Objectives

• Learn the diagnostic criteria of Pediatric Autoimmune Neuropsychiatric Disorder Associated with Streptococcal infections (PANDAS)

• Review the proposed pathophysiology and clinical course of PANDAS

• Briefly discuss treatment of PANDAS
Our Patient

- DM initially presented to the PCP in 2008 at the age of 10 with “attention problems” in school and severe mood swings that “appeared overnight.”

- Previously straight A student

- No previous attention problems noted by the teachers.

- No Meds / NKDA
History:

- History of multiple documented strep pharyngitis infections
  - ~2-5 illness involving a sore throat per year

- Most recent strep infection one month prior
  - Given antibiotics

- The pediatrician recommended observation

- Attention problems and mood swings resolved over the next few months
Progression of Illness

- PCP a few months later
  - Return of vocal tics
  - “Fits of rage”
  - Noticed suddenly, 1-2 days

- Sore throat, fever, myalgia one week prior

- Rapid strep positive with elevated ASO titers

- Given Amoxicillin x 10 days
  - Vocal tics gradually resolved in next few months
Timeline:

- Recurrence of vocal tics during each recurrence of strep throat
  - strep throat infection about every 4-8 weeks over the next 8-10 months

- Vocal tics during “remissions” between episodes became more prominent

- Referral to ENT
  - Performed tonsillectomy
Referrals:

**Allergy/Immunology Labs:**
- IgGAME
  - Normal
- Pneumococcal antibodies
  - 12/14 protective
- ASO titers
  - Elevated
- Streptozyme titers
  - Positive
- Anti-DNAse B
  - Negative

**Psychiatry:**
- Medical management for tics → **Buspar**
- Vocal tics improved
  - Not interfering with daily activities
- Continued to have increased vocal tics with occurrence of strep throat
Patient diagnosed with PANDAS
What is PANDAS?

• **Pediatric Autoimmune Neuropsychiatric Disorder Associated with Streptococcal infections**

• Earliest reported cases by Dr. Laurence Selling in 1929 describing 3 cases of a potential correlation between the onset of tics and sinusitis

• First officially reported by Swedo et al in 1998 in the American Journal of Psychiatry
  ▫ Retrospective study evaluating 50 cases of children meeting the initial **diagnostic criteria** set by a committee reviewing hundreds are cases
Proposed pathophysiology:

- Swedo et al suggested molecular mimicry
  - Somatic epitopes of the group A beta-hemolytic streptococcus evoke antibodies that are capable of cross-reacting with areas of the brain, specifically the basal ganglia, to produce neuropsychiatric and behavioral symptoms

- Similar mechanism is thought to cause Syndenham’s chorea (known variant of rheumatic fever)
5 Diagnostic Criteria
Diagnostic Criteria

1. **Presence of Tic disorder or OCD**

   Tic = sudden, rapid, recurrent, non-rhythmic, stereotyped motor movements or vocalizations
Presence of Tic disorder or OCD

Must meet DSMV IV criteria

- Transient Tic Disorder
  - Motor and/or vocal tics 1-12 month
- Chronic Motor or Vocal Tic Disorder
  - One form of tic for > 1 year
- Tourette’s Disorder
  - Both motor and vocal tics for > 1 year
- OCD
  - Obsessions AND Compulsions
  - Interferes with daily life
Diagnostic Criteria

1. Presence of tic disorder or OCD
2. Pre-pubertal symptom onset
Onset of PANDAS

• Pre-pubertal onset
  ▫ Average age 7 years old
  ▫ Most common from ages 3-12
  ▫ Has been documented in adolescence/young adulthood in a few cases

• Onset of OCD
  ▫ Young adulthood

• Onset of Tourette’s syndrome
  ▫ Adolescence/young adulthood
Diagnostic Criteria

1. Presence of tic disorder or OCD
2. Pre-pubertal symptom onset
3. Episodic course of symptom severity
Episodic course of symptom severity

• Abrupt onset and/or dramatic symptom exacerbation

• Symptoms decrease significantly/resolve within 6-8 weeks of symptom onset

• Symptoms decrease/resolve between episodes

• Often described as sawtooth pattern
Diagnostic Criteria

1. Presence of tic disorder or OCD
2. Pre-pubertal symptom onset
3. Episodic course of symptom severity
4. Association with GABHS infections
Timeline:

- Exacerbations with neuropsychiatric symptoms usually begin **within 7-14 days** after streptococcal infections (can be up to 4 weeks)

Data to support timeline:
- Nephritis 10 days after infection
- Rheumatic fever 2-3 weeks after infection
- Chorea can occur months later
Testing:

- Symptoms of pharyngitis
  - rapid strep and throat culture

- History of recent strep infection
  - Antistreptolysin O (ASO)
  - Anti-deoxyribonuclease B (anti-DNAse B)
  - Anti-A Carbohydrate (anti-A CHO)

- One positive test is NOT considered sufficient to determine association between symptoms and infection
Need documentation of the following for diagnosis of PANDAS

- Presence of streptococcal infection in conjunction with at least one episode of neuropsychiatric symptoms
- Negative throat culture and/or decreased titers during times of symptom remission
  - Documents patient is not a carrier
Diagnostic Criteria

1. Presence of tic disorder or OCD
2. Pre-pubertal symptom onset
3. Episodic course of symptom severity
4. Association with GABHS infections
5. Association with neurological abnormalities
Neurologic Abnormalities

- 95% have Choreiform movements
  - Piano playing movements of the fingers
  - NOT present at rest (unlike Sydenham’s chorea)
  - Elicited through stressed postures

- Related to dysfunction of basal ganglia (just as Sydenham’s chorea)
Neurologic Abnormalities

- Motoric hyperactivity
- Fine motor skill loss (handwriting deterioration)
- Disturbances in math and science skills
- Frequent daytime urination without UTI
- Separation anxiety/ Emotionally labile
- Anger outburst/ temper tantrums (after initial resolution)
Diagnostic Criteria: Recap

1. Presence of tic disorder or OCD
2. Pre-pubertal symptom onset
3. Episodic course of symptom severity
4. Association with GABHS infections
5. Association with neurological abnormalities
Treatment:

- Initial course of antibiotics for 10 days
  - Penicillin, Amoxicillin, Azithromycin, Cephalosporin

- Referral to psychiatrist for persistent symptoms
  - SSRI
  - Cognitive Behavioral therapy

- Controversial treatment: Daily prophylaxis antibiotic
  - Study of 23 children in 2005 over 2 years
    - Decreased GABHS infections 96%
    - Neuropsychiatric symptoms declined 61%
Prognosis:

• Many have minimal/no symptoms following acute resolution within 6-12 weeks

• Number of prior episodes of GABHS infection prior to diagnosis directly correlated with a more severe relapsing course
Back to our patient:

- Seen in Allergy/Immunology Clinic almost 2 years following initial episode for follow-up and repeat titers

- Returned due to 2 more infections associated with increased tics

- Titers
  - ASO elevated
  - DNAse B elevated
  - Streptozyme positive

- Given Amoxicillin prophylaxis for 6-8 weeks and symptoms resolved
• Returned 4 months later for repeat titers

• Unfortunately, patient had strep throat 2 weeks prior
  ▫ Associated with increased vocal tics one day prior to infection and throughout infection
  ▫ Resolved with antibiotics

• Offered daily prophylactic antibiotics
  ▫ patient refused

• Continues Buspar and follows with psychiatry

• Plans to follow-up with A/I for repeat titers without recent streptococcal infection
Discussion/Questions:
References:

References:


• Murphy, Pichichero. Prospective Identification and Treatment of Children With Pediatric Autoimmune Neuropsychiatric Disorder Associated With Group A Streptococcal Infection (PANDAS). *JAMA*. 2002

• Murphy, et al. Tonsillectomies and Adenoidectomies Do Not Prevent the Onset of PANDAS. *Pediatric Infectious Disease J*. 2013.