"Seesaw effect" between the host immune response and tic expression in a *Staphylococcus aureus* intermittent carrier with Tourette Syndrome

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BACKGROUND

Different studies support the etiologic role of group A beta-hemolytic streptococcal (GAS) infections, in PANDAS (Pediatric Autoimmune Neuropsychiatric Disorders Associated with Streptococcal infection) (1) and in a sub-group of patients with Tourette syndrome (2). Additionally, other pathogens can also induce post-infectious Tourette-like syndromes, including *Mycoplasma pneumoniae*, *Borrelia burgdorferi*, and assorted viruses (1). Basal ganglia autoimmunity, triggered by these infectious agents, can result in movement and neuropsychiatric disorders, but no conclusive data are available.

AIMS

To focus on the possible associations between bacterial pathogens in nasopharyngeal and tonsil swabs, serological immune and autoimmune responses against brain antigens and tic severity in an adolescent girl with TS, during exacerbations and remission phases (3).

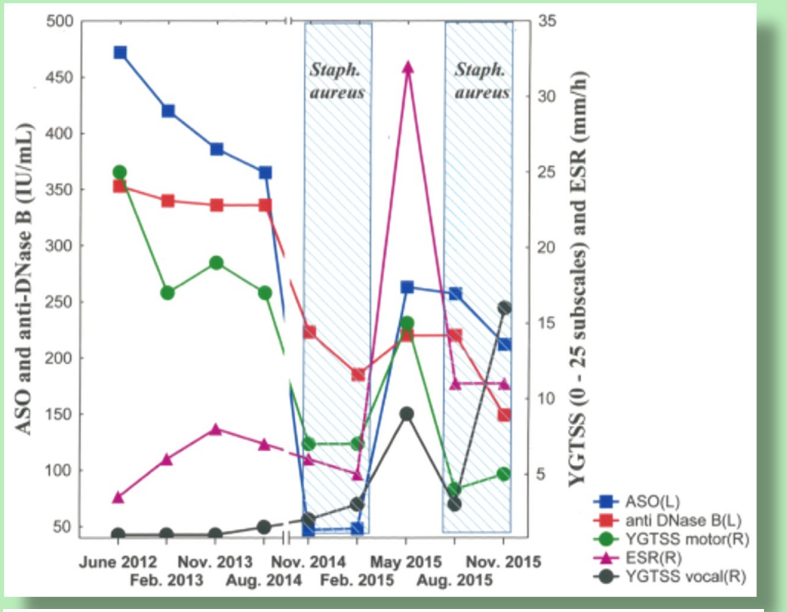


Fig. 1. Tic severity rating, laboratory records and *S. aureus* carriage pattern in a girl with Tourette syndrome

ASO = Anti-Streptolysin O; anti DNase B = Anti-Deoxyribonuclease B YGTSS (motor) = Yale Global Tic Severity Scale (motor tics subscale) ESR = Erytrocyte Sedimentation Rate; YGTSS (vocal) = Yale Global Tic Severity Scale (vocal tics subscale)

Table 1. Autoimmunity testing against brain antigens

	Before Colonization (November 2014)	Colonization phase (January 2014)	Decolonization phase (March 2014)
Dopamine D1R (titer)	**8000** Pos.>2000	Neg. ≤ 2000	Neg. ≤ 2000
Dopamine D2R (titer)	**16000** Pos.>8000	Neg. ≤ 8000	Neg. ≤ 8000
Lyso-ganglioside (titer)	Neg. ≤ 320	Neg. ≤ 320	Neg. ≤ 320
Tubulin (titer)	**2000** Pos. >1000	**4000** Pos. >1000	**4000** Pos. >1000
CaM Kinase II (% of baseline)	**156** Pos. >130	**160** Pos. >130	**190** Highly Pos. >180

Titers are given as the minimum serum dilution required in ELISA assays to achieve a positive reading, compared with standard values of normal controls in a test panel provided by Moleculera Labs, Inc. (Oklahoma City, OK, USA)

CONCLUSIONS

A correlation was observed in a girl with TS between *S. aureus* colonization/tic improvement and decolonization/tic exacerbation. During the colonization phase anti-streptococcal antibody titers as well as autoantibodies against dopamine receptors D1 and D2 were downregulated and dropped to normal values.

S. aureus nasal carriage possibly provides a new human model for the *in vivo* study of the interplay between infection, immunity, autoimmunity, and tic disorders.

RESULTS

Here, we longitudinally investigated a 9-year-old girl with Tourette syndrome and elevated levels of antibodies against *Streptococcus pyogenes*. Microbiological monitoring indicated that the child was an intermittent nasopharyngeal carrier of S. aureus. Clinical improvement in the frequency and severity of motor tics was observed during the *S. aureus* colonization phase (Figure 1) and were temporally correlated with downregulated production of anti-streptococcal (Figure 1) and anti-D1/D2 dopamine receptor antibodies (Table 1). After decolonization, clinical conditions reverted to the poor scores observed previously, suggesting a possible role for the immune response during bacterial clearance as a trigger of symptom recrudescence. This hypothesis is consistent with data from animal models showing that a pro-inflammatory Th17 cell-associated immune response is ultimately required for *S. aureus* nasal decolonization. These findings imply a cause-effect relationship between *S. aureus* colonization and motor tic improvement, as well as between decolonization and tic exacerbation. A shift from an anti-inflammatory modulatory response during the colonization phase (induced by *S. aureus*) to a pro-inflammatory state during the clearing process (induced by the host) occurred.

REFERENCES

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