Prevalence of Ganglionic AChR Antibodies in Postural Tachycardia Syndrome (POTS)

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Objectives
- Determine a better estimate of the prevalence of ganglionic AChR antibody in patients with POTS
- Determine if POTS patients with ganglionic AChR antibody have clinical differences compared to other POTS patients

Design/Methods
Prospective study of POTS volunteers
- Participants at 2014 meeting of Dysautonomia International (a patient support and advocacy group) were invited to participate in a serological study
- Demographics and supine/standing vital signs
- All subjects completed VOSS (Vanderbilt Orthostatic Symptoms Score); a rating of 9 common POTS symptoms on a scale of 0-10 (max score is 90)
- Blinded serum sample sending for antibody testing
- 102 POTS patients (self-reported diagnosis)
- 5% male, mean age 29.5; range 14-56
- Mean VOSS = 25.3
- 64 control subjects (healthy family members)
- 18% male, mean age 50 yrs
- Mean VOSS = 3.5

Results
- 11 POTS patients had gAChR antibody (> 0.02)
- 5 controls with gAChR antibody (0.02 – 0.10)
- 5 POTS with Ab level > 0.05 (0.06 – 0.13 nmol/L)
- Ab-positive POTS more likely to be male (but the number of male subjects in this study was small)
- The clinical characteristics of POTS with gAChR antibodies were otherwise different

Clinical characteristics of POTS

<table>
<thead>
<tr>
<th>Antibody Status</th>
<th>Demographics</th>
<th>Voss Score</th>
<th>VOSS STAND</th>
<th>Symptoms Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>+</td>
<td>Males %</td>
<td>22%</td>
<td>30%</td>
<td>32% ± 14</td>
</tr>
<tr>
<td>+</td>
<td>Height (in)</td>
<td>65.3 ± 0</td>
<td>65.3 ± 0</td>
<td>121 ± 15</td>
</tr>
<tr>
<td>+</td>
<td>Weight (lbs)</td>
<td>168 ± 5</td>
<td>149 ± 35</td>
<td>90 ± 13</td>
</tr>
</tbody>
</table>

AChR Ab Titers

<table>
<thead>
<tr>
<th>Antibody Status</th>
<th>AChR Ab POS</th>
<th>AChR Ab NEG</th>
</tr>
</thead>
<tbody>
<tr>
<td>(n=11)</td>
<td>(n=91)</td>
<td>P value</td>
</tr>
<tr>
<td>Age (y)</td>
<td>29 ± 11</td>
<td>30 ± 12</td>
</tr>
<tr>
<td>Males (%)</td>
<td>22%</td>
<td>3%</td>
</tr>
<tr>
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<tr>
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POTS vs Controls

<table>
<thead>
<tr>
<th>Antibody Status</th>
<th>Controls</th>
<th>POTS</th>
<th>NS*</th>
<th>10.8%</th>
</tr>
</thead>
<tbody>
<tr>
<td>n=6</td>
<td>12.0%</td>
<td></td>
<td>8.7%</td>
<td>4.9%</td>
</tr>
<tr>
<td>n=5</td>
<td>10.0%</td>
<td></td>
<td>3.1%</td>
<td>4.9%</td>
</tr>
<tr>
<td>n=13</td>
<td>6.0%</td>
<td></td>
<td>4.9%</td>
<td>3.1%</td>
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NS* = No significant differences antibody > 0.05 nmol/L

Anecdotal case

- 17 y male - onset of orthostatic intolerance after recovery from a food injury
- gAChR antibody positive – 0.13 nmol/L
- Autonomic testing normal aside from postural tachycardia (HR increase from 77 to 117 bpm on tilt)
- Plasma NE normal: 284 (supine), 641 (upright)
- Trials of iv and oral steroids and 5 days of IVIG produced no subjective or objective benefit

Specificity of low level gAChR antibodies
- High levels of gAChR Ab (≥ 0.5 nmol/L) are frequently associated with autoimmunne autonomic failure
- Low Ab levels < 0.1 nmol/L are much less specific
- Patients with low Ab have various disorders, including degenerative and non-neurological disorders
- False positives (in healthy controls) do occur, ranging from 0.6% (8) to 3% (this study)
- Low level gAChR antibody may be a useful non-specific marker of autonomic but needs to be interpreted critically, according to the clinical context
- Very low gAChR Ab levels ≤ 0.05 nmol/L appear to have questionable significance

Summary
- A small minority of unselected patients with POTS and healthy controls were seropositive for gAChR antibodies.
- Prevalence of gAChR antibody in POTS patients (5%, using a 0.05 nmol/L cut-off) was lower than previous reports.
- All had low antibody levels (≤ 0.13 nmol/L)
- Neither the seroprevalence nor antibody level was significantly different from the healthy control group.
- Seropositive POTS patients were not different in clinical characteristics compared to seronegative POTS, except for a greater number of males.
- Limitations of the study:
  - POTS diagnosis and healthy controls were self-reported.
  - All patients were treated at time of symptom assessment.
- However, only one patient (seronegative) on IVIG
- Low level gAChR antibody appears to have little clinical significance in otherwise typical POTS.

References