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Tourette Syndrome Associated to Streptococcal Infections in 14 Years Old Male

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Abstract: ***Background: Tic is one clinical finding in pediatric autoimmune neuropsychiatric disorders associated with streptococcal infections (PANDAS). Tourette syndrome is complex tic that consist of vocal and motor tic. Prevalence of Tourette approximately 5 per 10,000school-age children (0.05%) and PANDAS was 1% in children. Case Presentation Summary: A 14-year-old boy complained of involuntary movement with sudden jerky neck contraction and uncontrolled repeated blinking eyes for 5 years before admission and getting worse in few months. History of sore throat and fever about 4 months before tic occurred. Physical examination showed involuntary movement with motor ticon the neck and eyes and vocal tic with repeated coughing. Laboratory test revealed ASTO400IU/ml. Patient diagnosed with Tourette syndrome et causa PANDAS. Antibiotic prophylaxis was given with erythromycin 250 mg every 12 hours orally, prednisone 2mg/kg/day for 7 days, haloperidol 0.02 mg/kg per day and clonazepam 1 mg every 12 hours.The purpose of therapy was to control tourette. After two weeks of treatment symptom was decreased. Learning Point/ Discussion: We report a14-year-oldmale with Tourette syndrome and ASTO400IU/ml was confirmed as a diagnostic marker of the streptococcal infection. Pharmacological therapy for PANDAS involved eradication of streptococcal infection by using antibiotic erythromycin upto 5 years duration, anti-inflammation with prednisone, and treating involuntary movement haloperidol. Our case achieved recovery after 2 weeks of therapy.***

Keywords: ASTO, PANDAS, streptococcal infection

1. Introduction

The pediatric autoimmune neuropsychiatric disorders associated with streptococcal infections (PANDAS) refers to children with abrupt onset of tics and/or obsessive-compulsive disorder (OCD) associated with a recent group-A beta-hemolytic streptococcal (GABHS) infection.[1] Prevalence of Tourette approximately 5 per 10,000school-age children (0.05%) and PANDAS has prevalence 1% in children.[2]

Tics are defined as involuntary, sudden, rapid, recurrent, nonrhythmic movements (motor tics) and vocalizations (vocal or phonic tics).[3]The chronic presence at least two motor tics and one vocal tic since childhood is recognized as the key feature of Tourette's syndrome (TS).[3]The pathogenesis of PANDAS is thought to be triggered by streptococcal infections that influence basal ganglia function and trigger excessive activity of glutamate circuit that regulate tic.[1] Because of the prevalence of PANDAS was seldom and awareness of diagnosis is low so this report aims to provide the symptomology and diagnosis of PANDAS in children.

2. The Case

A 14-year-old boy present with sudden jerky neck contraction for 5 years. This condition repeated every 15 minutes in a day. This condition disappears if the patient was sleeping or concentrating like praying and getting worse when the patient feels stressed or depressed. In this last month, jerky neck contraction getting worse and become more frequent. This condition disturbance learning activities at school.

Patient experienced uncontrolled repeated blinking eyes. Blinking eye occur every 15-30 minutes per day. If this condition is withheld, the patients feel uncomfortable. Blinking eye movements disappear if the patient sleeping and get worse when patient stressed. Patients also often experience repeated coughing. Coughing starts almost simultaneously with the appearance of jerky neck straining and blinking eyes. Coughing was not accompanied by an itchy throat or phlegm. Coughing was not accompanied by shortness of breath. Coughing appears repeatedly every 15-20 minutes. Recurrent cough also increased in the last 1 month.

Patient has previous sore throat and fever about 4 months before tic. History of seizures, decreased consciousness was denied. The patient was never taken certain drugs or alcohol before this complaint first appeared.

Patient was with normal history of antenatal. The patient is the second child of two siblings. The patient's sister was normal. The patient's uncle experiences uncontrolled blinking eye movements but the frequency more seldom than patient. The patient had been treated by several doctors before such as adult neurologists, internal medicine but the complaints had not improved yet.

On physical examination, patient was alert with GCS $E_4V_5M_6$, heart rate was 74 beats/minute, blood pressure 110/60, respiratory rate 18 breaths/minute, axillary temperature was 36.6ºC. Head size was within normal limit. There is no strasbismus. Lung examination was normal. In cardiac examination, there is no ictus cordis seen and palpable withfirst and second heart sound was normal without murmur. On abdominal examination there is no hepatomegaly or splenomegaly and peristaltic sound was

normal. On neurologic examination,motor strength was 555 with normotonic and tropic on upper and lower limb. Physiologic reflex was normal and no patologic reflex in four extremities. There are motor tic noticed with neck jerking, and eyes blinking and also vocal tic as coughing. Yale Global Tic Severity Scale for motor tic was 11 (multiple tic 2, frequency 4, intensity 3, complexity 0, and interference 2), vocal tic was 10 (single tic 1, frequency 4, intensity 3, complexity 0, and interference 2), and impairment severity 10 and total score of motor tic, vocal tic and impairment was 31 classified as moderate tic severity. On laboratory examination revealed anti streptolysin O (ASTO) was 400 IU/ml.

Patient was diagnosed with Tourette's syndrome et causa Pediatric Autoimmune Neuropsychiatric Disorders associated with Streptococcal infections (PANDAS). Patient got therapy oral prednisone 2mg/kg/day for 7 days, haloperidol 0.02 mg/kg per day and clonazepam 1 mg every 12 hours oral and erythromycin 250 mg every 12 hours for three months. Two weeks after treated, all symptoms were improved. After two months therapy, patient got pyoderma on lower limb and ASTO titer evaluation showed increment to 800 IU/ml. In the same month, patient had history not consume medication for two weeks and tic manifestation getting worse. After patient continued the medication the symptom decreased in severity and resolved. Patient medication until now and was planned 5 years therapy of prophylactic antibiotic.

3. Discussion

Tourette's syndrome (TS) is voluntarily suppressible, urge-driven motor and vocal tics and repeated complex movements. Tics are defined as sudden, non-rhythmic, stereotyped motor movements or vocal productions that are performed repetitively. The prevalent and severity are more often in males than females, and often childhood-onset.[4]Current diagnostic criteria for Tourette's syndrome based on Diagnostic and statistical manual of mental disorders (DSM) V. Based on this criteria, there are at least two motor and one vocal tic, presence of tics for at least 12 months, onset before age 18 years, and tics not caused by the physiological effects of substances (such as stimulants) or other medical conditions.[3] **In this patient** there were two motor tic that manifest as sudden neck jerking and eye blinking and one vocal tic as coughing started when patient 9 years old. There is no history of substance and drug use before symptom onset. These conditions were appropriate for diagnostic of Tourette's syndrome.

The pediatric autoimmune neuropsychiatric disorders associated with streptococcal infections (PANDAS) refers to children with abrupt onset of tics and/or obsessive-compulsive symptoms (OCD) associated with a recent group-A beta-hemolytic streptococcal (GABHS) infection.[1] Based on Diagnostic and Statistical Manual of Mental disorder (DSM) IV, criteria diagnostic for PANDAS were:[1]

1) Presence of OCD and/or a tic disorder
   The patient must meet diagnostic criteria for OCD or a tic disorder.
2) Pediatric onset
   Symptoms of the disorder first become evident between 3 years of age and the beginning of puberty.
3) Episodic course of symptom severity
   Clinical course is characterized by the abrupt onset of symptoms or by dramatic symptom exacerbations. Often, the onset of a specific symptom exacerbation can be assigned to a particular day or week, at which time there is variety of severity of symptoms. Symptoms usually decrease significantly between episodes and occasionally resolve completely between exacerbations.
4) Association with Streptococcal infection
   Symptom exacerbations must be related to Streptococcal infection with positive throat culture and/or rising antistreptococcal antibody titers.
5) Association with neurological abnormalities
   During symptom exacerbations, patients will have abnormal results on neurological examination. Motoric hyperactivity and adventitious movements (including choreiform movements) are particularly common.

In this patient, fulfill diagnostic criteria for Tourette's syndrome, with onset of symptoms begin at 9 years old and become more evident at puberty period. The frequency and severity of symptom increased or decreased in particular day or week. This neurologic symptom was associated with Streptococcal infection with laboratory result revealed ASTO 400 IU/ml. All the sign and symptom fulfill diagnostic for PANDAS. To describe accuracy of Antistreptolysin O (ASTO)to detect Group A β-hemolytic Streptococcal Infection, we perform journal searching which concluded that ASTO has Sensitivity 75%, Specificity 84%, likelihood ratio for a positive test result 4.6, likelihood ratio for a negative test result 0.29, pretest probability 1% (0.01), posttest probability 12% (0.12).[5]

The pathogenesis of PANDAS is thought to be triggered by streptococcal infections. Specifically, antibodies raised in response to the infection of group A beta-hemolytic Streptococcus (GABHS) that cross-react with autoantigens in the basal ganglia and cortical structures and yield the motor and behavioral abnormalities.[4]GABHS antigens are mimic neural antigen in basal ganglia such as human neural dopamine receptor 1 and 2, lysoganglioside and tubulin. Furthermore, antibody that produced to GABHS antigens will also cross react to neuron antigen especially in basal ganglia.[6]In basal ganglia, there is specific circuits that control and select goal-directed motor, cognitive and motivational behavior. Furthermore, the circuits are involved in inhibitory control and habit formation.[4]The antibody stimulates hyperactivity effect of the circuit that control unvoluntary movement.[6]

Symptoms of PANDAS are hypothesized to result from immune dysfunction at multiple levels. Local dysfunction related to cross-reactive antibodies that recognize specific central nervous system (CNS) antigens and regional dysfunction related to inflammation within neuronal tissues in the basal ganglia and possibly vasculature of the basal ganglia and systemic abnormalities of cytokines or chemokines, with resultant disruption of the blood–brain barrier (BBB) and CNS functions. Corticosteroid use in this condition is still controversial. Some studies report significant improvement in patients receiving steroid, other

show deteriorations. Steroid can no longer be used long term due to its side effects. If clinical improvement after steroid administration occurs, then the diagnosis of immune system-based disease can be confirmed, which in this case immune-based therapy can be very beneficial. **In this case**, patient received corticosteroid prednisone therapy for 7days and showed improvements. To understand the effectiveness of corticosteroid in the treatment of PANDAS, a journal search was conducted that concluded corticosteroid can shorten the duration of PANDAS symptoms. Early corticosteroid administration results in better therapy response, similar to corticosteroid use in most inflammation-based diseases (asthma, jouvenile arthritis, etc).[7]

Therapy for PANDAS include pharmacological andnon-pharmacological (cognitive-behavioral therapy). Pharmacological therapy targeted for streptococcal eradication, treatment to improve tic or OCD and to treat neuro-inflammation. Streptococcal eradication therapy use antibiotic. Antibiotics prescribed for these subjects included penicillin, amoxicillin, clarithromycin, erythromycin, amoxicillin/clavulanate, azithromycin, clindamycin, and cefadroxil. The duration of antibiotic treatment ranged from brief courses (1 week) to long-term prophylaxis for up to 4 years.[8]Based on American Academy of Pediatrics reported a prophylactic antibiotic use for up to 5 years after the last episode of disease until the age of 21 years old, depending on which takes the longer time.[9]**This patient** was treated with antibiotic erythromycin for three months. On last follow up, tic symptom improved and all daily activity was back to normal.

Therapy for PANDAS also targeted for symptom relieve. Neuroleptic drug use for tic relieve is haloperidol. Many studies have investigated the efficacy of haloperidol, which can provide an estimated78-91% reduction in tics. This medication was still considered the most effective tic suppressants. This medication act as dopamine antagonize, through the blockade of type 2 dopamine receptors. The higher the potency of dopamine blockade, the more effective drug is in tic. However, these agents are also known to alter cholinergic, serotonergic, histaminergic and alpha-adrenergic transmission, thus leading to side effects.[10]Tounderstandtheeffectivenessof haloperidol in tic treatment, a journal review was conducted concluded that antipsychotic drugs and alpha-2agonists can improve the symptoms of tic significantly.[11]

The most common side effects associated with these drugs are relatively mild and include weight gain and drowsiness, although some patients may experience excessive sedation. The greatest concern relating to the use of neuroleptics is the potential for them to lead to hyperprolactinaemia, which is associated with amenorrhoea, galactorrhoea and gynaecomastia. Another side effect is extra pyramidal symptoms, such as dystonia, parkinsonism, akathisia and tardive dyskinesia.[10] **In this patient** was used haloperidol with dose 0.02 mg/kg per dayand clonazepam 1 mg every 12 hours oral. Tic was getting better after two weeks treatment without significant side effect.

4. Summary

A14-year-old boy complained of involuntary movement of with sudden jerky neck contraction and uncontrolled repeated blinking eyes for 5 years before admission and getting worse in few months. History of sore throat and fever about 4 months before tic occur. Physical examination showed involuntary movement with motor ticon the neck and eyes and vocal tic with repeated coughing. Laboratory test revealed ASTO400IU/ml. Patient diagnose with Tourette syndrome associated to PANDAS. We treated with erythromycin 250 mg every 12 hours orally, prednisone 2mg/kg/day for 7 days, haloperidol 0.02 mg/kg per day and clonazepam 1 mg every 12 hours. The involuntary movement decreased after treated for two weeks.

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