DISORDERS OF REDUCED ORTHOSTATIC TOLERANCE: AN EXAMPLE OF (DYS)FUNCTIONAL AUTONOMIC SYNDROMES

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Orthostatic intolerance (OI) is a fairly generic term often loosely used to describe symptoms occurring upon standing and relieved by recumbency ranging from uneasiness, discomfort, lightheadedness, palpitations, head pressure, anxious feeling, a multitude of somatic complaints referable to sympathetic activation (i.e., shakiness, peripheral vasoconstriction, clammy feeling, etc.) to frank symptoms suggesting cerebral hypoperfusion and even syncope. These disorders have been variably labeled in the past as neuroasthenia, mitral valve prolapse syndrome, sympathotonic hypotension, etc., based on specific aspects that can either be associated or presumably responsible for the manifestations. Patients with orthostatic intolerance often present with complaints of exercise intolerance, lightheadedness, cognitive difficulties, and may be labeled (oftentimes incorrectly) as panic disorder or chronic anxiety. Simple activities of daily living such as eating, showering, or low intensity exercise may profoundly exacerbate these symptoms and may significantly impair the patient’s functional capacity. The magnitude of these symptoms and functional impairment is often significantly greater than those observed in patients with obvious orthostatic hypotension and more generalized autonomic failure. This apparent dissociation has led many to believe such entity is not organic in nature. Undoubtedly many patients presenting with this symptoms complex have underlying psychological traits predisposing to somatoform disorders, but in other the picture is quite different, and, as often occurs in medicine, others have mixed features.

Over the past 2 decades, improved testing has allowed us to recognize there is indeed an entity which became labeled as postural tachycardia syndrome (POTS) that represent the most common variety of orthostatic intolerance, but still belonging to the spectrum of autonomic dysfunction, with autonomic failure being at the other end of the spectrum. This is not a specific disorder, but a syndrome, much more benign from a prognostic standpoint than autonomic failure obviously, but nonetheless quite disabling for the affected individuals.

Key feature of this disorder is the inappropriate tachycardic response that occurs upon standing without decrement in blood pressure. OI/POTS are defined by heart rate (HR) increment of at least 30 bpm (40 bpm in the pediatric population) for at least 50% of the standing time. Syncope can occur in a subset of these patients if forced to stand for a long enough time. The striking apparent paradox is the fact patients describe symptoms suggestive of cerebral hypoperfusion besides palpitations, even if BP is maintained at baseline level as mentioned. Often however marked oscillations in HR and BP are present during standing, suggesting instability in the system that struggles to maintain its homeostasis.

Another key characteristic of this syndrome is its polysymptomatic nature, which may account at least in part for the marked QOL and functional impairment. This is again in striking contrast to isolated OH or syncope.

OI can be seen as part of more pervasive conditions such as chronic fatigue syndrome, probably more as secondary effect of it, but there is also some data suggesting a possible direct involvement of autonomic pathways.

Finally, clinicians and investigators alike have noted the frequent coexistence of other dysfunctional syndromes with OI/POTS, namely migraine, vasomotor phenomena like vasospasm, and gastrointestinal disorders like irritable bowel syndrome (IBS), functional dyspepsia and abdominal pain, fatigue, cognitive complaints, and sleep disturbances.

Abnormalities within the autonomic nervous system have been suggested to be of importance in some patients with functional dyspepsia, such as efferent vagal dysfunction. There is evidence of an association between psychopathology and functional dyspepsia and between psychological factors and gastric functioning and symptoms in functional dyspepsia. Many posit therefore some patients are predisposed to these entities possibly due to a familial trait of vasomotor instability and labile autonomic system, in a sense similar to what happen in subjects with autoimmune disorders.

Personality traits and psychological disorders can certainly contribute, coexist, possibly be causative in some patients and we do not want to discount that.

The presentation will cover the following topics:
1) clinical features
2) subtypes based on pathophysiology, proven or presumed
3) spectrum of clinical manifestations
4) suggested evaluation
5) treatment

Clinical features

OI/POTS are a condition affecting predominantly young women. Onset is acute or subacute in up to 50% of cases, being preceded by an intercurrent illness (known or suspected). Others have a more insidious onset and course, and some may have a constitutional trait to it, as also suggested by some familial cases.

Table 1 summarizes the various complaints reported by patients with POTS in a large series published in 2007.

POTS subtypes

Three phenotypes have been described.

1) Neuropathic POTS
2) Hyperadrenergic POTS
3) POTS with excessive venous pooling

Quality of life

Patients with POTS reported impairment across multiple domains on the SF-36. Modifiable psychological factors play a role in the functional limitations experienced by patients with POTS and could be the target of specific treatment.

Genetics

A single POTS gene probably does not exist, but there a genetic predisposition is likely.

Evaluation

1. Autonomic Reflex Screen
2. Plasma catecholamines: supine and standing
3. 24-hr urinary sodium
4. ECG
5. Exercise testing
6. Cardiac echo and Holter
7. Thermoregulatory sweat test (opt.)

Treatment

Volume expansion, physical retraining, “life coaching” and selected medications (tailored to specific subtypes when possible) are critical for a good functional outcome.
Prognosis

The syndrome is more likely controlled rather than cured, thus stressing the importance of patients' education, lifestyle modifications and retraining.

| TABLE 1 |
| Orthostatic Symptoms as Frequency (%) in Patients with POTS |

<table>
<thead>
<tr>
<th>Orthostatic symptoms</th>
<th>Frequency</th>
</tr>
</thead>
<tbody>
<tr>
<td>Light headed or dizziness</td>
<td>118</td>
</tr>
<tr>
<td>Palpitations</td>
<td>114</td>
</tr>
<tr>
<td>Syncope</td>
<td>92</td>
</tr>
<tr>
<td>Exacerbation by heat</td>
<td>81</td>
</tr>
<tr>
<td>Exacerbation by exercise</td>
<td>81</td>
</tr>
<tr>
<td>Sense of weakness</td>
<td>76</td>
</tr>
<tr>
<td>Tremulousness</td>
<td>57</td>
</tr>
<tr>
<td>Shortness of breath</td>
<td>42</td>
</tr>
<tr>
<td>Chest pain</td>
<td>37</td>
</tr>
<tr>
<td>Exacerbation by meals</td>
<td>36</td>
</tr>
<tr>
<td>Exacerbation associated with menses</td>
<td>22</td>
</tr>
<tr>
<td>Hyperhidrosis</td>
<td>14</td>
</tr>
<tr>
<td>Loss of sweating</td>
<td>8</td>
</tr>
<tr>
<td>Nonorthostatic symptoms</td>
<td></td>
</tr>
<tr>
<td>Nausea</td>
<td>59</td>
</tr>
<tr>
<td>Blotting</td>
<td>36</td>
</tr>
<tr>
<td>Diaphoresis</td>
<td>27</td>
</tr>
<tr>
<td>Constipation</td>
<td>23</td>
</tr>
<tr>
<td>Abdominal pain</td>
<td>23</td>
</tr>
<tr>
<td>Bladder symptoms</td>
<td>14</td>
</tr>
<tr>
<td>Vomiting</td>
<td>13</td>
</tr>
<tr>
<td>Papillary symptoms (glare)</td>
<td>5</td>
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<tr>
<td>Diffuse associated symptoms</td>
<td></td>
</tr>
<tr>
<td>Fatigue</td>
<td>73</td>
</tr>
<tr>
<td>Sleep disturbance</td>
<td>48</td>
</tr>
<tr>
<td>Migraine headache</td>
<td>42</td>
</tr>
<tr>
<td>Myofascial pain</td>
<td>24</td>
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<tr>
<td>Neurologic type pain</td>
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</tbody>
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References

