Overview

- Review of Definitions - tics and Tourette syndrome (TS)
- Etiology of TS - focus on possible post-infectious mechanism
- Treatment of TS - medication, immune modulation, behavioral, surgical
- Stimulant use with TS and tics

What is a Tic?

- Sudden, brief, intermittent movement or sound, semivoluntary
- Non-rhythmic, unpredictable
- Mimic fragments of normal behavior
- Wax and wane
- Increase with stress, excitement, fatigue, relaxation
- Decrease with concentration

Primary Tic Disorders

- Transient tic disorder 3 - 15% of children
- Chronic Motor Tics 2 - 5%
- Tourette Syndrome 0.5 - 1%
- M: F 2:1 to 10:1

Natural history of TS

- Onset 3 and 8 years
- Peak severity age 9-11
- ADHD predates tics
- Simple tics first
- Complex tics, OCD later
- Tics decrease after puberty, remission in 60-80%
- Comorbidities persist for lifetime

CoMorbidities

- Up to 50% of patients with TS
- Attention deficit/hyperactivity disorder
- Obsessive compulsive disorder
- Learning disabilities
- Mood disorders, behavioral issues
- Sleep abnormalities, migraine
Differential Diagnosis of TS

- Other Primary Tic disorders
- Secondary Tic disorders
  - autism/PDD, neurodegenerative disease, chromosomal anomalies, infection, injury, medication and toxins

Pathophysiology of TS

- Dysfunction cortex striatum-thalamus circuitry
- Abnormality of dopamine release and uptake

Experimental Diagnostic Testing

- Volumetric MRI with subtle difference in striatum
- PET and fMRI with metabolism difference in frontal cortex
- Blink reflex
- Transcranial magnetic stimulation

Genetic and Environmental Factors

- Twin concordance high
- Bilateral inheritance, multilocus likely
- Two genes associated - CNTNAP2, SLITKRI
- Risk factors - maternal morning sickness and tobacco/caffeine use, LBW, low APGAR scores

Neuroimmunology

- Exacerbation of tics with Group A beta-hemolytic strep infection
- Elevated ASO titers, antineuronal antibodies in TS; not confirmed in all studies
- Two studies of infusion of TS sera in rats - one paper with behavior change, other paper no change

PANDAS

- Pediatric Autoimmune Neuropsychiatric disorders Associated with Strep Infection
- OCD or tic with sudden onset or exacerbation related temporally to documented strep infection
### Diagnostic Evaluation of TS
- History - including development, family history
- Complete neurologic examination
- Consider imaging and laboratory testing only if signs of secondary Touretteism by history or abnormal neurologic examination

### Treatment of TS
- Address comorbidities
- Educate family and child
- Clarify goals - cannot eliminate tics
- Multimodal - lifestyle, education, social, behavioral, medication
- 60-80% of children do not need specific treatment of tics

### Tic Treatment- Pharmacologic
- Moderate efficacy at best
- Several weeks to achieve effect
- Natural waxing and waning
- Multiple medications, variable quality of studies
- Most effective medication 60% benefit, with significant side effects and risk

### Consensus Medication Treatment of Tics
- First line - adrenergic agonists (guanfacine, clonidine)
- Second line - non-dopamine receptor blocking agents (SSRIs, topiramate, botox, baclofen)
- Third line - dopamine receptor blocking agents (haldoperidol, risperidone)

### Immunomodulation
- 2 controlled trials of antibiotics in patients with TS - no change in tics or OCD
- Swedo 1998 - trial of 29 children with PANDAS
  - IVIG, saline, pheresis
  - decrease in tics with pheresis only (30%)
  - decrease in OCD with IVIg and pheresis (40%)
- Recommend only in research setting

### Tic Treatment- Surgical
- Still experimental, small #s
- Limited to adults
- Prior lesion surgery - frontal lobe, thalamus, cerebellum
- Deep brain stimulator first 1999
### Deep Brain Stimulator for TS
- 6 published papers - 7 patients, all adults
- Unilateral or bilateral stimulator
- globus pallidus interna, thalamus, internal capsule
- tic reduction 40-90%, also reduction of OCD

### Tic Treatment - Behavioral
- Habit reversal therapy - awareness training and competing response training (55% reduction in tics)
- Self-monitoring (44%)
- Relaxation training (32%)

### Stimulant Treatment with Tics
- Estimated 50% of patients with Tourette syndrome have ADHD
- ADHD may cause more morbidity than tics
- Stimulant treatment can alleviate ADHD symptoms, but have been shown to unmask new tics or exacerbate tics in individuals

### Stimulant Side Effects
- The TS Study Group, 2002.
  - 136 children with TS enrolled.
  - Tx with methylphenidate alone, clonidine alone, or MPH+clonidine, or placebo
  - At 16 weeks, no different in percentage of children who had experienced an increase in tics (20-26%)

### Recommendations - Stimulants and TS
- No contraindication to stimulant treatment in TS
- If tics increase in the first 4 weeks of treatment, a possible medication effect
- Trial discontinuation and rechallenge later
- Take into account natural waxing and waning nature of tics

### Summary
- TS is a clinical diagnosis, multiple etiologies
- Most children do not need treatment of tics
- Pharmacologic treatment of tics of limited efficacy
- Behavioral therapy may be as effective
- Surgical options are experimental, limited to adults
- No current recommendation for immunomodulation therapy, but research is ongoing
- Comorbidities should be addressed
- No contraindication to stimulant treatment for ADHD
Thank You

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