Childhood Post-infectious Autoimmune Encephalopathy: Telehealth Opportunities

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Agenda

Condition

- History of PANS/PANDAS/CPAE
- Pathophysiology
- Diagnosis
- Treatment
- Role of IVIG
**Terms**

**PANDAS:** *Pediatric Autoimmune Neuropsychiatric Disorders Associated with Streptococcus*

**PANS:** *Pediatric Acute-Onset Neuropsychiatric Syndrome*

**CPAE:** *Childhood Postinfectious Autoimmune Encephalopathy*
Based on experience at NIMH after an outbreak of Rheumatic Fever/Sydenham’s Chorea in the late 1980’s

- Abrupt onset OCD after streptococcal infections (PANDAS) in prepubertal children

- Later expanded to OCD after other infections (PANS)

- National university-based network:
  - Harvard
  - Stanford
  - University of Wisconsin
  - University of Arkansas
  - Dartmouth
  - Columbia
  - UCLA
“Controversy”

- Biological explanation
- Overtreatment
Response to Controversy

- Mouse models
  - Injury to BBB mediated by IL-17
- Serum from patients causes OCD in mice
- Clinical research (BG imaging)
- Clinical outcomes research
  - Response to anti-inflammatories
  - IVIG
Pathophysiology
Pathophysiology

- Rheumatic fever
- Sydenham’s Chorea

Sweeten, Nature Medicine 9(7):823-5
Diagnosis
Prospective community cohort study: 693 school-aged children followed for 8 months, strep cultures, movement, behavior assessments

- 3 months post-streptococcal infection:
  - 3x as likely to have movement problems
  - 2x as likely to have behavior problems
  - Children with more strep infections had greater symptoms


doi:https://doi.org/10.1016/j.biopsych.2006.08.031
Denmark: January 1, 1996 to December 31, 2013, all children who received a throat culture (1,067,743 children, over 600,000 had throat culture)

- Presumed strep if given antibiotics in 2 weeks
- Presumed not strep if no antibiotics

- OCD increased 51% in presumed strep, 28% in not strep group
- Tics increased 35% in presumed strep, 25% in not strep group

Diagnosis

- **Dramatic onset of OCD/severely restricted food intake**
- Presence of *at least two* of the following:
  - Anxiety
  - Emotional lability and/or depression
  - Irritability, aggression, oppositional behavior
  - Behavioral/Developmental regression
  - Deterioration in school performance (ADHD, memory, cognition)
  - Sensory or motor abnormalities (tics, chorea)
  - Somatic signs and symptoms (sleep, enuresis, urinary frequency)

Somatic

- Tics
- Urinary frequency/enuresis
- Handwriting changes
This completed worksheet is due Wed., April 8 at the beginning of class.

Projects are mainly done in class: present week of May 18-22

April 18, 2011
6:30

This project will be graded based on the following:

1. Accuracy of information
2. Presentation
3. Participation

Due dates:

- May 18: First draft
- May 22: Final draft

This project will be submitted electronically.

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Country: Bolivia
Population: 10,631,416

Main Language(s): Spanish, Aymaran, Quechua, and thirty-four other native languages

Other Native Languages: Aymara, Quechua, and thirty-four other native languages

Spanish: Hello, Adios = Goodbye, Por favor = please, Gracias = Thank you, Si = yes, No = no

Main Religion(s): Roman Catholic 85%, Protestant 6%

Facts: Bolivia is located in South America. It is bordered by Brazil, Peru, Chile, Argentina, and Paraguay.

Bolivia is a landlocked country. It has a temperate climate in the highlands and a tropical climate in the lowlands.

Bolivia has a rich cultural heritage. The indigenous people have a long history of agriculture and craftsmanship.

Bolivia has a diverse range of flora and fauna, including many unique species of cacti and birds.

Bolivia has a rich history of mineral resources, particularly silver and tin. It is the world's largest producer of tin.

Bolivia has a democratic government. The president is the head of state and government.

The capital of Bolivia is Sucre. La Paz is the seat of the government.

The population of Bolivia is estimated to be 11,000,000.

Daily Life: Include at least 10 ideas of food, clothing, shelter, schools, sports & activities, holidays, animals, plants, etc., and discuss how they are different from or similar to the U.S. (Don't have to write down similarities/differences.)

The Bolivian diet revolves around potatoes. These are more types of potatoes in the Andes than anywhere else in the world. The Bolivian people usually have soup with many different kinds of vegetables.
Handwriting Changes

Country: Bolivia
Population: 10,631,454

Languages: Spanish, Aymara, Quechua, and thirty-four other native languages.

Religious: Roman Catholic 98%, Protestant 2%.

Geographical: Lake Titicaca is the highest navigable lake in the world.

Government: The President of Bolivia is Evo Morales, Head of Government.

Daily Life: The Bolivian diet centers on the potato. There are many potatoes in the Andes that are different sizes, shapes, and colors. The Bolivian people usually have soup, which has different kinds of vegetables.

The volume goes up that as the density does not.

1) The 2 numbers are not the same but not so different.

2) We took our objects density will we found number 5 is closest to it.
Cognitive/Behavior

- Separation anxiety
- ADHD
- Developmental regression
- Academic regression
Theory: Reduce inflammation

• Tiered treatment:
  • Antibiotics
  • Nonsteroidal medications (ibuprofen, naproxen)
  • Less common, Prednisone
  • Much less common, Intravenous immune globulin
Immunology, Immunomodulation, and IVIG
What we ask our immune system to do every day

- Bacteria
- Viruses
- Parasites
- Fungi
100,000 different possible house keys

1,000,000 different possible car keys

1,000,000,000,000-10,000,000,000,000,000,000 different possible antibodies
Sometimes one key fits two locks
If we can’t change the lock, can we stop the key?

Antibiotics

Blocking antibodies

Immune suppression
Why is this so hard?

• The bacteria that are triggering the autoimmune reaction are everywhere
• Other types of infections can trigger the same immune cross reaction issues
• The antibodies can last months, but the cells that produce them can live for decades
• Late recognition and delayed treatment can lead to damage and persistent defects
Telehealth
Case 1

- 10 year old boy
- Strep pharyngitis
- 10 days later, he had overnight refusal to eat anything that his sister breathed on
- Seen in clinic 4 months after onset
- Treated with naproxen and symptoms resolved in one week
- Naproxen with flares for 2 years with viral illness
Story: 7-year-old girl with 3 siblings

• Influenza

• 1 week later:
  • OCD
  • Restricted eating
  • Tics (eye blinking, throat clearing)
  • Anxiety
  • Bedwetting
Symptoms

- Weight loss
- Weather obsession/compulsions
- School refusal
- Handwriting decline
- Slept on parents’ floor
- To bathroom with mother
Treatment

- Naproxen
- Azithromycin
- Prednisone
Resolution

- Resolved symptoms
- Refused to return to previous routine
Accommodations

- Served all meals in her room watching videos
- No school
- No chores
- Routine expectations for other children
Case 3: Severe PANS

- 7 year old boy
- Previously healthy, normal frequency/severity of infections
- Family history of autoimmune diseases
- 6 year old sibling, overall healthy also
- Several strep infections this year
Symptoms at onset

• Strep pharyngitis
• Sudden onset of all symptoms, over a 48 hour period
• Fear of flies because of germs and uncleanliness
• Fear of food contamination
  • Food restriction and refusal
  • Weight loss
• Separation anxiety, mood swings
• Developmental regression, loss of math skills, baby talk
• Increased urinary frequency
• Thoughts of self harm
Symptoms continued

• OCD
  • Thinks about death, afraid of harming others
  • Disgusted with body waste, toilet routines
  • Hand washing rituals
  • Licks hands because they always feel sticky
  • Compulsive counting, ordering, and sorting
  • Eating toilet paper
  • CY-BOCS 35
Prior treatments

• Seen by outside physician, collaboration with Tucson via telehealth
  • Azithromycin
  • Ibuprofen
  • Melatonin

• Initially improved
  • Less OCD
  • Improved appetite
  • Reduced thoughts of self harm
Exacerbation and enrollment in clinical trial

- Contracted COVID, immediately back to severe symptoms including food refusal, thoughts of self harm, and severe OCD
- Because of severity of illness and the sudden onset of OCD was We elected to begin IVIG treatment
- 2g/kg IVIG over 2 days q3 weeks x3 treatments
- Objective improvement based on CGI and CYBOCS scores, mother estimates him to be ‘90 percent’ better
Conclusion

• PANS/PANDAS is a treatable condition

• Requires a diverse team
• Families are very stressed

• UA/Banner CPAE team is available to telehealth consultation to providers.
• We do need to see patients in person initially if we are going to provide direct care.
Team

- Michael Daines, MD (immunology)
- Sydney Rice MD, MS (developmental pediatrics)
- Pawel Kiela DVM, PHD (microbiome and mice)
- Andrew Gardner, PHD, BCBA (psychology)
- Chelsea Carr, PHD, BCBA (psychology)
- Fayez Ghishan, MD (GI)
- Jessica West, RN
- Linnette Ortiz, MPH
- Joann Schultz
- Many students, residents, fellows
Connections

- CPAE@bannerhealth.com
- Jessica West, RN
- https://peds.arizona.edu/cpae