Pediatric autoimmune neuropsychiatric disorders associated with streptococci (PANDAS) are important neuropsychiatric disorders in childhood. Streptococcus pyogenes infection associated with tics, obsessive-compulsive disorders, and chorea co-occurrence is important. Swedo et al. have increased the awareness of this situation since 1998. How streptococcal infections give rise to this condition is not clear yet, but the severity of the symptoms is reduced by the treatment of streptococcal infections is important. Eight-year-nine-month-old girl presented with complaints of a 2-year history of upper respiratory tract infections and increased severity of blinking of eyes, throat cleaning, tic disorder and obsession with hand cleaning. In addition, choreiform movements were present and fluoxetine did not improve the symptoms. The patient was followed-up and treated with PANDAS pre-diagnosis. Streptococcus treatment and prophylaxis decreased the patient's complaints.

A six-year-four months old boy, admitted with abnormal hand and body movements, which increased severity after the school period, and causing deteriorated fine motor skills during infectious periods for two years. There were also complaints with vocal tics and obsessive-compulsive disorder in the form of throat cleaning. Treatment of S. pyogenes was administered in throat culture. After the penicillin prophylaxis, the complaints decreased.

In this study, two patients were presented with choreiform movements, obsessive-compulsive disorder and tic disorder due to follow-up PANDAS diagnosis. PANDAS should be considered in children with neuropsychiatric disorders, especially symptoms associated with infection periods.

Keywords: Neuropsychiatric; PANDAS; streptococci.

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Pediatric autoimmune neuropsychiatric disorders that are associated with streptococci (PANDAS) are significant concerning possible complex history of the disease and relation to Streptococcus pyogenes (group A streptococcus - GAS) infection, tics, obsessive-compulsive disorders (OCD) and Sydenham’s chorea (SC) as a neurological sign of acute rheumatic fever (ARF).[1] There used to be many confusing clinical situations before the discovery of PANDAS, but as Dr. Susan Swedo described the first 50 cases (Swedo et al. 1998), these patients, similar to SC, were distinguished from the cases with tic disorders and OCD. For this purpose, five diagnostic criteria were defined to define PANDAS by evaluating other criteria and studies related to SC and OCD:[1,2]

1. Obsessive-compulsive disorder and/or tic disorder (Tourette, chronic motor or vocal tic disorder)
2. Pediatric onset (between 3 years-onset of puberty)
3. Sudden onset and episodic course of the symptoms
4. The close association between GAS infection and onset or increase of symptoms
5. Presence of neurological abnormalities during exacerbations (motor hyperactivity, choreiform movements and/or tics)

PANDAS is more common in men (2.6: 1) compared to women. Although the prevalence and incidence of PANDAS are not completely known, the prevalence in tic disorder and OCD in childhood is approximately 10%. In this study, we present two patients who were referred to our pediatric psychiatry clinic for the treatment of OCD, tic disorder and choreiform movements.

Case Reports

Case 1 – An 8-year-9-month-old female patient presented to our clinic with complaints of blinking, tic disorder in the form of hawking and perpetual urge for hand cleaning, which increased in intensity with a throat infection. The patient described deterioration in dexterity and involuntary hand and body movements, which became evident during the periods of exacerbation, indeed. The patient had been started on fluoxetine before, but despite using fluoxetine for six months, her symptoms did not improve, and the family discontinued the treatment voluntarily. He did not have a family history of psychiatric illness, especially OCD, Tourette syndrome, or a tic disorder. Thus, the patient stated that she had not undergone regular check-ups before. Physical examination of the patient revealed choreiform hand and body movements, vocal and motor tics. In the oropharynx examination, the tonsils were markedly hyperemic and hypertrophic. Then, the patient was asked for antistreptolysin-O (ASO), anti-nuclear antibody, rheumatoid factor, C-reactive protein, hemogram, biochemistry tests and a throat culture was sent to the laboratory. ASO level was 615 IU-ml (0-200 IU-ml) and C-reactive protein was 38 mg/L (0-5 mg/L). White blood cell count increased (19,800). Anti-nuclear antibody, rheumatoid factor and biochemistry tests were normal. Echocardiography showed no cardiac involvement. Cranial magnetic resonance imaging and electroencephalography were normal. GAS-Streptococcus pyogenes grew in throat culture. Ampicillin-sulbactam was started intravenously. On the 3rd day of the treatment, his symptoms started to improve. Monthly Depot penicillin prophylaxis was started. Significant improvement was observed in the choreiform movements after six months.

Discussion

A group of researchers, including Swedo et al., identified a subgroup of children presenting with OCD and/or tic disorders following streptococcal infections in the last half of the 1990s and used the term PANDAS for this subgroup. In the following years, the concept of PANDAS has become very popular. Numerous studies have also been published on different aspects of PANDAS.

The frequency of obsessive-compulsive disorder is 1-3% in the general population. The presence of obsessions (repetitive and persistent impulses and/or thoughts) and/or compulsions (repetitive behaviors that a person strongly wants to perform in response to the obsession or according to the rules that must be applied) are the main components. The obsessive-compulsive disorder peaks in childhood and adolescence in the 2-year age group: 8-12 years before puberty and secondly postpubertal period. In typical OCD, however, the onset of symptoms is gradual and usually postpubertal. These cases respond better to the treatment. Although OCD is described as a chronic course in some cases, fluctuation of symptoms (decreasing-increasing) is especially noteworthy, particularly in...
PANDAS,[2, 4, 5] Both of our patients were diagnosed with OCD. Thus, they were administered treatment. However, PANDAS was supported given that their symptoms were fluctuating with the periods of infection and regressed with the antibiotic prophylaxis.

Chorea is seen after ARA, which is a poststreptococcal condition, mostly in the form of SC in childhood. Chorea is often monophasic. However, PANDAS and PANDAS related chorea have a chronic course concerning the infection periods or present with exacerbations associated with infection periods. Perhaps the most important difference between PANDAS and chorea in ARA is the presence of cardiac involvement in ARA.[6] Both of our patients had recurrent choreiform movements that increased during the periods of infection. Echocardiographic examinations were normal.

Tics are fast, repetitive, non-rhythmic and stereotypic motor movements or vocal movements. Tics are usually impulsive and can be terminated voluntarily. Tick disorders are generally childhood and adolescent disorders. In chronic forms, the onset of tics is 2-7 years. The most severe period of symptoms is pre-adolescence (9-12 years) period. Then, there is a phase of alleviating and balancing the symptoms in early adulthood (>14 years). The emergence of the definition of PANDAS and the subsequent investigations tell us that this natural course of tic disorders is not actually present in these patients. This is because there is an increase in these complaints with periods of infection.[1, 7] In our study, it was important that the patients’ movements in the form of tic disorder increased with periods of infection and regressed after the treatment.

In many studies, researchers have reported that streptococcal infections may play a role in many neuropsychiatric disorders, such as SC, and this situation should be paid attention to, especially in childhood. In the emergence of Sydenham chorea, it was observed that the reaction of monoclonal antibodies with the surface of neuron cells and cross-reaction with N-acetyl-beta-D-glucosamine and lysoganglioside, group A carbohydrate epitope. The reason for this was not fully elucidated, but the most emphasized hypothesis was on the immune response that is likely to occur in the basal ganglia. Another hypothesis suggests that antibodies crossing the blood-brain barrier increase antibody-mediated cell signaling and trigger movement of dopamine in the caudate-putamen region of the brain, causing movement impairment. In many studies, an increase in the immune response to streptococcal antigens (ASO), which is commonly used as an indicator of S. pyogenes infection, is considered as a finding of infection. The gold standard method is the isolation of bacteria in a culture medium.[7-9] ASO level, which was higher in the second patient, and S. pyogenes growth in throat cultures examined in both patients were the evidence of infection.

In recent studies, the benefits of antibiotic therapy, adenotonsillectomy, intravenous immunoglobulin (IVIG), and cognitive behavioral therapy in the effective treatment of PANDAS have been investigated. While the potential effects of adenotonsillectomy are uncertain, other treatment options are effective, but further clinical studies are needed.[10] In our study, antibiotic therapy prophylaxis was administered to the patients and evaluated by the child psychiatry clinic for the follow-up and treatment.

Conclusion

In this study, PANDAS, which is crucial in childhood and difficult to diagnose because of a complex clinical presentation, is of considerable importance for both pediatric psychiatrists and pediatricians. PANDAS are especially noteworthy because they affect school success and attendance; however, the regression of complaints with proper treatment is pleasing.

Disclosures

Informed Consent: Written informed consent was obtained from the patient for the publication of the case report.

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