MCPAP Clinical Conversations:

Pediatric Neuropsychiatric Disorders [Associated with Streptococcus]: PANDAS/PANS

Presented by

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Outline

- Introductions
- Discussion of Format
- Presentation
- Comments and Questions (15-20 mins)

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PANDAS/PANS

- Long and well documented history:

  Sydenham Chorea post Rheumatic Fever

  NMDAR Autoimmune Encephalitis "Brain on Fire" [psychosis, mania]

  Others auto immune meditated disorders: including MS [mood disorders 50%], SLE [VH/paranoia], Syrogren, Temporal Arteritis, Sarcoidosis [5% psychosis, behavior], Scleroderma, Hashimoto's [psychosis, mood], Myasthia Gravia. As a result, screening labs not limited to strep titers.

- PANDAS result of cross reactivity of antibodies in the Basal Ganglia [Caudate, GP and Putamen] and binding to multiple targets including gangliosides, tubulin and particularly dopamine receptors.
- Caudate Nucleus is the source of obsessive thoughts and tics.
- Systemic abnormalities of cytokines that cause disruption in BBB.
- Estimated that >80% PANDAS patients have immunological abnormalities. Additionally, increase of autoimmune disorder in family members [particularly maternal].
- Infections including mycoplasma pneumonia, malaria, legionnaires, syphilis, lyme, HIV, herpes, typhoid, diphtheria, influenza, parasitic infections.
- Increased risk of schizophrenia in child with intra utero exposure to Herpes 2 [6 fold increase], Lyme, influenza, toxoplasmosis [4.5 fold increase].
- Link between some psychotropic medications [Thorazine, Clozaril, Depakote] can inhibit viral replication in neuropsychiatric illnesses.

PANDAS/PANS

1. Defined by the abrupt onset of obsessive/compulsive symptoms and/or severe eating disorder as well as 2 of the following symptoms:

   Decline in academic functioning, attention, visual spatial and executive skills, handwriting, regressive and oppositional behaviors, emotional lability, irritability, depression, aggression, obsessive anxiety [particularly separation anxiety] with resultant compulsions and rituals, movement disorders including tics, hyperactivity, akathetic like restlessness, sensory integration difficulties, sleep disturbances, enuresis/encopresis, urinary frequency and somatic complaints/arthralgias

   Typical "waxing and waning" course over time.

   Can be difficulty to illicit in older children who have a history of prior undiagnosed episodes. Consider PANDAS in kids who are intermittently presenting with complaints of anxiety or behavioral issues.

2. Onset entry to school [4-6 yr.] but can and should be considered in any pre adolescent [< 13 yrs.] child presenting with OCD or tics.

3. Males > Females.

4. Is thought to account for up to 30% of OCD seen in children.

5. Heterogeneous both in severity as well as symptoms.

   Symptoms may even vary with subsequent episodes.

PANDAS/PANS

- Although helpful in confirmation, diagnosis based on constellation of symptoms not lab work.
- Even in absence of clear infectious cause, course of antibiotics is recommended.
- Because of symptoms of transient vomiting, headaches, low grade fevers, rashes are thought to be viral in nature, 50% of strep infections are undiagnosed.
- Can see streptococcal pharyngitis, perianal dermatitis, post streptococcal arthritis.
- Streptococcus not always precipitant for children [i.e. designation of PANS in some] and work up should include strep cultures, titers including ASO, Dnase, Lyme, Mycoplasm, TSH, RPR, ANA, RF, Complement panel, CBC with differential, CMP [fasting glucose].
- Viral illnesses including influenza and cocksackie [hand/foot/mouth] can lead to PANDAS, particularly with recurrent exacerbations.
- Although they may be negative, consideration of additional testing including imaging/MRI and EEG.

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- Tics can occur alone or in conjunction with OCD and can include simple motor, vocal or more complex tics.
- Tics occur in 30 % of PANDAS patients as initial presenting symptom.
- Presence of tics predicts more significant cognitive decline and eating issues.
- Tics can be difficult to differentiate from compulsions and rituals- particularly more complex tics.
- Cognitive issues including attentional issues, decline in school performance and handwriting.
- Associated comorbidity with ADHD in many [particularly young children], can complicate diagnosis.
- Sensory issues [can contribute to eating issues], secondary enuresis/encopresis, polyuria, arthralgia and somatic complaints of headaches/stomach aches [may be related to undiagnosed strep infections].
- Impaired eye contact, atypical behaviors/mannerisms [complex tics], regressive behaviors, obsessive rigidity around routines and obsessive interests may be confused for ASD in young children.

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- Clinical Picture is variable and ranges from mild to severe illness.
- Course also variable. Range from only single or sporadic episodes, frequent recurrent episodes [school year], chronic/difficult to treat.
- Time line also unclear. Initial NIMH studies suggested 2-3 year course but clinically often longer.
- Common obsessive fears include separation anxiety, school refusal ["fears of harm to self or others", night time rituals, need for reassurance/"suicidal thoughts"], contamination, choking/vomiting [eating disorders], symmetry ["just right" rituals around routines/self care/eating (body dysmorphia)/environment/handwriting], superstitious ["special numbers", checking, tic like movements/behaviors], fear of insects [VH/TH related to intrusive images in young children].
- Behavioral issues can include panic attacks, prolonged tantrums, aggression, oppositional behaviors [related to need to engage in rituals], insomnia [delayed onset, early morning awakenings and obsessive themed nightmares, refusal to sleep alone], mood issues [lability and depression], hyperactivity, restlessness, refusal to eat.

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- Development of treatment guidelines by consensus board compromised of specialists from across subspecialties published September 2017.
- PCP can manage majority of uncomplicated mild/moderate cases.
- Consider consultation from specialist with multi team approach.
- Recommended first line is 2 week course of antibiotics. Options including Amoxil, Augmentin, Cephalosporin, Azithromycin.
- First choice may not be effective and require second alternative course of antibiotic.
- Prophylaxis with Zithromax, Ceftriaxone or Augmentin when patients experience 3 or more exacerbations during the school year.
- Prophylaxis with daily once a day dosing from September to June with break over summer.
- Addition of Probiotics for those with Perianal Dermatitis.
- Safety issues for more severe cases including hospitalization either psychiatrically or medically.
- Additionally, anti inflammatory treatment with immunomodulatory medications such as NSAID [first line].

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- All children and families, regardless of age, should be referred for cognitive, exposure relapse preventive therapy for OCD. Psycho educates children and families around illness, allows children to develop effective coping skills for current and potential exacerbations and gives parents guidance around behavioral interventions including how to avoid re-enforcing rituals and obsessions.
- Medications for sleep and insomnia including Benadryl, Clonidine [short acting preparation/patch], Ativan.
- Alpha adrenergic medications have the additional benefit of treating tics and decreasing hyperarousal.
- Once episode resolves, can "wait and see" approach.
- Low threshold for screening going forward.
- For older children who have more significant or protracted episodes, consideration of SSRI.
- Consideration of consultation with child psychiatrist for those presenting with symptoms of hallucinations, school refusal, thoughts of self harm and significant mood lability with aggression.

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- Prophylaxis with once a day dosing of antibiotics and NSAIDs [Alleve] throughout school year in children with recurrent episodes.
- Course or burst of steroids, IVIG or Retuxan in severe or chronic cases.
- Treatment with an SSRI for chronic and protracted illness or those with persistent depressive symptoms.
- Consideration of atypical neuroleptics or mood stabilizers for severe episodes with lability, aggression and self harm.
- Screen for carriers, both in child as well as family members.
- Family history should include screening for OCD, ADHD, Tics as well as autoimmune disorders- thyroid disease is the most frequently reported autoimmune disorder in family members.
- Controversy over role for elective tonsillectomy in children with persistent streptococcal related illness.
- No controlled studies and variability among case reports and series with some showing dramatic improvement or remission 24-36 months post tonsillectomy to others showing no improvement.
- PANDAS Physician Network: www.pandasppn.org provides support, guidelines and current research for physicians.
- www.pandasnetwork.org : Provides local chapters, resources, support information for parents.

Resources

1. Swedo, Frankovich, Murphy, *"Overview of Treatment of Pediatric Acute-Onset Neuropsychiatric Syndrome"*, J. of Child and Adol Psychopharm, 1 Sept. 2017, Vol. 27, No. 7. pp.1-6. *
2. Thienemann et al., *"Clinical Management of Pediatric Acute-Onset Neuropsychiatric Syndrome: Part I-Psychiatric and Behavioral Interventions"*, J. of Child and Adol Psychopharm, 1 Sept. 2017, Vol. 27, No. 7. pp. 1-13. *
3. Frankovich et al. *"Clinical Management of Pediatric Acute-Onset Neuropsychiatric Syndrome: Part II- use of Immunomodulatory Therapies"*, J. of Child and Adol Psychopharm, 1 Sept. 2017, Vol. 27, No. 7, pp. 1-45. *
4. Cooperstock et al. *"Clinicial Management of Pediatric Acute-Onset Neuropsychiatric Syndrome: Part III- Treatment and Prevention of Infections"*, J. of Child and Adol Psychopharm, 1 Sept. 2018, Vol. 27, No. 7, pp. 1-23. *
5. Rajor, AD et al, *"Pediatric Autoimmune Neuropsychiatric Disorders Associated with Strep: An Indication for Tonsillectomy. A Review of the Literature"*, Int. J. Otolaryngol, 2018, Feb. 21.

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Questions and Comments

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