Is it PANDAS? How to confirm the sore throat/OCD connection

Antibiotics are indicated in only a minority of cases

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John, age 6, presented for psychiatric evaluation with acute, incapacitating obsessive-compulsive symptoms. For 4 weeks he washed his hands compulsively and had pervasive obsessions about death by choking.

These symptoms had suddenly worsened over 2 days. At first, he washed his hands more than 35 times per day in rituals lasting several minutes each. Then, within 2 weeks, John’s handwashing spontaneously decreased, but his choking fears dramatically increased. He refused all solid foods and continuously sought reassurance from his parents that he would not choke or die.

Approximately 1 week before these symptoms began, John had a sore throat and tested positive via throat culture for group A beta-hemolytic streptococcal infection (GABHS).

continued
few controlled studies have examined treatment response
• using antibiotics and immunotherapies to treat or prevent PANDAS symptoms remains controversial because of unproven efficacy and potential adverse effects.

To help you diagnose and treat patients with suspected PANDAS, this article examines the limited evidence for the disorder, discusses diagnostic guidelines, and reviews preliminary indications for behavioral and medical treatments.

**CASE REPORT CONTINUED: PANDAS CLUES**

John’s sudden-onset compulsive behaviors and obsessive thoughts exemplify the rapid symptom onset often seen in children with PANDAS. His medical records showed a temporal relationship between his streptococcal infection and symptom exacerbations, which his parents confirmed. On examination, we noted choreiform movements when we asked John to extend his hands in a supinated position.

Because this was John’s first documented presentation of PANDAS-like symptoms, an additional episode would provide more convincing support for classifying his OCD as the PANDAS subtype.

**DIAGNOSTIC CRITERIA**

National Institute of Mental Health (NIMH) diagnostic guidelines for PANDAS, initially proposed as working guidelines by Swedo and colleagues, are listed in Table 1, page 39.

Time between GABHS infection and symptom onset varies, but post-streptococcal diseases generally emerge after a few days to several weeks. Because this latent period makes retrospective assessment difficult, NIMH guidelines require a prospective link between GABHS infection and at least two OCD/tic symptom episodes. These additional criteria are necessary continued on page 39
to avoid misdiagnosing PANDAS in cases when the GABHS infection/OCD connection is spurious.

PROSPECTIVE DIAGNOSIS

Neuropsychiatric symptoms. Early PANDAS symptoms are often similar to those of pediatric OCD and tic disorders (Table 2, page 40). Notable differences include:

- Sudden onset of obsessive-compulsive or tic behaviors shortly after GABHS infection, as opposed to OCD’s typical insidious course.
- Prepubertal onset (average age 7, as with Tourette’s syndrome7,8), compared with average age 10 of childhood OCD.12

Other psychiatric symptoms frequently reported in PANDAS patients include separation anxiety, hyperactivity, inattention, and emotional lability.4 Some researchers, therefore, suggest

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Table 1

Guidelines for PANDAS diagnosis

<table>
<thead>
<tr>
<th>Presence of obsessive-compulsive disorder and/or tic disorder</th>
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<tbody>
<tr>
<td>Pediatric symptom onset (age 3 years to puberty)</td>
</tr>
<tr>
<td>Episodic course of symptom severity</td>
</tr>
<tr>
<td>Prospectively established association between group A beta-hemolytic streptococcal infection (GABHS)—as shown by positive throat culture and/or elevated anti-GABHS antibody titers and at least 2 separate OCD/tic symptom episodes</td>
</tr>
<tr>
<td>Association with neurologic abnormalities (motoric hyperactivity or adventitious movements, such as choreiform movements)</td>
</tr>
</tbody>
</table>

PANDAS: pediatric autoimmune neuropsychiatric disorders associated with streptococcus
Source: References 7, 8, and 11
the PANDAS syndrome should include primary diagnosis of late-onset attention-deficit/ hyperactivity disorder and age-inappropriate separation anxiety disorders.8,13

Compulsions reported in PANDAS include germ-related behaviors such as hand washing, hoarding, and excessive toilet hygiene rituals. Most studies show consistent gender differences, with more washing behaviors by girls and more checking behaviors, aggression, and tics among boys.13

**Recurrences.** PANDAS has an episodic course, and approximately 50% of patients experience recurrences.13 Whether PANDAS remits completely, becomes dormant when neuropsychiatric symptoms are waning, or consistently progresses to a more chronic illness is unclear.

Because young children diagnosed with PANDAS often have repeated, frequent GABHS infections,2 give careful attention to:

- unexplained abdominal pain accompanied by fever
- history of scarlet fever
- brief episodes of tics, OCD, or compulsive urination that remitted
- illness accompanied by sudden onset of OCD or tic-like behaviors
- history of sore throats not severe enough to seek medical attention

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<table>
<thead>
<tr>
<th>Characteristic</th>
<th>OCD</th>
<th>Tourette’s/tic disorders</th>
<th>PANDAS</th>
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<tbody>
<tr>
<td><strong>Typical age of onset</strong></td>
<td>10 years</td>
<td>7 years</td>
<td>7 years</td>
</tr>
<tr>
<td><strong>Gender relatedness</strong></td>
<td>Slightly higher prevalence in boys than girls before age 15; female-to-male ratio increases after puberty</td>
<td>2:1 male-to-female ratio</td>
<td>5:1 male-to-female ratio before age 8; thereafter, boys slightly outnumber girls</td>
</tr>
<tr>
<td><strong>Course</strong></td>
<td>Typically unremitting, though some episodic cases reported</td>
<td>Peak severity at age 10; 50% of cases remit by late teens</td>
<td>Episodic or sawtooth course; long-term prognosis unknown</td>
</tr>
<tr>
<td><strong>Involvement of basal ganglia</strong></td>
<td>Strong evidence</td>
<td>Strong evidence</td>
<td>Good evidence</td>
</tr>
<tr>
<td><strong>GABHS trigger</strong></td>
<td>Reported; cause uncertain</td>
<td>Reported in some cases; cause uncertain</td>
<td>Proposed association</td>
</tr>
<tr>
<td><strong>Neurologic findings</strong></td>
<td>Increased findings of NSS, including choreiform movements</td>
<td>Increased findings of NSS, including choreiform movements</td>
<td>Choreiform movements</td>
</tr>
</tbody>
</table>

GABHS: group A beta-hemolytic streptococcal infection
NSS: neurologic soft signs
OCD: obsessive-compulsive disorder
PANDAS: pediatric autoimmune neuropsychiatric disorders associated with streptococcus
• dramatic improvement in behavior/neuropsychiatric symptoms following standard antibiotic therapy for unrelated infection.

WEIGHING TREATMENT OPTIONS

**Antibiotics.** Antibiotic treatment of GABHS infection has been thoroughly studied among patients with rheumatic fever. American Heart Association guidelines for preventing rheumatic fever after GABHS infection recommend oral penicillin, 250 mg bid. Studies also indicate that using azithromycin, 500 mg once weekly, can protect against GABHS infection but may also increase resistance to macrolide antibiotics.

Because antibiotic prophylaxis for GABHS infection is effective for rheumatic fever, some researchers have hypothesized that similar treatment would reduce neuropsychiatric symptoms in PANDAS patients.

In a double-blind, randomized, controlled trial, Snider et al found significant decreases in GABHS infection and neuropsychiatric symptoms in 23 PANDAS patients who took penicillin (250 mg bid) or azithromycin (250 mg bid on one day of the week) for 12 months.

An earlier study using penicillin for PANDAS prophylaxis was inconclusive. Its design limited more-definitive conclusions by allowing a high rate of antibiotic use during the placebo phase.

An uncontrolled prospective study by Murphy et al documented rapid resolution of primary OCD, tic, and anxiety symptoms after appropriate antibiotic treatment in 12 children with PANDAS. Obsessive-compulsive symptoms remitted 5 to 21 days after patients received penicillin, amoxicillin/clavulanate potassium, or a cephalosporin. Symptoms resolved much more quickly than non-PANDAS obsessive-compulsive and tic disorders usually remit with cognitive-behavioral, habit reversal, and/or drug treatment. One-half of patients had at least one OCD recurrence, all documented as GABHS-positive with throat culture or rapid antigen-detection assay.

**Recommendation.** Obtain a GABHS culture if a child presents with sudden-onset OCD. If positive, treat with a standard course of antibiotics. Caution is strongly recommended when using antibiotics in children, as antibiotic-resistant organisms may develop. Collaborate with the child’s pediatrician to ensure that strep infections are treated consistently.

CASE CONTINUED: USING CBT FOR PANDAS

Giving John antibiotics when he had the sore throat might have been a rational choice to manage acute OCD symptoms. However, the scant literature on antibiotic prophylaxis for PANDAS subtype OCD led us to also consider cognitive-behavioral therapy (CBT).

CBT alone or with a selective serotonin reuptake inhibitor (SSRI) is first-line therapy for pediatric OCD. We hypothesized, therefore, that CBT might also be useful in PANDAS and provided John with five CBT sessions within 1 week, without giving an antibiotic or other medication. [See our study for therapy details.]

At baseline, John’s score on the Children’s Yale-Brown Obsessive-Compulsive Scale (CY-BOCS) was 34, indicating severe OCD symptoms, and his score on the Anxiety/Depression subscale of the Child Behavior Checklist (CBCL) was elevated (t = 66). After five CBT sessions, John’s CY-BOCS score decreased by 75% to 8 and his CBCL Anxiety/Depression score decreased into the average range (t = 50).

Given PANDAS’ fluctuating course, his symptoms could have remitted spontaneously. His symptoms remained in remission 6 months later.
As stated, CBT alone or with an SSRI is first-line therapy for pediatric OCD, and CBT alone or with an SSRI reduces pediatric OCD symptoms more effectively than antidepressants alone. Because no published reports of SSRI use in PANDAS exist, we recommend treating a child with PANDAS as you would any child presenting with OCD and tics:

- **For milder cases** with recent onset, begin with clinical monitoring for GABHS, without using SSRIs or antibiotics. Early CBT may prevent symptom worsening.
- **For more severe** cases of longer duration, continue with CBT, then consider adding an SSRI.

When using SSRIs in pediatric patients, be mindful of recent literature on increased suicidality in children and adolescents taking these antidepressants. Use SSRIs judiciously, monitor dosages closely, and watch for suicidal thoughts.

**Immunomodulatory therapies?** Immunomodulatory therapies such as IV immunoglobulin (IVIG) and plasma exchange are not appropriate for refractory OCD or tic cases that have no clear GABHS association and a relapsing/remitting course. No studies support using immunomodulatory agents in disorders without an immune-mediated cause.

You might consider these therapies for severe, clearly established PANDAS only when less-invasive treatments (antibiotics, standard OCD therapies) have been ineffective and then only under research protocols and by physicians experienced in giving them.

Immunomodulatory therapies interrupt autoantibodies’ actions on the CNS and have shown moderate (40% to 50%) symptom reduction in some CNS diseases. In the NIMH trial, plasma exchange was better tolerated than IVIG and provided greater symptom relief. However, at least one

Box 2

**Recommended guidelines for treating PANDAS with antibiotics**

**Assess for GABHS infection** in young children with abrupt-onset, obsessive-compulsive/tic-like behaviors (suspected PANDAS), using a 48-hour throat culture. If positive, promptly give a 10-day course of antibiotics effective for acute GABHS treatment (penicillins, cephalosporins, azithromycin).

**Attempt to document** a preceding GABHS infection if neuropsychiatric symptoms began abruptly 4 to 6 weeks ago. Perform a 48-hour throat culture and a blood test for antistreptococcal antibody titers (ASO and anti-DNase B). Do not give antibiotics unless GABHS culture is positive.

A rising titer 4 to 6 weeks later would suggest a recent infection. A single elevated titer does not adequately support a recent strep infection, as some individuals have elevated titers 6 months or longer after GABHS infection.

**Consider prospective assessment** for GABHS infections in children with episodic symptoms. Obtain throat cultures when neuropsychiatric symptoms return/exacerbate, as even untreated strep infections are usually self-limited.

**Reserve antibiotic prophylaxis** for use under research protocols and based on solid evidence of PANDAS diagnosis.

**Use immunomodulatory therapies** under research protocols and only for children with acute, severe symptoms who fit the PANDAS designation.

Source: Reference 24.
study has shown plasma exchange to be ineffective for chronic OCD.23

**USING ANTIBIOTICS FOR PANDAS**

Snider and Swedo24 recommend guidelines for treating PANDAS, based on risks of using antibiotics in children, research and clinical experience, and American Academy of Child and Adolescent Psychiatry practice parameters (Box 2, page 42).

Elevated streptococcal titers are common in the community population25 and are not necessarily diagnostic of PANDAS. Thus, it is important to demonstrate a change in titer levels (such as a 4-fold dilution rise in antistreptococcal antibody titers 4 to 6 weeks after infection).

In patients with new-onset OCD/tics or recent symptom exacerbation, a positive throat culture provides support that symptoms were triggered by subclinical GABHS infection but does not rule out the possibility that the child is a GABHS carrier.

After streptococcal infections, titers may remain elevated for 6 months to 1 year. Murphy et al25 found persistent elevations in one or more strep titers in patients with dramatically fluctuating neuropsychiatric symptoms, compared with those whose course was inconsistent with PANDAS. It is unclear if these children had undetected, frequent GABHS infections or the elevated titers reflect a chronic immune activation to GABHS.

**References**


PANDAS is characterized by abrupt onset/exacerbation of neuropsychiatric symptoms following GABHS infection. Consider CBT, with or without SSRIs, as part of initial treatment. In patients with documented GABHS, antimicrobial treatment by standard clinical guidelines is most appropriate. Immunomodulatory therapies are rarely appropriate.

Related resources

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