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Increased anti-streptococcal antibodies in patients with Tourette's syndrome

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Abstract

Infection or postinfectious phenomena have been postulated to play a role in the pathogenesis of children afflicted with the typical symptoms of Tourette's syndrome (TS). We investigated whether an increase of titers of antistreptococcal antibodies can be reproduced in our children with TS, and whether this increase is restricted to children. We examined the titers of two different antistreptococcal antibodies, antistreptolysin (ASL) and antiDNase B, both in children and adults. Titers of ASO and antiDNase B were measured (1) in 13 children/adolescents suffering from TS and in an age-matched comparison group; (2) in 23 adult patients, a comparison group of 23 age-matched controls, and in another group of 17 age-matched, non-medicated acute schizophrenics. ASO and antiDNase B titers were determined by laser nephelometry using a commercially available kit. Two antistreptococcal cut-off levels were compared (>250 U/ml and >400 U/ml). As expected, increased ASO titers (>400 IU/ml) were found in a higher proportion of children/adolescents with TS compared to healthy controls. In parallel, high antiDNase titers (>250 U/ml or >400 U/ml) were also observed in significantly more children/adolescents with TS compared to controls. Regarding adults, titers >250 U/ml for both antistreptococcal antigens were found in significantly more TS patients than in schizophrenic patients or healthy control subjects. The mean values of ASO and antiDNase titers were significantly higher in both groups of TS patients compared to control children/adolescents, to the comparison groups of healthy adults and to schizophrenics. No difference in antistreptococcal titers was found between schizophrenics and the group of healthy adults. TS patients exhibited higher antistreptococcal titers than age-matched

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comparison groups of both children/adolescents and adults using different types of calculation. Our findings support the theory that a postinfectious immune mechanism may play a role in the pathogenesis of TS. The mechanism still needs to be elucidated.

Keywords: Tourette's syndrome; Schizophrenia; Autoimmunity; Anti-streptococcal antibodies; PANDAS

1. Introduction

Typical features of Tourette's syndrome (TS) include simple and complex motor tics, vocal tics, and echolalia. Obsessive–compulsive symptoms are frequent (Müller et al., 1997b; Robertson and Stern, 1998). The onset of the disorder is before the age of 21. Typically TS shows a waxing and waning course, but the chronic presence of tics even during later life is not unusual (Shapiro et al., 1988).

The pathoetiological mechanism is still unclear. Neuroanatomical as well as neuroimaging studies (Haber et al., 1986; Peterson et al., 1993; Singer et al., 1993) and effective neuroleptic treatment in many cases (Shapiro et al., 1988) suggest that a disturbance of the dopaminergic system in the basal ganglia plays a role in the pathogenesis of TS (Singer, 1994).

Several possibly causative mechanisms of the disturbed dopaminergic neurotransmission are discussed. One is an infection-triggered immune process (Hallet and Kiessling, 1997). Extrapyramidal movement disorders are known to occur as a symptom of post-streptococcal disease as in Sydenham's chorea (Nausidea et al., 1983; Kiessling et al., 1993; Swedo et al., 1994; Toren et al., 1994). Cases of childhood TS were recently proposed to be caused by such a post-streptococcal mechanism (Allen et al., 1995; Allen, 1997), these cases being part of a spectrum of childhood neurobehavioral disorders termed PANDAS (Pediatric Autoimmune Neuropsychiatric Disorders Associated with Streptococcal infection; Swedo et al., 1997; Kurlan, 1998).

Since TS has its onset in childhood or adolescence but is also a disorder of adulthood, we evaluated one common feature of post-streptococcal disorder, titers of antistreptococcal antibodies, both in children/adolescents and in adult TS patients in comparison to healthy children/adolescents and to healthy adults regarding the antistreptococcal antigens Antistreptolysin O (ASO) and antiDNase B. To study the specificity of this phenomenon in TS patients, we compared the adult TS patients with age-matched schizophrenics, since a disturbance of dopaminergic neurotransmission is also involved in schizophrenia.

2. Methods

We examined two different groups of TS patients, two healthy age-matched comparison groups, and one adult schizophrenic comparison group. All TS patients fulfilled the diagnostic criteria of DSM-III-R. The severity of the TS was assessed by the Tourette syndrome global scale (TSGS; Leckman et al., 1988).

The group of children/adolescents with TS consisted of 13 (four female, nine male) children/adolescents, their ages ranged from 9 to 15 years, and the mean age was 12 ± 2 years. The onset of the motor tics ranged from the age of 4 to 10 years (mean: 6.2 ± 1.9 years), and the onset of the vocal tics ranged from the age of 5 to 13 years (mean: 8.1 ± 3.7). The severity of the tics ranged from 7 to 58 points (mean: 30.9 ± 14.7) on the TSGS. Clinical symptoms of obsessive–compulsive disorder were presented by two (15%) of the children. Four of the children (31%) showed signs of an attention deficit/hyperactivity disorder. TS children/adolescents joined the TS outpatient program from a wide region of upper Bavaria and northern Swabia. No two TS children attended the same school.

The comparison group consisted of 12 healthy children/adolescents (five female, eight male), their ages ranged from 7 to 17 years, and mean