A Rare Manifestation of 'Complex' Post Streptococcus Infection Movement Disorder in Paediatric Patient a Case Report

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Abstract

Background: Post Streptococcal Movement Disorder (PSMD) is a rare disease. One of the PSMD diagnosis is Pediatric Autoimmune Neuropsychiatric Disorders Associated with Streptococcal Infection (PANDAS).

Case Description: 10 year old female with involuntary movement including myoclonic jerks, chorea and stereotype. Movement duration is 5 minutes, repetitive and sensitive to loud noise. Patient has history of respiratory infection 2 weeks ago with Positive ASTO test. Patients showed improvement after treatment with antibiotics, corticosteroids and antipsychotics.

Conclusion: The pathophysiology of PANDAS begins with Group A beta-hemolytic infection that causes cross reaction in cortical structures and basal ganglia due to molecular mimicry. Currently there is no definitive test for PANDAS,where diagnosis is primarly confirmed by identifying signs, symptoms and physical neurological examination.

Introduction

Post streptococcal movement disorder (PSMD) is a rare movement disorder following streptococcus infection. PSMD includes Sydenham's chorea, tics, dystonia, tremor, and stereotypy. One of the diagnoses included in the PSMD category is Pediatric Autoimmune Neuropsychiatric Disorders Associated with Streptococcal Infection (PANDAS).

The main symptoms experienced by PANDAS patients are obsessive-compulsive disorder and/or tic disorder and may be accompanied by attention deficit disorder, oppositional behaviour, emotional lability, and impulsivity after the patient experiences a streptococcus infection. Overall, the symptoms experienced by PANDAS patients are nonspecific, ranging from hyperactivity, chorea movements, loss of fine motor skills, and motor disorders resembling seizures. These symptoms also have a temporal relationship with the presence of infection, where more severe symptoms are found in patients with a longer duration of GHABS infection.

Comorbidities that can be caused by PANDAS are ADHD, Oppositional Defiant Disorder, and depression.[1,2]

Group A B-Hemolytic Streptococcus (GAHBS) is the main cause of bacterial pharyngitis. According to previous research, the incidence of PANDAS is 1 in 200 children. The age of the PANDAS patient population is 1-13 years with a sex ratio of 2:1, with a higher incidence in males. A previous study also found that the average age of PANDAS incidence is 6.3 years. The incidence at this age correlates with the frequency of GHABS infections occurring in the prepubertal age group.[1,2]

Pathogenesis of PANDAS has the same mechanism as Sydenham's chorea. When infection with streptococcus bacteria (Group A beta-hemolytic) occurs, an antibody response occurs that cross-reacts with cortical structures due to molecular mimicry. This cross-reaction causes the neurological symptoms found in PANDAS patients. Previous studies have found two immunological components that play a role in the pathophysiology of PANDAS, namely Lysoanglisodie GM1 and Calcium Modulin Kinase II. Lysoanglisoside GM1 is an antigen that causes a cross-reaction in monoclonal antibodies. Another pathophysiological mechanism of Lysoanglisode GM1 is to stop the reaction of autoantibodies in the putamen caudate nucleus, causing movement disorders and cognitive impairment. Another immune component that plays a role in the pathophysiology is CaMKII. The binding of tyrosine kinase is carried out by CaMKII, resulting in the conversion of tyrosine to dopamine, which affects patient movement. GHABS has the ability to activate CaMKII.[3]

The cortical structure affected by this autoimmune process is the basal ganglia. This structure plays a role in motor learning, motor control, behaviour, and executive function. When the physiological function of the basal ganglia is disrupted, symptoms such as movement disorders (tic disorder, chorea) and behavioural disorders such as OCD, impulsivity, and hyperactivity.[3]

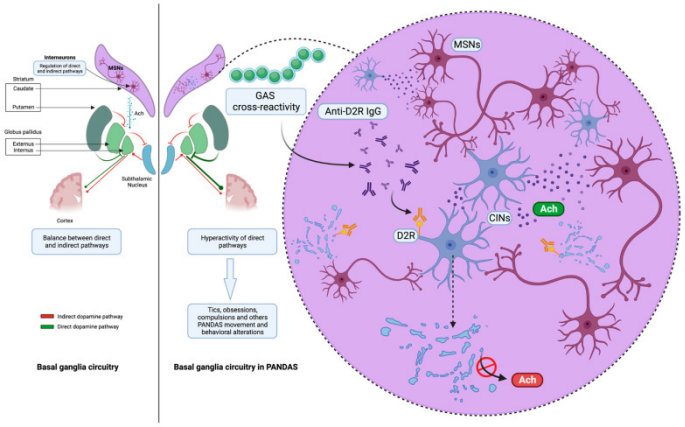

Figure 1. PANDAS Patophysiology[2]

Other types of PSMD that can be found are Pediatric Acute-onset Neuropsychiatric Syndrome (PANS), Childhood Acute Neuropsychiatric Symptoms (CANS), and Pediatric Infection-Triggered Autoimmune Neuropsychiatric Disorders(PITAND).[2,3]

Table 1. Diagnostic Criteria in PSMD

PANDAS	PANS
- OCD dan/atau Tic Disorder(DSM-IV) - Prepubertal onset of symptoms - Episodic Symptoms - Hubungan dengan infeksi GHABS(hasil kultur positif/ peningkatan titer antibodi GABHS) - Ditemukan Gejala Neurologis seperti hiperaktivitas motorik, tics atau chorea	- OCD present on onset or sudden food intake disorder - ≥ 2 Neurological symptoms: 1. Anxiety 2. Emotional lability and/or depression 3. Irritability, aggression or oppositional behavior 4. Behavioral Regression 5. Performance issues at school 6. Motoric or sensoric disturbance 7. Somatic symptoms such as sleep disturbance or enueresis 8. Symptoms are not caused by other diseases

CANS	PITAND
Acute onset of Symptoms Main Diagnostic Criteria: OCD Secondary Diagnostic Criteria : - Tics - Dysfagia - Hyperactivity - Anxiety - Psychosis - Emotional Lability - Growth Regression - Sensitivity towards sensory stimulus - Monophasic or polyphasic disease course	Pediatric Onset, lifelong OCD or tic disorder. Sudden onset with recurrent relapsing/remitting disease pattern - Symptom exacerbations that may last up to 4 weeks. - Neurological findings when patient during exacerbation of OCD and Tic disorder. - History of infection prior to symptoms - Patient did/did not experience significant symptoms between exacerbations of OCD/ tic disorder

The treatment of PANDAS consists of three main pillars: antibiotics, psychotherapy, and immunomodulatory drugs. Antibiotics are given to treat GHABS infection. The types of antibiotics used are beta-lactams such as azithromycin and clindamycin. Previous studies have shown that patients have excellent symptom resolution after antibiotic therapy. The use of antibiotics as prophylaxis can also be considered because reinfection with GHABS can re-trigger PANDAS symptoms in patients who are already asymptomatic. Other modalities that can be used to prevent infection besides antibiotics are tonsillectomy and/or adenoidectomy.[2,4]

Immunomodulatory therapy is given to reduce the severity of the patient's symptoms. The most commonly used immunomodulatory modality is corticosteroids, but other modalities can also be used such as IVIG and plasmapheresis. Previous research has found IVIG effectiveness of 45% and IVIG effectiveness of 56% in terms of symptom reduction. Other pharmacogenomic immunomodulatory therapies that can be used are rituximab and mycophenolate mofetil.[2,4]

Psychotherapeutic management of PSMD is cognitive behavioral therapy (CBT) used to treat tic disorders and OCD in patients. Selective Serotonin Reuptake Inhibitors are the first-line drugs used for OCD therapy in PANDAS patients. Both psychotherapeutic modalities need to be tailored and adjusted according to the patient's needs.[4]

Case Report

We report a 10-year-old female patient with the main complaint of involuntary movements in the trunk and upper and lower extremities in the past 2 months before the examination. The movement manifestations were complex and unusual tics: tonic-clonic movements in both upper and lower extremities, accompanied by back flexion such as opisthotonus, tongue fasciculation, and oculogyric tic. The duration of the movement was 5 minutes with 1-minute intervals without movement. During the movement, the patient could be questioned, was relevant, and remained oriented. The patient had a history of respiratory tract infection 2 weeks before the onset of the movement disorder. The patient also had a history of verruca vulgaris therapy surgery before the onset of symptoms.

On physical examination, the patient's weight was 27 kg, blood pressure 110/70 mmHg, pulse 72 x/min, respiratory rate 19 x/min, and temperature 36.4'C. The patient's consciousness was E4M6V5. The results of the patient's general status examination were within normal limits. In the supporting examination, the results of MRI and EEG were within normal limits. The ASTO examination showed positive results.

Therapy given to the patient:

- Methylprednisolone 1x800 mg -> taper off 4x125mg per day
- Ranitidine 3x30 mg
- Clonazepam 2x0.5 mg -> 1x0.5 mg
- Haloperidol 1mg - 0 - 0.5mg
- Valproic Acid 2x5 cc
- Ampicillin 4 x 750 mg -> switched to phenoxymethyl penicillin 3 x 500 mg after discharge.

Figure 2. Patient experiencing tonic clonic tic in both upper and lower extremities

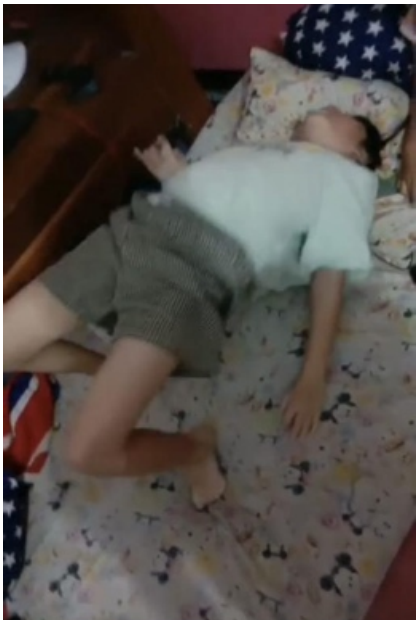

Figure 3. Patient experiencing opisthotonus like tic

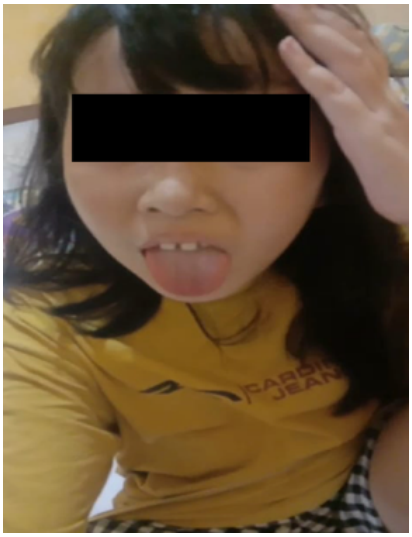

Figure 4. Patient experience tic in the for of tongue fasciculation.

Discussion

The diagnosis of PANDAS is established through the patient's clinical symptoms. There are five diagnostic criteria for PANDAS[5,6]:

- Presence of OCD and/or tic disorder
- Pediatric onset (age 3 years - puberty)
- Episodic severity of symptoms, acute onset with high severity
- Symptoms have a temporal relationship with group A beta-hemolytic streptococcus infection
- There are neurological symptoms such as motor hyperactivity, tics, or chorea.

The severity level in PANDAS patients has 3 levels[6]:

1. Mild Case
    - Symptoms are significant and interfere with activities at school/home.
    - Patients experience symptoms for a few hours a day.
2. Moderate Case
    - Symptoms are difficult and inhibit daily activities.
    - Patients experience symptoms 50-70% of their waking hours.
3. Severe Case
    - Symptoms are very difficult and life-threatening.
    - Patients experience symptoms 50-70% of their waking hours.

This patient has clinical signs that meet the diagnostic criteria for PANDAS. The main symptom in this patient is a movement disorder in the form of complex and unusual tics such as tonic-clonic movements of the upper and lower extremities, back flexion like opisthotonus, tongue fasciculation, and oculogyric tics. The patient's age (10 years) is also a population that fits the diagnostic criteria for PANDAS, which is 3 years to puberty. The characteristics of the symptoms experienced by the patient, where there is a duration of movement for 5 minutes with periods without movement, and the onset of symptoms, are included in the diagnostic criteria for an acute and episodic onset of the disease course. The patient's symptoms also have a temporal relationship where the onset of symptoms occurs after streptococcus bacterial infection. This temporal relationship is also a diagnostic criterion. This patient also has neurological symptoms, namely involuntary

movements in the form of tic disorder. The severity level experienced by this patient is moderate because the patient's movement disorder interferes with daily activities and is experienced approximately 50-70% of the waking hours. Currently, there are no supporting examinations that can be used to establish the diagnosis of PANDAS.[5,6]

The treatment given to this patient was antibiotics (ampicillin and phenoxy methyl penicillin), corticosteroids (methylprednisolone), and antipsychotic medication (clonazepam and haloperidol). The therapy given to this patient is in accordance with the three main modalities of PANDAS therapy that have been established in previous studies, namely antimicrobial therapy, immunomodulatory therapy, and psychotherapeutic therapy. The patient showed improvement after undergoing treatment until symptom-free. Patients can have a good prognosis with immediate therapy and prevention of recurrent GHABS infection. Although PANDAS is a rare disease, this diagnosis still needs to be considered in paediatric patients diagnosed with GHABS infection.[3]

Conclusion

PSMD is a spectrum of movement disorders that occur following streptococcus bacterial infection. A type of PSMD that is commonly found is PANDAS. Due to the high prevalence of GAHBS infection this can be the underlying etiology of OCD and tic disorders in the pediatric population. Currently there are no specific tests to confirm the diagnosis of PANDAS, where diagnosis can only be given through clinical examination and history of infection. Therefore

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