

February 2019

November Clinical Conversation: Understanding PANS and PANDAS

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Presented by Michele Casoli Reardon, MD, MCPAP Medical Director and Pediatric Liaison, MGH
for Children at North Shore Medical Center*

A child is happy and easygoing one day, then literally overnight refuses to eat, sleep alone, or go to school. He or she may have tics, difficulty sleeping and headaches. The sudden, dramatic onset of symptoms, particularly following an infectious disease, should alert pediatricians to a possible diagnosis of pediatric acute-onset neuropsychiatric syndrome (PANS) or pediatric autoimmune neuropsychiatric disorder associated with streptococcal infections (PANDAS).

With symptoms that resemble many neurological and psychiatric conditions, PANS and PANDAS are often misdiagnosed or overlooked by clinicians. They are relatively new diagnoses: While first reported in 1995, they have only received medical validation since 2012 and had treatment guidelines established in 2017.

At the MCPAP November Clinical Conversation, Michele Casoli Reardon, MD, MCPAP Medical Director and Pediatric Liaison, MGH for Children at North Shore Medical Center, discussed these conditions.

What are PANS and PANDAS?

There is a long, well-documented history of infectious diseases, such as syphilis and rheumatic fever, that spread to the brain, causing autoimmune neuropsychiatric disorders such as Sydenham chorea. PANS and PANDAS result from the cross-

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reactivity of antibodies in the basal ganglia, which includes the caudate, putamen, and globus pallidus in the cerebrum. The caudate nucleus is the source of obsessive thoughts and tics. The systemic abnormalities of cytokines



cause disruption in the blood brain barrier. While PANDAS is associated with a Group A streptococcal (GAS) infection, PANS is believed to be triggered by a variety of infections such as mycoplasma pneumonia, Lyme disease, HIV, herpes, and influenza. Evidence of post-infectious autoimmunity and/or neuroinflammation is found in more than 80 percent of PANS patients. Many patients also have a family history of an autoimmune disease, especially hypothyroidism.

Diagnosis

PANS Diagnostic Criteria

An abrupt onset of obsessive/compulsive disorder or a severely restricted food intake, typically within a 24- to 48-hour period, and at least two of the following symptoms:

- Obsessive anxiety, especially separation anxiety
- Emotional lability and/or depression
- Irritability, aggression and/or severe oppositional behaviors
- Decline in academic performance and attention
- Motor or sensory abnormalities – hypersensitivity to light and sounds, visual distortions, occasionally hallucinations
- Somatic signs – headaches, sleep disturbances, enuresis, or urinary frequency

Obsessions and compulsions can include fear of contamination by food, household cleaners, or germs, to name a few, fear of harming oneself or others, and ritualized behaviors. The child may have panic attacks, prolonged tantrums, hyperactivity, and restlessness.

PANDAS Diagnostic Criteria

As in PANS, PANDAS onset is abrupt and can include:

- OCD
- Tics, particularly multiple, complex, or unusual tics -- present in 30 percent of PANDAS patients as initial, presenting symptom which predicts more significant cognitive decline and eating issues
- An episodic (relapsing-remitting) course of symptom severity
- Pre-pubertal onset -- post-streptococcal reactions are rare after age 12

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- Association with a GAS infection which may have been asymptomatic and untreated or without pharyngitis (50 percent are undiagnosed)
- Neuropsychiatric symptoms similar to PANS
- Neurological abnormalities – which are reflected on neurological examinations

PANS and PANDAS are more prevalent in boys and are believed to account for 30 percent of pediatric OCD. The clinical picture is variable and ranges from mild to severe illness. Initial NIMH studies suggested a two- to three-year course, but it may be longer.

Diagnostic Guidelines

PANS and PANDAS are diagnoses of exclusion based on clinical presentation. To establish that they are the correct diagnosis, conduct a comprehensive evaluation, including:

- A complete medical and psychiatric history
- Physical examination
- Laboratory tests to detect any prior or current infection, such as GAS, mycoplasma pneumonia, Lyme, herpes
- Paraclinical tests such as MRI, electrocardiogram, electroencephalography, if indicated

It is important to rule out other neurological or medical disorders, such as Sydenham chorea and autoimmune encephalitis, which require different treatments. PANS and PANDAS are sometimes misdiagnosed as

OCD, Tourette's syndrome, autism spectrum disorder (ASD), ADHD, anorexia, and other psychiatric disorders. Comorbidity with ADHD, particularly in young children, can complicate the diagnosis. The presence of obsessive rituals and interests, rigidity around routines, and impaired eye contact may be confused with ASD in young children.

“Pediatricians should consider the possibility of PANS and PANDAS for any child who presents with sudden changes in behavior or mood, especially when there is a family history of autoimmune disorders,” advises Dr. Casoli Reardon.

Treatment

Pediatricians are in the best position to care for and treat children with mild to moderate PANS/PANDAS, according to Dr. Casoli Reardon.



Treatment for PANS/PANDAS includes three areas:

1. Antibiotics – First-line treatment is a two-week course of antibiotics which can sometimes bring about complete symptom remission. Options include Amoxil, Augmentin, Cephalosporin, and Azithromycin. If the first course isn't effective, a second alternative course is

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needed.

2. Immune therapies – Used when there is clear evidence of neuroinflammation or post-infectious autoimmunity. Options can include NSAIDs (first-line) and oral corticosteroids. In moderate to severe cases, intravenous immunoglobulin (IVG) may be used.
3. Symptomatic treatment – SRIs for depression and OCD in older children (children with these syndromes are more sensitive to these medications, so start at a low dose). Benadryl or Clonidine can be used for sleep disturbances. Atypical neuroleptics or mood stabilizers can be used for lability, aggression, and self-harm. Alpha-adrenergic medications can be used for tics and hyperarousal.

When a child presents with hallucinations, school refusal, thoughts of self-harm, and significant mood lability with aggression, Dr. Casoli Reardon suggests an MCPAP consultation with a child psychiatrist.

Other treatments

Cognitive exposure relapse preventive therapy is recommended by Dr. Casoli Reardon for all children and families. Provides education, coping skills for children, and guidance for parents in dealing with symptoms, especially how to avoid reinforcing rituals and obsessions.

Tonsillectomy – not studied but case reports show dramatic improvement or remission in some patients

Prophylaxis – Patients with recurrent episodes can have daily prophylaxis with NSAIDs and prophylactic antibiotics Zithromax, Ceftriaxone, or Augmentin during the school year when they are more vulnerable to infection.

Case examples

A nine-year-old girl presents with increasing agitation, labile, and anxious behaviors with panic-like symptoms, refusal to eat, and weight loss due to obsessive fear of vomiting. Her symptoms appeared in June after a bout of sinusitis, then improved, then recurred and worsened in August when she had a “viral like” illness. She is hospitalized for depression and the desire to harm herself. She is placed on Zoloft, Zyprexa, and Clonidine but continues to struggle.



Referred to North Shore Medical Center for outpatient follow up, she is diagnosed with PANDAS and started on Zithromax, which isn't effective, then Augmentin and Aleve.

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Her behavior and mood improve and she gains weight and is able to transition back to school.

A 10-year-old boy with an ASD diagnosis presents with aggression, agitation and hyperactivity. He hits his father, has vocal tics, and crawls on the floor during the exam. He also has secondary enuresis and encopresis. His parents report a similar history of behavioral dysregulation and intermittent obsessive fears since early childhood.

After positive laboratory results, he is treated with a course of antibiotics and NSAIDs, and, after a diagnosis of ADHD, he is also placed on stimulants. His symptoms resolve.

Supporting children and families

While having PANS or PANDAS is distressing for children, it is even more upsetting for parents, who are often in a state of desperation from trying to help their child without success. Having their child diagnosed helps along with attending cognitive therapy sessions to learn how to cope with the child's behavior. "Dealing with the family is very important," says Dr. Casoli Reardon.

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Resources

The following provide comprehensive information about PANS/PANDAS:

- PANDAS Physician Network, www.pandasppn.org, provides support, guidelines and current research for physicians.
- For parents, www.pandasnetwork.org, provides local chapters, resources, and support information.
- Swedo, Frankovich, Murphy, "Overview of Treatment of Pediatric Acute-Onset Neuropsychiatric Syndrome." *Journal of Child and Adolescent Psychopharmacology*, Sept. 2017, Vol. 27, No. 7. pp.1-6.
- Thienemann et al., "Clinical Management of Pediatric Acute-Onset Neuropsychiatric Syndrome: Part I-Psychiatric and Behavioral Interventions." *Journal of Child and Adolescent Psychopharmacology*, Sept. 2017, Vol. 27, No. 7. pp. 1-13.
- Frankovich et al. "Clinical Management of Pediatric Acute-Onset Neuropsychiatric Syndrome: Part II- use of Immunomodulatory Therapies." *Journal of Child and Adolescent Psychopharmacology*, Sept. 2017, Vol. 27, No. 7, pp. 1-45.
- Cooperstock et al. "Clinical Management of Pediatric Acute-Onset Neuropsychiatric Syndrome: Part III- Treatment and Prevention of Infections." *Journal of Child and Adolescent Psychopharmacology*, Sept. 2018, Vol. 27, No. 7, pp. 1-23.
- Rajor, AD et al, "Pediatric Autoimmune Neuropsychiatric Disorders Associated with Strep: An Indication for Tonsillectomy. A Review of the Literature." *International Journal of Otolaryngology*, Feb. 21, 2018.

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“As the family’s lifeline, the pediatrician plays the most important role in supporting parents and reassuring them that things will get better.”

Children usually rebound well following treatment but parents never forget the experience and may be traumatized, reports Dr. Casoli Reardon.



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**DMH Services for Kids, Changes
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