Sydenham's chorea
Immune modulation treatment of severely affected children

Hilla Ben-Pazi, MD

Movement Disorders Clinic,
Neuropediatric Unit,
Shaare Zedek Medical Center,
Jerusalem, Israel

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Tele-neurology services
Immune modulation
treatment of severely affected children

Treatment

Clinical symptoms

Pathophysiology

References

5 cases
Clinical symptoms

Chorea definition
ongoing random-appearing sequence of one or more discrete movements

Sangr TD et al 2009
Structural/ Congenital- Hypoxic ischemic, kenicterus

Immune/Acquired Chorea - SLE, NMDA

Genetic - DYNC1H1, NKX2.1
Sydenham’s Chorea

1686

The child with Sydenham chorea is punished three times - once for general fidgetiness, once for breaking crockery, and once for making faces at his grandmother.
30% RF single item for Jones criteria

SC - clinical diagnosis

Chorea
Tics,
Dystonia,
Parkisonism

No clear criteria
### Recurrence - Risk factors

#### Comparison between recurrent and non-recurrent patients.

<table>
<thead>
<tr>
<th></th>
<th>SC with recurrence (n = 14)</th>
<th>SC without recurrence (n = 71)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Female, n (%)</td>
<td>12 (85.7)</td>
<td>46 (64.8)</td>
<td>0.12</td>
</tr>
<tr>
<td>Mean age at onset (years), mean ± SD</td>
<td>10.2 ± 2.6</td>
<td>11.2 ± 2.5</td>
<td>0.15</td>
</tr>
<tr>
<td>Duration of chorea until admission (days), mean ± SD</td>
<td>18.75 ± 19.32</td>
<td>15.31 ± 20.24</td>
<td>0.59</td>
</tr>
<tr>
<td>Patients who had symptoms for 20 days and more before first admission, n (%)</td>
<td>2 (14.3)</td>
<td>17 (23.9)</td>
<td>0.43</td>
</tr>
<tr>
<td>Time to onset of clinical recovery (days), mean ± SD</td>
<td>12.5 ± 9.1</td>
<td>21.5 ± 20.3</td>
<td>0.173</td>
</tr>
<tr>
<td>Patients who had complete remission, n (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>In 1-6 months</td>
<td>10 (71.4)</td>
<td>67 (94.3)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>In 6-12 months</td>
<td>1 (7.1)</td>
<td>3 (4.2)</td>
<td>0.63</td>
</tr>
<tr>
<td>In &gt;12 months</td>
<td>3 (21.4)</td>
<td>1 (1.4)</td>
<td>0.001</td>
</tr>
<tr>
<td>Persistent chorea, n (%)</td>
<td>3 (21.4)</td>
<td>1 (1.4)</td>
<td>0.001</td>
</tr>
<tr>
<td>Cardiac involvement, n (%)</td>
<td>12 (85.7)</td>
<td>62 (87.3)</td>
<td>0.87</td>
</tr>
<tr>
<td>ASO titer at initial evaluation</td>
<td>415.4 ± 291.1</td>
<td>539.1 ± 370</td>
<td>0.24</td>
</tr>
<tr>
<td>Patients taking regular prophylaxis, n (%)</td>
<td>9 (64.3)</td>
<td>68 (95.8)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Severe chorea, n (%)</td>
<td>2 (14.3)</td>
<td>4 (5.6)</td>
<td>0.24</td>
</tr>
</tbody>
</table>

SD, standard deviation.

**Key findings:**

- Persistent chorea
- Irregular penicillin prophylaxis

Gurkas E et al 2016
Penicillin prevents recurrence

Steroids don’t
UFGM Sydenham's chorea rating scale -USCRS

I-Behavior
1. Irritable behavior
2. Attention deficit
3. Hyperactivity
4. Obsessions
6. Verbal fluency

II-Activities of Daily Living
7. Dysarthria
8. Chorea
9. Handwriting
10. Cutting food & handling utensils
11. Hygiene
12. Dressing
13. Walking

III-Motor Assessment
14. Ocular pursuit
15. Dysarthria
16. Chorea (face & 4 limbs)
17. Tongue protrusion
18. Finger taps (R+L)
19. Leg agility (R+L)
20. Muscle tone (R+L)
21. Gait (10 m)

Information obtained from patient and/or relatives

Teixeira ALJ, Maia DP and Cardoso F, 2005
USCRS example Tongue protrusion

0 = can hold tongue protruded for more than 1 minute
1 = can hold tongue protruded for more than 30 seconds
2 = can hold tongue protruded for more than 10 seconds
3 = can hold tongue protruded for less than 10 seconds
4 = cannot protrude tongue
Non motor symptoms

- 46% of children had **behavioral change** (n=144)
  - Emotional labiality
  - Irritability
  - Age-regressed behavior

- Impaired **verbal fluency & comprehension**
  - Correlated with motor symptoms
  - Also in RF

*Zomorrodi, 2006; Harsanyi 2015*
Yale-Brown Obsessive-Compulsive Scale (n=73)

- 34% OCD (DSM-IV)
- **Compulsions**
  - Checking (56%)
  - Cleaning (42%)
  - Repeating (36%)
- **Obsessions**
  - Aggressive (63%)
  - Contamination (34%)
- ^ also in RF without SC

Asbahr, 2005; Hounie, 2004
- social phobia
  - 24%
- depression
  - 14%
- anxiety
  - 16%

Remission = persistent

Moreira et al 2014
Psychosis
- Case report (n=1)
- Psychiatric patients
  - Higher incidence of a history of SC
    - Retrospective (n=369)
  - Higher risk of developing schizophrenia
    - Prospective controlled study (n=29)

Ridel 2010; Maia 2005; Teixeira, 2007; Wilcox 1986

ADHD
- Prior to chorea (4/14)
- 60% persistent SC (n=56)

non motor symptoms over time
Standard treatment do not alter recurrence.

Abnormal neurological history

Long term psyc issues
• Not related to chorea

Penicillin prevents recurrence

Not steroids
Auto immune
Pathophysiology

streptococcus
13 year old child
ADHD?

Tonsillitis

Temper tantrums

Referred: hemichorea

Haloperidol treatment

Insects crawling

Haloperidol - discontinued

Psychosis:

Heard voices
Locked doors
Couldn’t stay alone

Risperidone and Olanzapine - ineffective
Lab:
- Antistreptolysin titer
  - 722; N<200 IU/ ml
- Borderline antinuclear antibody titer
  - 1:200
- Mild aortic and mitral regurgitation

MRI T2 hyperintense lesion in the left caudate nucleus
Parallel and integrative processing of motor, cognitive, and psychiatric pathways

**Parallel**
- Emotional processing
  - Motivation
  - Cognitive & executive function
  - Motor planning
  - Motor execution

**Integrative:**
- Emotional -> cognitive -> motor

*Substantia nigra* - Midbrain
*Haber, 2003*
“I go home today. They cured me using this new miracle drug. I’m afraid it’ll be years before it’s approved for humans.”
Basal ganglia staining

Anti Basal Ganglia antibodies presence in serum from a child with SC

Mimicry and autoantibody-mediated neuronal cell signaling in Sydenham chorea

Christine A Kirvan¹, Susan E. Swedo², Janet S. Heuser¹ & Madeleine W. Cunningham¹

2006
Anti-D1R and Anti-D2R IgG antibody titers of Sydenham’s chorea patients (n=22) and Controls (n=22).

Surface D2R IgG antibody 30% SC 9% Tourette’s syndrome
Dopamine receptor antibody ratio (D2R/D1R) correlate with neuropsychiatric symptoms (USCRS score)

Antibodies and behavior

- **GABHS homogenate immunized mice**
  - IgG deposits in deep cerebellar nuclei
  - Increased rearing behavior
    - Blocked with Haloperidol
  - Rearing correlated with IgG deposits

Hoffman et al 2004; Brimberg et al 2012
Ben-Pazi H and Cunningham M unpublished data

* $p<0.05$  **$p<0.001$
Composite Measure (D1R + D2R + LysoGN)
Not one antibody

Abnormal neurological history

Long term psych issues
- Not related to chorea

Penicillin prevents recurrence

Not steroids

Standard treatment do not recur
Not one antibody

Abnormal neurological history

familial

Long term psyc issues

- Not related to chorea

Penicillin prevents recurrence

Not steroids

Standard treatment do not recurence
Treatment
**Penicillin**

Acute disease

Prophylaxis
IM Penicillin G 1,200,000 U/mo
PO Penicillin V 500 mg/d
For ???
5 years
Age 21

**Symptomatic**

Anti epileptic drugs
- Carbamazepine
- Valproic acid
**Antidopaminergic**
- Haloperidol

**Immunosuppression**
- Plasmapheresis
- IVIG
- Steroids (3w)

Garvey et al. Treatment of SC with IVIG, plasma exchange, or prednisone. J Child Neurol 2005
Not one antibody

Abnormal neurological history

Long term psych issues
- Not related to chorea

Familial

Penicillin prevents recurrence

Not steroids

Standard treatment do not alter recurrence
Case 3

Pulse steroids (30 mg/kg)

After 48 hours: "this is the first day that thoughts do not enter my head"

Prednisone 1 mg/kg a year

Follow up MRI T2 hypointense lesion in the left caudate -> gliosis

5-year follow up ruled out SLE.
14 y/o girl - persistent SC & behavioral problems

3 Mo after RF > personality changed

- Irritability, sensitivity, immaturity

- Deteriorated participation
  - Did not initiate activity
  - “would break into tears when requested to clear her dinner plate off the table”

Abulia: apathy with loss of initiative and spontaneous thought & emotional responses
Typical of caudate nucleus lesions (Bhatia, 1994)
Motor (USCRS)

Valproic acid
Haloperidol -> tiredness

Motor (USCRS)
Depression (CDI)
Inattention (DBDRS)
Hyperactivity (DBDRS)

VPA + psychological therapy
HPA

Percent

Time (months)
Haloperidol -> tiredness
Risperidone
^ depression -> Fluoxetine

Motor (USCRS)
Depression (CDI)
Inattention (DBDRS)
Hyperactivity (DBDRS)

VPA + psychological therapy
HPA
Risperidone
Fluoxetine

Percent

Time (months)
Haloperidol -> tiredness
Risperidone
^ depression  -> Fluoxetine
after 6 months-> steroids (2mg/kg↓ 3mo)

Motor (USCRS)
Depression (CDI)
Inattention (DBDRS)
Hyperactivity (DBDRS)

VPA + psychological therapy
HPA
Risperidone
Fluoxetine

resolution (motor and behavior)
Does long term treatment have long term effects? prevention? Motor psyc?
Not one antibody

Long term psych issues
- Not related to chorea

Abnormal neurological history

familial

Penicillin prevents recurrence

Not steroids

Long protocol for severe Psych symp

Standard treatment do not alter recurrence
Immune modulation treatment of severely affected children

- Use USCRS
- Look for psych symptoms
- Consider underlying factors: various Ab, Genetic factors
- Consider long term steroids in selected cases

Take home message
Thank you

Benpazi@gmail.com