Case report

A case of pediatric autoimmune neuropsychiatric disorder associated with streptococcal infection

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ABSTRACT

Pediatric autoimmune neuropsychiatric disease associated with streptococcal infection (PANDAS), is a subtype of acute-onset obsessive-compulsive disorder (OCD) induced by an immunological reaction to group A streptococcal infection. These diseases may be worsen by an autoimmune response brought on by streptococcal infections. One of the recurring diseases linked to PANDAS is recurrent streptococcal tonsillitis. "Strep throat" (acute suppurative tonsillitis) is a tonsil infection typically caused by Group A Beta-Hemolytic Streptococci (GABHS) bacteria, often leading to intense throat pain, fever, and difficulty swallowing for a few days. Health care providers frequently use a rapid strep test to check the tonsils of patients experiencing a sore throat for GABHS, as untreated infections can lead to more severe health issues. Occasionally, strep throat can result in a body rash (known as scarlet fever) and can also lead to more severe health issues such as arthritis in children, rheumatic fever that can cause long-lasting heart problems, and post-streptococcal glomerulonephritis which may result in kidney failure. Here we present a case of 20-year-old male patient with PANDAS, who underwent tonsillectomy. The morbidity associated with this neuropsychiatric condition can be reduced with prompt management.

***Key words*:** Obsessive compulsive disorder, Tonsillectomy, Streptococcal infection

Pediatric autoimmune neuropsychiatric diseases associated with streptococcus (PANDAS), which explains a collection of illnesses, including scarlet fever and strep throat, that are believed to afflict certain children who have streptococcal infections. Although a direct correlation has not yet been shown, there have been some reports of tics, obsessive-compulsive behaviour, and other neurological and mental symptoms developing following PANDAS. Following an infection with Streptococcus pyogenes, children experience abrupt and typically substantial changes in personality, behaviour, and mobility. [1]

The signs and symptoms occur during a PANDAS episodes are Moodiness and irritability, Separation anxiety, ADHD (Attention Deficit Hyperactivity Disorder)symptoms, Sleep disturbances, Night-time bed wetting and/or day-time urinary frequency, Fine motor changes (writing), Joint pain, Trouble eating, Concentration difficulties and loss of academic abilities. Children may have tics, which are uncontrollable, abrupt motions or sounds that they repeatedly make. They could jerk their head or blink a lot. They could repeat sentences, growl, or continuously clear their throat. The child's immune system generates antibodies that specifically attack GABHS bacteria when they are infected. In PANDAS, it is thought that these antibodies also coincidentally target and cause inflammation in a region of the brain known as the basal ganglia. This region of the brain is responsible for refining deliberate muscle actions and managing behaviour within the realm of thinking and logic. If this area of the brain is affected, its performance decreases and changes, leading to specific involuntary actions and motions.

To determine whether the kid has PANDAS, which can resemble other diseases, a strep bacterial test or a history of the bacterium is required. The doctor should examine additional areas where strep tends to hide, such as the sinuses or child's genitalia and but if a throat swab or antibody test yields no results. Even if the child recovered, a blood test might reveal if they had a recent strep infection. If child does not or did not have strep throat, then they do not have PANDAS. However, their symptoms may still be a result of a malfunctioning immune system response. PANDAS is a member of a broader category of autoimmune illnesses impacting the brain known as pediatric acute-onset neuropsychiatric syndrome (PANS). The symptoms may be alike, but they could be caused by a different factor rather than strep. Physician might request blood tests or brain scans to determine if another infection or a different underlying cause is responsible for the symptoms.[2,3]

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Despite its rarity, some experts believe it may be responsible for 10% of childhood obsessive-compulsive disorder (OCD) and tic disorders. [4] It affects roughly 1 in 1000 children, and boys are three times more likely than girls to get it. Because most children have established streptococcus immunity by adolescence, it is considered a pre-pubertal condition. As a result, the onset is unlikely to occur again, while PANDAS symptoms may continue to appear on a regular basis.[5] The National Institute of Mental Health's (NIMH) criteria for PANDAS includes: [6]

1. Presence of tic disorder and/or OCD (obsessive compulsive disorder)
2. Prepubertal onset of neuropsychiatric symptoms
3. Abrupt onset and a course characterized by dramatic exacerbations
4. The onset or exacerbation is temporally related to group A beta haemolytic streptococci (GABHS) infection
5. Neurological abnormalities- hyperactivity, fidgetiness, restlessness or abnormal movements such as choreiform movements may be present during symptom exacerbation.

The principle evidence-based therapies for OCD are cognitive behaviour therapy (CBT), which includes exposure and response prevention (ERP), and selective serotonin reuptake inhibitors (SSRIs). [7] Antibiotics or tonsillectomy to treat and/or prevent GABHS infection are additional or alternative therapy options when PANDAS is suspected. [8] Therapeutic plasma exchange (TPE), intravenous immunoglobulin (IVIG), or anti-CD20 monoclonal antibodies (rituximab) have been used to suppress the immune system in patients with potential autoimmune-based OCD corticosteroids. [9] Nonsteroidal anti-inflammatory medicines (NSAIDs) have also been recommended to help with the psychiatric symptoms of PANDAS and PANS, which is in keeping with the autoimmune etiology explanation. [10]

CASE REPORT

A 20-year old male patient was admitted to neurological department, who had history of episodes of sudden staring with deviation of right eye to right side in 2002, when he was 2-year-old and was diagnosed as probable absence seizure though no treatment was started. While initially, these episodes were 1-2 per day, these increased to 5-10 episodes per day over a period of two years, and patient was put on valparin. He had history of aggressive behaviour, which would increase in presence of any infection (had two attacks of hand-foot-mouth disease <5-year age, croup at 6-year age) with EEG report of parieto-occipital spikes and MRI brain showing no significant abnormality, and he was diagnosed as having probable ADHD (Attention-Deficit/Hyperactivity Disorder). From 2006 onwards (6-year age), he started having behaviour disturbances with fluctuating mood, biting clothes, bruxism. He underwent squint surgery in 2008. Since 2010 (10-year age), he had significant worsening of scholastic performance, would drink milk excessively, developed slurred speech, memory issues and episodes of bed wetting.

Over the years, he developed abnormal eye movements, delayed speech and language and was diagnosed as regressive autism and homeopathic treatment was started. In 2014 (14-year age), he had increase in aggressive behaviour and was taken to USA for further management. In 2019, Cunningham panel- anti dopamine receptor D1 increased; anti-tubulin increased; anti-dopamine receptor D2 normal. He had received Rituximab, IV steroid, IV-Ig, Bortezomib. CSF was negative for IgLON 5 antibody, GFAP, GABA-B, NMDA Glutamate receptor antibody, CASPR 2, Protein 2, LGI 1, AMPA-1 & 2 antibodies. Lupus anticoagulant was negative. FDG-PET MRI whole body on 21th February 2021- hyper metabolism in bilateral striatal nuclei- consistent with limbic encephalitis. He was diagnosed as auto immune encephalitis- G6PD deficiency- seborrheic dermatitis- PANDAS (Pediatric Autoimmune Neuropsychiatric Disorder Associated with Streptococcal infection). He was on Tab.Clonidine 0.1 mg, Tab. Divalproex 250 mg, Tab. Risperidone 1 mg. He had received 9 doses of rituximab (last- 29th April 2021), 7 cycles of Bortezomib (last- 19th July 2021) and he was on regular IV Ig monthly (last- 1-3rd September 2021) and weekly IV methyl prednisolone.

Therapeutic plasma exchange is the primary treatment for severe and life-threatening PANDAS, and may be used alone or alongside IVIG, high-dose IV corticosteroids, and/or rituximab. Along with IVIG, patients were given preventive antibiotics to avoid worsening of symptoms triggered by infection in the future. They were also provided with typical psychiatric treatment, which involved utilizing anti-obsessional drugs and cognitive-behavioural therapy. In order to achieve the best relief from symptoms, a combination of immunomodulatory therapy, antibiotic prophylaxis, and targeted symptom treatments is essential.

Patient thus came to our neurology department for further evaluation on 7th September 2021. On examination, the patient was conscious and agitated, with bilateral plantar flexor response and no signs of neck rigidity. Routine investigation- vitamin B12-657, ammonia-42, vitamin D-70.04, TSH-3.15, C-reactive protein (CRP)- negative, Antistreptolysin O (ASO) titre- positive (215.07 IU/ml). Patient was managed with continuation of Tab.Resperidal 1 mg, Tab. Clonidine 0.1 mg, tab. Divalproex 250 mg. patient was discharged on 13th September 2021 with advice for OPD follow up and review with plan for FDG PET MRI and monthly IVIg. Patient was again admitted for IVIg therapy between 29th September to 4th October 2021 and discharged in stable condition and again admitted for monthly IVIg cycle (total 120g over 3 days) on 12th November 2021 and patient was managed with ongoing treatment and was discharged on 15th November 2021 with advice for OPD follow up and next IVIg after 6 weeks (2g/kg total dose, divided over 3 days).

On 7th December 2021, patient was admitted for tonsillectomy. During the admission, routine hematological and biochemical investigations were normal. Serum ASO (Antistreptolysin O) titre and CRP (C-reactive protein) were negative. Gram stain, fungal stain, AFB stain and stain for cryptosporidium and nocardia were negative from tonsillar pus. Serum EBV virus and HV virus RT PCR were negative. Aerobic culture from tonsillar pus show growth of alpha hemolytic streptococci, klebsiella, E.coli, rest fungal and AFB. Anerobic culture shows no growth. Serum TPO and anti-thyroid antibody was positive on background of T3-3.2, T4-1.44 and TSH-5.76.

Patient was managed with appropriate antibiotics, antipsychotics, thyroid replacement and other symptomatic and supportive treatment. On 29th December 2021, patient was again admitted for IVIg therapy. Immunoglobulin immunorel-10 10g (total 10 vials) thrice a day for 3 days were given. Serum TSH-1.06, T4-1.48, T3-3.5. Advised Tab.Erythrocin 250 mg twice a day to continue as streptococcal prophylaxis. After receiving the full course of IVIg therapy, the patient was discharged in a stable condition. Follow up advised after one month. Patient condition improved and no notable symptoms showed.

DISCUSSION

During childhood, tics and obsessive-compulsive disorders (OCD) are rather frequent. They affect 1% to 4% of the pediatric population and 2% to 3% of the pediatric population, respectively.[11] Swedo[12] discovered a subset of patients whose tics and/or obsessive-compulsive disorder worsened briefly following group A beta hemolytic Streptococcus infections. The acronym PANDAS has been coined to describe this illness.[12] Anxiety, emotional lability, focus issues, hyperactivity, and other symptoms are common in these patients.[13] Our patient had a background of autoimmune encephalitis following criterias of prepubertal onset of neuropsychiatric manifestations, vocal repetitive spells (tics disorder), temporal association between onset or exacerbation of symptoms and prior infection.

Orvidas et al[13] reported two clinical cases of two siblings who suffer from recurrent tonsillitis as well as the PANDAS syndrome. Due to repeated streptococcal pharyngitis, two siblings—one with a tic problem and the other with obsessive-compulsive disorder (OCD)—had tonsillectomy. Both patients showed notable improvement in their mental health conditions at the most recent follow-up appointment, which was held 11 months after surgery. Their neuropsychiatric problems resolved after their tonsillectomy.[13] Heubi et al[14] describe clinical improvement in two patients with OCD and tics who had recurrent tonsillitis. Two siblings who met the criteria for the diagnosis of PANDAS and had recurrent tonsillitis whose symptoms, which were linked to TS and OCD, were made worse by tonsil infections. According to the PANDAS diagnostic criteria, a patient must already had a neurological disorder, usually TS or OCD. Patients with problematic obsessions and compulsions were said to have OCD, here their tonsils were removed.[14]

Our patient also underwent tonsillectomy to prevent further throat infection. We presented this case to increase awareness of this disorder, which can lead to major declines in academic performance and social adjustment in prepubescent and early adolescent children. After taking antibiotics, some kid's condition improves fast, but if they have streptococcal infection again, their symptoms can reappear. The majority recover with few long-term problems. For others, it may develop into a persistent issue that need the occasional prescription of antibiotics to manage infections that might result in flare-ups. Some children may be unable to function in social or academic settings due to PANDAS symptoms. If left untreated, PANDAS symptoms might get worse and cause irreversible cognitive impairment, thus can develop into a chronic autoimmune disease in certain children.

CONCLUSION

Limited reports of PANDAS in India may stem from inadequate awareness and under-recognition among healthcare providers. In any child presenting with abrupt onset or exacerbation of tics, OCD or late onset of Attention-Deficit/Hyperactivity Disorder (ADHD), clinicians need to focus on the history of throat infection and evidence for GABHS infection. PANDAS is a condition characterized by episodic episodes that can resolve spontaneously; if the child is not in distress or facing disruptions in daily activities, observation may be enough. Early consideration of immunomodulatory therapy is recommended, as NSAIDs or a brief course of oral corticosteroids may be effective for symptom relief in new cases, while individuals with long-standing symptoms may need more intensive and prolonged immunotherapeutic treatments. A proper cross referral between the pediatricians and the psychiatrists can aid in minimizing and eliminating the morbidity and the impairment which are connected with this disease.

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