dystonia (one), seizures (one), and insomnia (one). Eight of the 16 patients (50.0%) had a first-degree relative with tics, OCD, ADD, ASD, anxiety, or depression. Other neurological and psychiatric disorders in first-degree relatives included schizophrenia (one patient) and bipolar disorder (one patient).

The mean age at exacerbation was 40 years old. The mean latent period was 16 years (range 3–35 years); two patients did not have specifically recorded latent periods but the notes indicated that it was “years”. Ten out of 16 (62.5%) patients reported one or more identifiable stressor(s) that may have induced the exacerbation, including work-related stress (four), comorbid psychiatric disease (three), illness of a family member (one), marital problems (two), medication cessation or reduction (two), high caffeine intake (two), alcohol cessation (one), smoking cessation (one), and poor sleep (one). Six of fifteen patients (37.5%) were unable to identify a trigger.

The phenomenology of tics was the same as had been present when the patient was a child in eight patients (50.0%). In four patient charts (25.0%), the phenomenology of the childhood tics was not clearly documented. Three patients (18.8%) had clear documentation of tic evolution, such that a set of tics in childhood changed to more varied tics in adulthood. In one patient (6.3%) with a history of multiple types of vocal and motor tics in childhood, one tic in particular (winking) became more prominent and bothersome in adulthood. Seven patients (43.8%) had clearly reported that their adult tics were worse than those they had experienced as children; these patients reported that their tics were more prominent, loud, violent, frequent, or varied. The remaining nine patients (56.3%) either reported that their tics were of the same severity (four), were better (one), or it was not documented (four). Fourteen patients (87.5%) reported both motor and vocal tics in adulthood, while the remaining two patients (12.5%) had motor tics only, by report.

Six patients (37.5%) sought treatment at the time of their exacerbation because their tics (both motor and vocal) interfered with work, particularly with public speaking and interacting with clients and coworkers. One patient (6.3%) reported social embarrassment related to her tics (winking). For the remaining patients, a clear precipitant for presentation to a medical professional was not documented, other than exacerbation of tics.

Ten of sixteen patients (62.5%) had not been treated with any medications for tics as children, while six (37.5%) had been treated with medications during childhood. On presentation to our clinic, eleven patients (68.9%) were on a medication for tics or mood including: clonidine (two), benzodiazepines (three), pimozide (one), selective serotonin–norepinephrine reuptake inhibitors (two), bupropion (one), haloperidol (one), and topiramate (one). Fourteen patients (87.5%) were treated with medication for their tics by their Yale movement disorders physician at the time of their exacerbation. One patient (6.3%) underwent lifestyle modifications, and two patients (12.5%) received botulinum toxin injections (one in addition to medication). The medications prescribed were clonidine (six), benzodiazepines (three), guanfacine (two), levitiracetam (two), topiramate (two), tetrabenazine (one), haloperidol (one), bupropion (one), amantadine (one), and pimozide (one). Medication responses are recorded in Table 2. Excluding patients without follow up and one non-adherent patient, medications were effective in about half of

Table 1. Group Clinical Characteristics of 16 Adult Patients with a History of Childhood Tics and Subsequent Tic Exacerbation in Adulthood

Characteristic	Data
Mean age at presentation (years)	47
Mean age at exacerbation (years)	40
Male gender (N)	12 (75.0%)
Tourette syndrome diagnosis (N)	16 (100.0%)
Psychiatric comorbidity (N)	15 (93.4%)

Table 2. Individual Demographic and Clinical Information of 16 Adult Patients with a History of Childhood Tics and Subsequent Tic Exacerbation in Adulthood

Age at Presentation (years)	Age at Exacerbation (years)	Gender	Diagnosis	Latent Period (years)	Trigger for Exacerbation	Comorbidities	Family History	Medications Tried, Effectiveness
23	21	M	TS	3	Anxiety, high caffeine intake, cessation of alcohol and tobacco	Anxiety, ADD	None	Clonidine, not effective; clonazepam, effective
25	23	M	TS	5	High caffeine intake, poor sleep	OCD	None	No medications
30	28	M	TS	8	Work	Anxiety, multiple sclerosis	None	Clonidine, unknown
31	31	M	TS	10	New job	OCD, migraine	Mother (OCD, anxiety), father (anxiety), sister (OCD, anxiety)	Clonidine, not effective
32	29	M	TS	10	None	ASD, insomnia	None	Botulinum toxin, unknown
32	24	M	TS	6	New job	ADD	Father (tics)	Clonidine, unknown
33	32	F	TS		None	OCD, seizures	None	Clonidine, effective; levetiracetam, side effects
34	33	M	TS	12	None	OCD, ASD	Brother (tics)	Amantadine + botulinum toxin + topiramate, effective
38	33	F	TS	25	None	OCD	None	Clonidine, non-compliant
40	37	M	TS	19	New business, marriage	Anxiety, depression	Brother (tTics)	Bupropion, not effective

Table 2. Continued

	Age at Presentation (years)	Age at Exacerbation (years)	Gender	Diagnosis	Latent Period (years)	Trigger for Exacerbation	Comorbidities	Family History	Medications Tried, Effectiveness
11	47	41	F	TS	15	None	OCD, depression	None	Guanfacine, not effective; clonazepam + levetiracetam, not effective
12	56	48	M	TS		None	ADHD	None	Guanfacine, effective
13	62	61	M	TS	20	Depression with suicidality	OCD, depression	Sister (TS)	Haloperidol, effective
14	63	62	M	TS	30	Stopped meds; anxiety	OCD, anxiety	Sister (depression)	Topiramate, unknown
15	66	66	F	TS	30	Divorce, medication reduction	None	Father (OCD), sister (schizophrenia)	Pimozide, effective; tetrabenazine, not effective
16	69	66	M	TS	35	Ill family member	OCD, depression, anxiety	Father (anxiety), sister (bipolar)	Clonazepam, unknown

Abbreviations: ADD, Attention Deficit Disorder; ADHD, Attention Deficit Hyperactivity Disorder; ASD, Autism Spectrum Disorder; F, Female; M, Male; OCD, Obsessive Compulsive Disorder; TS, Tourette Syndrome.

the patients (seven or 46.7%). One medication was discontinued because of side effects. Patients tried an average of 1.25 medications, and only six of 15 patients who received pharmacologic treatment had a documented effective response at some point in their treatment. Five patients were lost to follow-up. With the exclusion of non-compliant cases and those lost to follow-up, clonidine was effective in one out of three cases (33.3%), benzodiazepines in one out of two cases (50.0%), guanfacine in one out of two cases (50.0%), and levetiracetam in zero out of two cases (0.0%). Botulinum toxin was effective in combination with medications in one patient, and there was an unknown outcome in the other patient.

Discussion

In this study, we retrospectively identified 16 patients who belong to a little-described subset of TS patients: those who are diagnosed with TS during childhood, then experience a period of relief from or absence of symptoms before tic re-emergence in adulthood. This temporal pattern has not been depicted as part of the natural history of tic disorders, mainly because there are no longitudinal studies of children with tics far into adulthood. Our study, which represents the largest single series to date of adults with tic recurrences, raises the possibility that, for some patients, the steady decline in symptoms many patients experience as they enter their early 20s may represent temporary improvement.

The major implication of this study relates to the way in which tic patients may be educated about their disorder, and managed into adulthood. Tic patients and their families are often educated about the natural history of their tic disorders using the classic paradigm that the tics will likely become less severe as the patients exit adolescence. It is important for neurologists to be aware that tics may recur or worsen in adulthood even after a significant latent period. The neurological community should therefore 1) consider that there may be more patients than expected who suffer from recurrences in adulthood, and 2) ultimately attempt to identify factors that predict which patients go on to have recurrences.

The mean age at onset of tic re-emergence in our patients was 40 years, very similar to the mean age of 47 years reported by Chouinard and Ford;⁸ the latency period was shorter for our patients, averaging 16 years (range 3–35 years) vs. 35 years (range 12–56 years). Notably, Klawans and Bari⁹ reported four patients, each with an age of exacerbation greater than 60 years, and latency periods exceeding 40 years in all cases. In each of these studies, adults experienced shifts in their symptomatology over periods of years or decades, unlike the more rapid fluctuations over weeks to months that has been observed in children.¹⁵

Day-to-day factors that influence variability of tics have been studied in adults and children,^{16,17} but there is little information in the literature on what factors may affect tic fluctuations over years. Sixty-three percent of our patients reported identifiable triggers linked to their tic exacerbations. These were often common life stressors of adulthood related to work and interpersonal relationships, which are similar to the psychosocial stressors that have been reported to induce tic exacerbations in children, namely school-related and interpersonal/family

stressors.¹⁸ Initiation, increase, or cessation of substances such as tobacco, alcohol, caffeine, and/or medications were found to temporally correlate with re-emergence of tics in five (31.3%) of our patients. Substance use is less prevalent in children, so it is important for practitioners to ask adult patients about use of neurologically active substances or medications, as these may influence tics. Patients with tic disorders have been shown to have heightened levels of internalizing disorders (e.g., depression, anxiety, OCD), and these have been correlated with more self-reported triggers for tic exacerbations.^{16,19} Twelve of 16 (75.0%) of our patients had one or more diagnoses of internalizing disorders, which may partially explain why these patients developed exacerbations later in life that warranted medical attention.

Studies have reported variable results regarding tic evolution from childhood to adulthood—that tics in adulthood are milder, more severe, or the same as those found in children.^{8,12,13} These studies did not compare the same patients over time. Slightly less than half of our patients (43.8%) reported a clear worsening. Nine patients for whom tics were milder, the same, or not documented accepted medical intervention for their tics, even though four of those patients (44.4%) had not received medications for their tics as children. Himle et al.¹⁶ found that older children reported more tic-exacerbating consequences for their tics (defined as outcomes that occur after tics, such as being stared at), and proposed that this may be due to an increasingly complex social environment that comes with age. It may be that, in adults, the social environment continues to increase in complexity, and with that, external exacerbating consequences may become more influential, particularly in those patients with internalizing disorders. The influence of social impact on the decision to seek medical attention is supported by the common theme that tics interfered with the ability to function at work, and/or caused embarrassment in social settings in seven (43.8%) of our patients. Future studies should aim to differentiate between objective tic severity and subjective tic impact, particularly as these factors relate to psychiatric comorbidities.

Ten different medications and botulinum toxin were used in the 15 patients who received medical therapy for their tics, and they were only effective about half of the time. In some cases, medications were not standard of care, but were used either because they were continued from a previous provider, or because multiple other medications had been tried prior to presentation to our center without success. At the time of the chart review, only six of the 15 patients (40.0%) who were treated pharmacologically were on treatments that were known to be effective for their tics. Past studies have demonstrated that adults may respond more poorly to medications than children, particularly neuroleptics.¹³ Two of our patients were treated with neuroleptics (pimozide, haloperidol), and both reported effectiveness of the medication. Alpha-2 agonists such as clonidine and guanfacine have been shown in several studies to be efficacious in less than half of patients, although some studies doubt their efficacy for tics at all.²³ Alpha-2 agonists were the most commonly prescribed medications for tics in our patients; eight of 16 patients were treated with either clonidine or guanfacine, and of those only two reported that they were efficacious. Control of tics in these patients was challenging and the

therapeutic strategies employed were highly variable, a situation unlikely to be unique to our institution.

The major limitation of our study is that it is a retrospective review of medical records and this resulted in incomplete data in some instances. Given the retrospective nature of the study, medications were not standardized and efficacy was difficult to determine. Patients often do not seek medical attention for tics, which makes a true incidence of tics difficult to assess.^{24,25} Ideally, the percentage of patients with tic disorders in childhood who experience re-emergence of tics as adults should be elucidated with a prospective study. Second, the sample size of 16 is small. Third, patients were not evaluated in clinic during their latent periods—the latency of tics was purely by patient report—so it is unclear to what extent the patients had a true abatement of symptoms. It has been observed that as many as 30–50% of patients were unaware of tics noted by examiners.^{6,25} Still, subclinical tics may be of little practical relevance. Likewise, tic severity in adulthood relative to childhood severity was by patient report and therefore may not be entirely reliable.

In conclusion, the improvement of tics as patients enter adulthood may, in some patients, represent a temporary process rather than a permanent resolution. Neurologists and patients should be aware that tics may recur in adulthood even after a significant latent period. More research is needed to better understand the many facets of this complex neuropsychiatric disorder in the adult population.

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