

## Case Report of Pediatric Autoimmune Neuropsychiatric Disorder Associated with Group A Streptococcus

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**Abstract:** Pediatric Autoimmune Neuropsychiatric Disorder associated with group A Streptococcus (PANDAS) is a term used to describe a subset of children whose symptoms of obsessive compulsive disorder (OCD) or tic disorders are exacerbated by group A streptococcal (GAS) infection. The association between PANDAS and GAS is controversial. Herein, we report a Ten year old boy who was complaining of fever and sore throat associated with tics and elevated titers of ASO leading to diagnosis of PANDAS and summarizes the definition, manifestations, pathogenesis, complications and treatment.

**Keywords:** Pediatric Autoimmune Neuropsychiatric Disorder (PANDAS), Group A Streptococcal (GAS) infection, Obsessive Compulsive Disorder (OCD), Antistreptolysin O titer (ASO)

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### INTRODUCTION:

Pediatric Autoimmune Neuropsychiatric Disorder associated with Group A Streptococcus (PANDAS) is a term used to describe the abrupt onset or exacerbation of neuropsychiatric symptoms, obsessive compulsive disorder (OCD) or tic disorders in a pediatric age group with a preceding infection of group A Streptococcal (GAS) infection [1]. The hypothesized association between PANDAS and GAS is controversial, as is the limitation of the diagnosis exclusively within the pediatric age group. Diagnosis of PANDAS requires documentation of an episode of neuropsychiatric symptoms or exacerbation of neuropsychiatric symptoms associated with evidence of GAS infection {Positive throat or skin culture, rapid antigen detection test, or rising Antistreptolysin O titer (ASO)}. Herein, we report a Ten year old boy who was complaining of fever and sore throat associated with tics and with elevated titer of ASO leading to diagnosis of PANDAS and summarize the definition, manifestations, pathogenesis, complications and treatment.

### CASE REPORT:

Ten year old boy complaining of fever of since before 12 days, about 6 episodes per day, relieved partially by antipyretics, with occasional chills associated with sore throat, anorexia, and fatigue. At day 4 of fever, he started to have a non-bloody watery diarrhea treated by an attending physician by Cefixime PO for 6 days, last dose 2 days prior to admission at our Hospital. Three days prior to his febrile illness, he started to complain of bilateral eye blinking or tics

(upper eyelids) treated with antihistamine eye drops for a possibility of allergic conjunctivitis. On physical examination, he looked pale, with anicteric sclera, poorly injected sclera, bilateral eye blinking with facial twitching were noticed. His ENT exam showed normal tympanic membranes, kissing tonsils with white patches over the posterior pharynx, and bilateral cervical posterior enlarged soft lymph nodes non tender and mobile. There was no neck stiffening but a mild hepatosplenomegaly. The lungs were clear on auscultation, with normal S1-S2 heart sounds and no additional murmur. As for his past history he had allergic rhinitis with previous hospitalization at 3 year of age for pneumonia, complicated with pleural effusion. His brother has an anxiety disorder. As for his neurodevelopmental history the patient was normally developed for his age. Laboratory data upon admission revealed Hemoglobin of 11 g/dl with WBC count of 9000 (70% Neutrophils and 30% Lymphocytes), Platelets count of 330x10<sup>9</sup>, CRP 22 mg/L, ASO 500 units/ml, ESR 33, Electrolytes and Creatinine were normal. Repeated laboratory tests after 5 days revealed Hemoglobin of 12, WBC 12000, Platelets 226x10<sup>9</sup>, CRP 380, ASO 864, and ESR 45. EBV IgM positive, CMV IgM slightly positive, Widal test and Wright serology repeated twice were negative. Blood culture showed no growth after 5 days. Throat culture revealed no growth as twice repeated. Ultrasound of abdomen and pelvis showed mild hepatosplenomegaly. Brain MRI, done to rule out any brain mass effect or abscess, was normal except for multiple cervical lymph nodes. Brain EEG showed no epileptic discharges.

The follow up of the ASO titers on day 4 and day 11 of hospitalization were 864 and 971 respectively. The patient was started on Ceftriaxone on day 7 of hospitalization for 5 days, the fever subsided, the tics improved and the patient was discharged on PO antibiotics for 10 to be followed up as outpatient within 1 week as he was diagnosed as having PANDAS. On his follow up after 1 week, he was completely free of tics and the ASO done to reveal 320. Four months later, the patient again started to have eye blinking and motor tics, his throat culture showed growth of GAS, ASO was above 1000, ANA and cANCA titers and the complement C3 and C4 were normal.

#### DISCUSSION:

In 1998, PANDAS as a syndrome was described by Swedo and colleagues, after they have been noted a different group that presented with abrupt onset of neuropsychiatric symptoms among prospectively followed children complaining of Obsessive Compulsive Disorder (OCD) [1].

PANS and CANS have been used to encompass the childhood age group (under 18 years of age) and a larger patient population by excluding the 'being pre-adolescence' requirement for PANDAS. PANDAS are characterized clinically by a "Saw tooth" pattern with episodes of symptom quiescence, followed by exacerbations with abrupt onset and gradual resolution (over weeks to months) [1]. Neuropsychiatric exacerbations in children with PANDAS begin at the time of GAS infection or within one to two weeks after GAS infection. If children with PANDAS develop another Streptococcal infection their symptoms suddenly worsen again [1].

Children with PANDAS and OCD are described as having an "explosion" of OCD symptoms, reaching clinically significant impairment in 24 to 48 hours. Because fever and other stressors of illness are known to exacerbate OCD and tic disorders, the exacerbations should have an association with GAS infection, documented by culture or serology to qualify as a possible case, to meet criteria for PANDAS [1]. In an epidemiological investigation Leslie et al investigated whether previous Streptococcal infection(s) increase the risk of subsequent diagnosis of OCD, TS, other tic disorders, attention-deficit hyperactivity disorder (ADHD) or major depressive disorder (MDD). Children with newly diagnosed OCD, TS, or tic disorder were more likely than controls to have had a diagnosis of Streptococcal infection in the previous year (Odds Ratio=1.54, CI 95% 1.29-2.15) [2].

In a case-control study of children 4 to 13 years old patients with OCD, TS, or tics these disorders were more likely than controls to have had prior Streptococcal infection (Odds Ratio=2.22; CI 95% 1.05-4.69) in the 3 months before onset date. The risk was higher among children with multiple Streptococcal

infections within 12 months (Odds Ratio=3.10; CI 95% 1.77-8.96). Similar results were found in patients with typical symptoms of Tourette's syndrome. The frequency of elevated ASO titers was also significantly higher (P-Value = 0.04) in patients with Attention-Deficit Hyperactivity Disorder (64%) than in a control group (34%). Overall, the available evidence does not totally support the concept that PANDAS are a well-defined, isolated clinical entity subdued by definite pathophysiological mechanisms. The etiology of OCD and Tics in the PANDAS subgroup is unknown, but is theorized to be a post-Streptococcal autoimmune process in a manner similar to that of Sydenham's chorea. The working hypothesis for the pathophysiology begins with a GAS infection in a susceptible host that incites the production of antibodies to GAS that cross react with the cellular components of the basal ganglia, particularly in the caudate nucleus and putamen. The Obsessions, Compulsions, Tics, and other Neuropsychiatric symptoms seen in these children are postulated to arise from an interaction of these antibodies with neurons of the basal ganglia [3]. The best therapy for acute episodes of PANDAS is to treat the bacterial infection with antibiotics. A throat culture should be done to document the presence of streptococcal infection. If it is present a single course of antibiotics is needed to allow PANDAS symptoms to subside. If throat culture is negative, an occult or a hidden Streptococcal infection should be ruled out such a sinus infection or Streptococcus bacteria infecting the anus, the vagina or a urethral opening of the penis, although the latter infections are rare, there have case reports of PANDAS symptoms in some patients of anogenital infections. The Streptococcus bacteria can be harder to eradicate in the sinuses and other sites, so the course of antibiotherapy may be longer than the usual course. Tonsillectomy should only be performed in those who are surgical candidates based on current published guidelines. Cognitive-behavioral therapy remains a low-risk option. Studies support the use of IVIG; however more investigation is needed prior to widespread adoption of this treatment given its potential risks [4].

#### CONCLUSION:

Fever and sore throats associated with Tics and elevated titer of ASO lead to the diagnosis of PANDAS. PANDAS are characterized clinically by a "Saw tooth" pattern with episodes of symptom quiescence, followed by exacerbations with abrupt onset and gradual resolution. Our patient had the PANDAS criteria associated with elevated titer of ASO and elevated EBV IgM titer.

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