Is there a role for Adenotonsillectomy for PANDAS/PANS

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What does the literature say about Tonsillectomy in PANDAS/PANS patients?

- Search for “pandas tonsillectomy” in PubMed revealed 16 articles
- **Case Reports**
  - Pediatric autoimmune neuropsychiatric disorders associated with streptococcal infections (PANDAS): an indication for tonsillectomy
    - 9 yr old with complete resolutions after tonsillectomy
  - A case of PANDAS treated with tetrabenazine and tonsillectomy.
    - *J Child Neurol*. 2010 May;25(5)
    - 9 yr old with complete resolution after tonsillectomy & decrease in antistrptolysin O titers
  - **PANDAS Syndrome: a new tonsillectomy indication?**
    - *Acta Otorrinolaringol Esp*. 2008 Aug-Sep;59(7)
    - 6 yr old with resolution after tonsillectomy
  - **PANDAS (Paediatric Autoimmune Neuropsychiatric Disorder Associated with Streptococcal Infection)**
    - *Ir Med J*. 2006 May;99(5)
    - 6 yr old with resolution after tonsillectomy
  - **PANDAS: pediatric autoimmune neuropsychiatric disorders associated with streptococcal infections--an uncommon, but important indication for tonsillectomy.**
    - 2 brothers, one with OCD & other with tics symptoms resolved after tonsillectomy
What does the literature say about Tonsillectomy in PANDAS/PANS patients?

- Tonsillectomies and Adenoidectomies Do Not Prevent the Onset of Pediatric Autoimmune Neuropsychiatric Disorder Associated with Group A *Streptococcus*
  - *Pediatr Infect Dis J.* 2013 Aug; 32(8)
  - Hypothesis was T&A does not reduce titer elevations or decrease neuropsychiatric symptoms
    - 112 patients 4-17 yr old with OCD or tics
    - 43 with PANDAS; 69 non-PANDAS pts (PANDAS 30 males, 13 females)
    - Surgery N=36 (4 tonsillectomy, 10 adenoidectomies, 22 T&A) – indications were not defined
    - Compared previous surgical patients to non-surgical pts and found no differences in strep antibody titers or symptoms
    - No difference in OCD/tics symptoms between surgery and non surgical groups
What does the literature say about Tonsillectomy in PANDAS/PANS patients?

- **Tonsillectomies and Adenoidectomies Do Not Prevent the Onset of Pediatric Autoimmune Neuropsychiatric Disorder Associated with Group A *Streptococcus***
  - *Pediatr Infect Dis J.* 2013 Aug; 32(8)
  - PANDAS onset pre or post-surgical onset
    - > 50% had surgery prior to onset of symptoms
  - Results:
    - No difference in the ASO titers between the groups
    - No difference in the OCD/tic symptoms
  - Acknowledged limitations of the study
    - “Lack of prospective follow-up data of the larger group with tonsillectomy for any indication and specifically neuropsychiatric conditions”
    - “lack of prospective measurement and analysis of antibody titer levels”
    - “if a subset of youth did have OCD/tic remission after surgery their study would not have detected them”
    - Titers were not obtained in proximity to OCD/tic flares & titers may remain elevated for months post flare
  - Concluded however “that removal of tonsils and/or adenoids is not associated with lower titers or with a decrease in the intensity of neuropsychiatric symptoms (eg. OCD or tics)”
What does the literature say about Tonsillectomy in PANDAS/PANS patients?

- Pediatric autoimmune neuropsychiatric disorder associated with group a streptococcal infection: the role of surgical treatment.
  - *Int J Immunopathol Pharmacol.* 2014 Jul-Sep;27
  - 120 patients with Pandas; 56 with tonsillectomy or adenoidectomy, 64 non-surgical
  - Followed every 2 months for > 2 yrs
  - Surgery did not affect symptomatology progression, streptococcal or neuronal antibodies, severity of neuropsychiatric symptoms
  - Concluded no difference in surgical and non-surgical cases
  - “cannot uphold surgical management as likely to impact positive remission rates, course of OCD/tics, or antibody concentrations in children with PANDAS”
What does the literature say about Tonsillectomy in PANDAS/PANS patients?

- The role of tonsillectomy in the treatment of pediatric autoimmune neuropsychiatric disorders associated with streptococcal infections (PANDAS)
  - Retrospective data 10 patients treated with antibiotics and 9 went on to tonsillectomy
  - Timeline data collected retrospectively
  - Parents asked to rate symptoms on scale of 0-10 with 10 = most profound symptoms (8 males, 2 females); age of onset 6.5 years
  - 50% had no response to antibiotics, no cures with antibiotics
  - All 9 patients showed improvement in their symptoms after tonsillectomy – 33% had complete resolution of symptoms
What does the literature say about Tonsillectomy in PANDAS/PANS patients?

- The role of tonsillectomy in the treatment of pediatric autoimmune neuropsychiatric disorders associated with streptococcal infections (PANDAS)
What does the literature say about Tonsillectomy in PANDAS/PANS patients?

- **Pediatric Autoimmune Neuropsychiatric Disorder Associated with Streptococcus Immunology: A Pilot Study.**
  - Prospective study on 23 patients
    - 12 with “experimental” PANDAS
    - 6 with group A beta hemolytic strep infections
    - 6 with OSA
    - Each assayed for human chemokines and cytokines
  - Found significant variation in the cytokines - Possible markers
    - Down-regulation of IP-10 & INF-γ
    - Increased eotaxin-3 and TNR-α
  - **Results of the tonsillectomy on PANDAS patients were not reported**
What does the literature say about Tonsillectomy in PANDAS/PANS patients?

• Characterization of B-Cells in tonsils of patients diagnosed with pediatric autoimmune neuropsychiatric disorder associated streptococcus.
  • Prospective study on 22 patients
    • 10 with clinical PANDAS
    • 6 Group A Streptococcus infections
    • 6 with obstructive sleep apnea
    • Each analyzed for B-Cell Activity Factor and B-Cell Activating Receptor or CD 19
  • PANDAS patients *did not demonstrate increased* number of B-Cells or B-Cell Activating Receptor as compared to Group A Strep. Patient or OSA patients
  • No data on post surgical symptoms or titers
What does the literature say about Tonsillectomy in PANDAS/PANS patients?

- **PANDAS: A systematic review of treatment options**
  - 5 articles regarding tonsillectomy treatments were found with level of evidence 4 but “not clear benefit could be determined”
  - Also assessed other treatment modalities
  - Concluded there is a paucity of high-level studies and no hard treatment recommendations can be made.
  - Recommended that tonsillectomy be performed only in patients who are candidates based on tonsillectomy guidelines

- Overall conclusion is: Data in the literature is conflicting regarding efficacy of tonsillectomy and adenoidectomy in PANDAS patients, requires good patient selection and prospective data in larger numbers to help clarify its role in treatment
Grace’s Story
July 2010

• 4 y/o female referred to Behavioral Health Clinic at Boys Town for evaluation from her pediatrician
• Noted to have strong intellectual and verbal skills
• Symptoms included:
  • **Excessive levels of worry** esp if parents are away
  • Must **know where parents are at all times**; excessive questioning regarding whereabouts
  • Parents had to return exactly on time or she would cry excessively, sometimes to the point of vomiting
  • **Required constant reassurance** by parents
August 2011

- Now at 6 years of age
- Started to express concerns of hurting herself – when angry she would make statements like “I should just shoot myself”
- Psychologist felt this was a manifestation of anger and not a true desire to harm herself or others
- Mother very alarmed.
- Behavioral assessment by parents revealed significant subsets of hyperactivity,
November 2012

- Teacher is noting greater **anxiety** based behaviors
- **Hyperfocused** on her body
- Scratch on her elbow became an **obsession** for her
- Starting to become **difficult for her to wear certain clothing** like:
  - Underwear
  - Labels really an issue for her
  - Wouldn’t wear socks or shoes at home
- **Behavior at home is more problematic**
  - Biting her fingernails and toes
  - Obsessing on insignificant things with tantrums when she is not getting her way
  - Frequent fights with her sister
  - Took three hours to get her to go to bed
Jan 2012

- **Referred to psychiatrist** for
  - Excessive worrying
  - Separation anxiety
  - Poor emotional regulation
  - **Rx** fluoxetine & methylphenidate

- Frequent outbursts of anger at home but manageable in public

- Concern about her anxiety, impulsivity, inattention and distractibility
May 2012

- **Returned to Psychologist for**
  - Picking at her skin, toes and feet, esp when on stimulant medication
  - Poor impulse control
  - ADHAD-IV Rating Scale moderate to high levels
    - Hyperactivity, inattention, impulsivity and distractibility
    - Frequently defiant at home
  - Recommended eval back to psychiatrist because of the need for multiple medications
  - Continued to have multiple issues at school and at home with marginal improvement on psychotropic drugs
My Nurse is Grace’s mother

• Started seeing multiple children with PANDAS syndrome which resulted in some increased awareness regarding Grace’s obsessive compulsive tendencies

• One day she came out of a patient room with a look of shock on her face and said “my daughter has PANDAS”

• This is the first time I knew of her daughters issues

• My reaction was something like “no she doesn’t!” You’re reading to much into this.
Grace’s Story

• But later on in the day I started discussing with her why she thought her daughter had PANDAS and she articulated her behavior’s to me.
• Mom had noted
  • Extreme anxiety
  • Aggressive behavior
  • Refusal to ware underwear
  • Picking at her fingers and toes
• The more I listened the more I thought she was right.
Grace’s Story

• I decided to send her to our allergist/immunologist and neurologist for further evaluation
• General consensus was that **she likely had PANDAS**
  • She did have recurrent strep throats – not enough to warrant a tonsillectomy by current standards
  • Recurrent sinusitis
  • Followed by one of my colleagues for most of her life
Grace’s Story

• We were doing a number of T&A’s on children with PANDAS and I started to discuss the option of a T&A with mom and her otolaryngologist.
• Grace was having problems with recurrent strep throats but not enough to warrant a tonsillectomy
• She was also having problems with recurrent acute sinusitis
• Mom started to track her symptoms
| Anxiety Symptoms: (Separation, generalized, irrational fears, worries or a specific phobia) |
|-----------------|---------|---------|---------|---------|
| Worries          | Death   | Incapacitated | Severe | Moderate | Mild | Resolved |
| Tears            |          |           |        |          |      |          |

| OCD symptoms: (OCD behaviors causing significant distress in the child's activities in the home, school and with peers) |
|-----------------|---------|---------|---------|---------|
| Chewing feet    |        |          |        |        |
| Bitting nails   |        |          |        |        |
| Bathroom, legs   |        |          |        |        |
| Feet             |        |          |        |        |

| Emotional Liability and/or Depression: (Sudden and unexpected changes in mood states, laughing to tears without reason/Depression-Self Inflicted Harm/Injury or suicidal ideation) |
|-----------------|---------|---------|---------|---------|
| Volatile        | Swings  |          |        |        |
| Kill myself     |        |          |        |        |
| Hitting siblings|        |          |        |        |

| Behavioral (developmental) Regression: (Abuse; increase in temper tantrums, loss of age appropriate talk "baby talk", artwork, handwriting regression) |
|-----------------|---------|---------|---------|---------|
| School home     |        | Incapacitated | Severe | Moderate | Mild | Resolved |

| Deterioration in School Performance: (Shortened attention span, problems with concentration and memorization/losses of math or visuospatial skills, Cognitive or Executive Functioning) |
|-----------------|---------|---------|---------|---------|
| Started IEP     |        |          |        |        |
| Dyslexia        | Special Ed. |

| Sensory or Motor Abnormalities: (Sensitivity to light, noises, smells, tastes, textures of foods/clothing; or conversely sensory seeking behaviors, must touch or feel a texture) |
|-----------------|---------|---------|---------|---------|
| Clothes, foods  |        |          |        |        |

| Somatic Signs and Symptoms: (Including: Sleep disturbances, bedwetting, or urinary frequency) |
|-----------------|---------|---------|---------|---------|
| Bed wetting     | Vomiting|          |        |        |
| Unable to sleep |         |          |        |        |
Grace’s Story

• Somewhat reluctantly after a couple of months and tracking her symptoms - she underwent a tonsillectomy, adenoidectomy, anterior ethmoidectomy and maxillary antrostomy
• Well it worked!
• Almost immediately she had a dramatic change in her symptoms.
**Sinusitis Tx with Antibiotics**
OCD behaviors:

*Compulsive Chewing on Feet

She has gone from the compulsive chewing on her hands & feet to doing pedicures with her sister over the summer.
Deterioration in School Performance

Post-Operative Improvement in handwriting and cognitive skills. (below)

02/19/2013

02/19/2013

02/19/2013

05/03/2013

08/21/2013

09/27/2013

10/02/2013 (wow!)
All those little things she could never do before she had surgery done...became possible this summer!

Sitting still for a haircut so she could be rewarded with pink hair, riding a bike, learning cheers, blowing bubbles and playing catcher...
Cognitive Skills
Before & After Math
Boys Town Research Hospital Experience

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• IRB approved
Introduction

• PANDAS – pediatric autoimmune neuropsychiatric disorder associated with streptococcal infections

I. Abrupt, dramatic onset of OCD or severely restricted food intake

II. Concurrent onset of at least 2 of these 7 symptoms (severe)

III. Symptoms are not better explained by a known neurologic or medical disorder, such as Sydenham chorea, systemic lupus erythematosus, Tourette disorder, or others

1. Anxiety
2. Emotional lability and/or depression
3. Irritability, aggression, and/or severely oppositional behaviors
4. Behavioral (developmental) regression
5. Deterioration in school performance
6. Sensory or motor abnormalities
7. Somatic signs and symptoms, including sleep disturbances, enuresis or urinary frequency
Objectives

• Hypothesis – T&A is an effective treatment for PANDAS
• Evaluate T&A efficacy for PANDAS
  • Neuropsychiatric symptoms
  • Efficacy of antibiotics
• Small retrospective study
Methods

- Records from BTNRH & AAIA
- 2009-2013
- Multidisciplinary - diagnosis
- T&A performed only for children who met the criteria for tonsillectomy
### Tonsillectomy Criteria

<table>
<thead>
<tr>
<th>Criterion</th>
<th>Definition</th>
</tr>
</thead>
<tbody>
<tr>
<td>Minimum frequency of sore throat episodes</td>
<td>7 or more episodes in the preceding year, OR 5 or more episodes in each of the preceding 2 y, OR 3 or more episodes in each of the preceding 3 y</td>
</tr>
<tr>
<td>Clinical features</td>
<td>Temperature &gt;38.3°C, OR Cervical lymphadenopathy, OR Tonsillar exudate, OR Positive culture for group A β-hemolytic streptococcus</td>
</tr>
<tr>
<td>Treatment</td>
<td>Antibiotics had been administered in conventional dosage for proved or suspected streptococcal episodes</td>
</tr>
<tr>
<td>Documentation</td>
<td>Each episode substantiated by clinical record notation, OR If not fully documented, subsequent observance by the clinician of 2 episodes of throat infection with patterns of frequency and clinical features consistent with the initial history.</td>
</tr>
</tbody>
</table>
Methods

• Data points
  • Age at onset of symptoms
  • Age at diagnosis
  • Symptoms – duration
  • ENT infections
  • ABX – duration, response,
  • Psychotherapy
  • Serologies
  • Size
  • Complications
Results

- Total of 16 patients had T&A
- Five had inadequate data for analysis
- N = 11
  - Male N = 9; 2 female
- Average age of presentation = 6.2 yr
- Average age at T&A = 9.4
- Average duration of symptoms = 3.2 yr at the time of surgery
Medications

• 73% (8/11) subjects – SSRI, SSNRI, Neuropsychiatrophic drugs – no improvement noted

• 11/11 used antibiotics - penicillin's, cephalosporin's, azithromycin, trimethoprim and sulfamethoxazole
  • Variable response – no single agent

• Improvement with antibiotics 91% (10/11) but had multiple relapses
Adenotonsillectomy

• Average tonsil size – 2+ (range 1-3+)
• ASO titers variable - <55-2300
• Variation in the response to antibiotics
• Pathology – showed typical lymphoid hyperplasia
• Many with deep crypts and tonsiloliths “stones”
## Duration of Symptoms vs Outcomes

### Duration in Yrs

<table>
<thead>
<tr>
<th>Duration</th>
<th>Improvement status</th>
<th>Resolution of Symptoms</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.25</td>
<td>unknown</td>
<td>unknown</td>
</tr>
<tr>
<td>3.00</td>
<td>unknown</td>
<td>unknown</td>
</tr>
<tr>
<td>5.00</td>
<td>improved</td>
<td>unknown</td>
</tr>
<tr>
<td>1.00</td>
<td>improved</td>
<td>unknown</td>
</tr>
<tr>
<td>4.00</td>
<td>unknown</td>
<td>unknown</td>
</tr>
<tr>
<td>0.50</td>
<td>99% improvement</td>
<td>none</td>
</tr>
<tr>
<td>5.00</td>
<td>excellent</td>
<td>none</td>
</tr>
<tr>
<td>0.00</td>
<td>slow improvement</td>
<td>none</td>
</tr>
<tr>
<td>4.00</td>
<td>excellent symptoms</td>
<td>3 weeks after</td>
</tr>
<tr>
<td>0.17</td>
<td>improvement</td>
<td>seizures, tic</td>
</tr>
<tr>
<td>6.00</td>
<td>improved</td>
<td>unknown</td>
</tr>
<tr>
<td>0.17</td>
<td>improvement</td>
<td>none</td>
</tr>
<tr>
<td>0.25</td>
<td>minor improvement</td>
<td>sinusitis - mouthing, pica, OCD</td>
</tr>
<tr>
<td>8.00</td>
<td>limited, ivig shortly</td>
<td>continued therapy</td>
</tr>
<tr>
<td>4.00</td>
<td>mild response</td>
<td>IVIG</td>
</tr>
</tbody>
</table>

- **Inadequate data**
- **Excellent result – Resolution of symptoms**
- **Improved but without resolution of symptoms**
- **No significant change and continued therapy required**
Adenotonsillectomy

- **Excellent**
  - 46% (5/11)
- **Good**
  - 27% (3/11)
- **Improvement with surgery 73%**
  - (8/11)
Symptom resolution vs duration of symptoms

Results vs Duration of Symptoms

Limited Data but no apparent correlation between duration of symptoms and success of surgery
Adenotonsillectomy

• Complications
• 2/11 (18%) - POD bleeding, dehydration
  • One patient required cauterization
  • Behavioral problems was an issue
• Complications with antibiotics, steroids, other medications, IVIG are unknown
Conclusions

• Pilot Data in a Case series
• Limitations
  • Small size, rare disease
  • Selection bias – T&A performed as last resort
• Improvement in majority
  • Defining improvement is challenging without prospective data
• T&A - more research is required by multiple institutions
• Continued conservative approach but T&A is warranted in children who meet the existing criteria
References