PANDAS With Catatonia: A Case Report. Therapeutic Response to Lorazepam and Plasmapheresis

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ABSTRACT

This is a report of an 11-year-old, prepubertal boy with acute-onset urinary urgency and frequency, obsessions and compulsions related to urination, severe mood lability, inattention, impulsivity, hyperactivity, and intermittent periods of immobilization. Fever, cough, otitis, and sinusitis preceded neuropsychiatric symptoms. Antistreptolysin O and DNAse B antibody titers were elevated, and magnetic resonance imaging revealed bilateral diffuse caudate nuclei swelling. Plasmapheresis resulted in significant and rapid clinical improvement of obsessive-compulsive disorder symptoms and a simultaneous decrease in basal ganglia swelling, consistent with an immune-mediated pathophysiological process involving group A β-hemolytic streptococci. Hyperactivity, impulsivity, and inattention improved with lorazepam, suggesting that the attention-deficit/hyperactivity disorder symptoms could be manifestations of catatonia. *J. Am. Acad. Child Adolesc. Psychiatry,* 2005;44(11):1145–1150. **Key Words:** PANDAS, catatonia, obsessive-compulsive disorder, attention-deficit/hyperactivity disorder, lorazepam, plasmapheresis, magnetic resonance imaging, basal ganglia.

Obsessive-compulsive disorder (OCD) with a unique clinical course is identified by the acronym PANDAS (pediatric autoimmune neuropsychiatric disorders associated with streptococcal infections; Swedo et al., 1998). Five criteria define PANDAS: (1) the presence of OCD and/or tic disorder, (2) prepubertal onset; (3) episodic course characterized by acute, severe onset, and dramatic symptom exacerbations; (4) adventitious movements (choreiform) present during the symptom exacerbation; (5) temporal association between group A β-hemolytic streptococcal infection and onset or exacerbation of symptoms (Swedo et al., 1998).

Additional neuropsychiatric conditions reported in PANDAS include mood lability, attention-deficit/hyperactivity disorder (ADHD), overanxious disorder, separation anxiety, tactile/sensory defensiveness, and enuresis (Perlmutter et al., 1998, 1999; Swedo et al., 1998). Catatonia, a nonspecific syndrome not previously described in PANDAS, is characterized by affective (intense and uncontrollable emotions), behavioral (perseverations, stereotypies), and motoric symptoms (immobility, posturing, or excessive purposeless movements; Gelenberg, 1976; Northoff, 2002). This state of hyperactivity could be misinterpreted as ADHD. Lorazepam, an effective treatment in 60% to 80% of cases (Bush et al., 1996; Northoff et al., 1995) potentiates γ-aminobutyric acid A receptors, which are thought to be decreased in catatonia (Northoff et al., 1999).

CASE HISTORY

An 11-year-old boy developed fever (103°F), cough, and otitis. One week after onset of symptoms, he was

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hospitalized because of increased sleepiness, atypical behavior (curling up with a blanket on the dog cushion), intermittent periods of decreased speech, difficulty speaking, staring episodes, tearfulness, and a constant, subjective need to urinate even when the bladder was empty. Sinusitis, revealed by computed tomography (CT), was treated with Augmentin. Three additional hospitalizations occurred in the following 2 weeks to evaluate the incessant need to void. Laboratory tests, abdominal CT scan, obstruction series, bladder scan, and sonogram were normal.

The patient was adopted at 2 days of age. His psychiatric history, with the exception of ADHD symptoms (five inattentive, two impulsive, and two hyperactive), was essentially negative. The biological family history was unavailable. Medical history was significant for beesting allergy, occasional otitis media, and a single seizure after his measles, mumps, and rubella vaccination at 15 months of age (EEG at that time was normal). Migraine headaches, diagnosed at age 7, had decreased in frequency from four times per year to once per year.

At the time of the fourth hospitalization, 21 days after the onset of symptoms, physical examination was unremarkable. Mental status examination showed a very restless 11-year-old boy who was constantly moving from place to place. He was impulsive, unable to focus his attention, and distracted by minimal stimuli. During several brief periods, he stared and became immobilized, maintaining his limb position in mid-motion. His cognition, comprehension, and receptive language were always intact. Expressive language was difficult, with decreased amount of speech. His voice was squeaky, thin, and barely understandable. At times, he used gestures (thumb up or down) to answer questions. His mood was markedly labile, with unprovoked brief crying spells immediately followed by unexplained calmness. He frequently reported the need to void and needed continual redirection not to constantly use the bathroom. There was no evidence of psychosis.

On a parent-structured interview (Schedule for Affective Disorders and Schizophrenia for School-Age Children (K-SADS; Ambrosini, 2000), he met criteria for ADHD (symptom count on K-SADS: nine inattentive, five impulsive, and four hyperactive symptoms) and OCD. On the Children's Yale-Brown Obsessive-Compulsive Scale (Scahill et al., 1997), he scored 34 out of 40, significant for OCD. The National Institute of Mental Health (NIMH) emotional lability scale showed a score of 4 (0 indicating no irritability and 4, extreme irritability; Perlmutter et al., 1999).

Normal laboratory studies included complete blood count with differential, erythrocyte sedimentation rate, C-reactive protein, hepatic and thyroid function tests, calcium, magnesium, phosphorus, heavy metal screen, toxoplasma immunoglobulin M (IgM), Lyme enzyme immunofluorescence assay IgG and IgM, Epstein-Barr and cytomegalovirus titers, and urine toxicology. The antinuclear antibody titer was elevated at 1:640 (normal 1:20), with a homogeneous pattern suggestive of PANDAS. Serum ammonia was elevated at 67.2 (normal 9–33 μmol/L). Urinalysis showed trace protein. Cerebrospinal fluid (CSF) had trace white blood cells but was colorless and clear; Venereal Disease Research Laboratory (VDRL) and herpes simplex virus were negative; and bacterial, viral, and fungal cultures had no growth. CSF and serum electrophoresis patterns were identical. Electrocardiogram and EEG were unremarkable. Urine copper and ceruloplasmin were within normal limits, and ophthalmological examination was negative for Kaiser-Fleischer rings, ruling out Wilson's disease.

Twenty-three days after onset of symptoms, antistreptolysin O (ASO) and DNAase B antibodies were 282 (reference 0–240 IU/mL) and 1:680 (reference range 1:170), respectively. Throat culture was negative. Twenty-one days after symptom onset, the first magnetic resonance imaging (MRI) showed significant swelling of both putamina and caudate nuclei, with increased signal intensity on T1-weighted images and on axial fluid-attenuated inversion recovery (FLAIR). The remainder of the brain was normal (Table 1, Fig. 1A and B). MRI before gadolinium injection included sagittal, axial, coronal T1-weighted images, and FLAIR images. After gadolinium injection, axial, coronal, and sagittal T1-weighted images as well as axial diffusion weighted images were performed. FLAIR was used for volumetric measurement, the volumes calculated from all axial images with abnormal signal in the basal ganglia. These were added together in a volume and cubic centimeters calculated. FLAIR uses an inversion pulse to null the signal of gross CSF, such as is found in the ventricles and sulci, so that only the abnormal increased water content that affects the tissue is seen as high signal intensity. This allows the calculation of the volume of affected tissue. In our patient, diffusion imaging indicated rapid movement of water within the