Postural Orthostatic Tachycardia Syndrome and Inappropriate Sinus Tachycardia

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Disclosures
I have nothing to disclose

MS, a 28 yo F, c/o palps, postural dizziness, severe fatigue, and inability to concentrate.

Supine: HR 73, BP 103/72
Upright: HR 106, BP 109/80

Most likely diagnosis:
A. Inappropriate sinus tachycardia
B. Postural orthostatic tachycardia syndrome
C. Autonomic nervous system failure
D. Chronic fatigue syndrome
Overlapping syndromes

POSTURAL ORTHOSTATIC TACHYCARDIA SYNDROME

POTS

Diagnosis
- HR increase ≥ 30 bpm from supine to standing with no orthostatic hypotension
- Symptoms worsen with standing and improve with recumbence
- Symptoms persist ≥ 6 months
- Absence of other overt cause of orthostatic symptoms or tachycardia

Clinical manifestations
- Postural:
  - Lightheadedness, (less commonly syncope,) palpitations, exercise intolerance
- Unrelated to standing:
  - Nausea, diarrhea, abdominal pain
- Systemic:
  - Fatigue, mental clouding, migraines
**Epidemiology**
- ~650,000 patients in the US alone
- Women > men (4:1)
- Usually presents at young age, 15-25yo
- Onset often following acute stressor
- Big impact on QOL
- No known mortality
- Many have eventual improvement

**Physiology of upright posture**
- Instantaneous descent of ~500mL of blood
- 10-25% shift of plasma into interstitial tissue
- Decreases venous return to heart (preload)
- Triggers compensatory sympathetic activation

**Lower extremity autonomic denervation**
- Sympathetic postganglionic fibers in LE
  - ↓ sympathetics -> ↓ venoconstriction -> venous pooling -> OI
  - Anhidrosis of LE
- Ganglionic acetylcholine receptor Ab
Blood volumes are decreased

Raj SR and colleagues, Circulation 2005

Renin-aldosterone paradox

Raj SR and colleagues, Circulation 2005

Increased sympathetic activity

- Elevated arterial norepinephrine levels at rest
- ↓ norepinephrine clearance
- Increased resting HR
- Larger amplitude sympathetic bursts in peroneal nerve recordings

Genetic abnormalities

- One kindred with identified mutation in norepinephrine transporter
- Frequent family history of orthostatic intolerance
The Grinch Syndrome?

Exclude other etiologies
- Medications
- Prolonged bedrest
- Dehydration
- Anemia
- Hyperthyroidism
- Pheochromocytoma
- Arrhythmia (IST, others)
- Cardiomyopathy (postpartum)
- Autonomic neuropathies

Agents that may worsen orthostatic intolerance
- ACE inhibitors
- Alpha receptor blockers
- Calcium channel blockers, Beta blockers
- Phenothiazines
- Tricyclic antidepressants, MAO inhibitors
- Bromocriptine
- Ethanol, Opiates
- Diuretics, Hydralazine, Nitrates, Sildenafil
- Ganglionic-blocking agents

Which HR + BP pattern with tilt is most likely POTS?
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A. B. C.*

Evaluation

- H+P, including orthostatic vital signs (I)
- ECG (I)
- CBC and TFTs (IIa)
- 24 hour Holter monitor (IIb)
- Autonomic testing (IIb)
- Echocardiogram (IIb)
- Tilt-table testing (IIb)
- Exercise stress testing (IIb)

Nonpharmacologic Treatment

- Reverse any contributing condition
- Avoid aggravating factors (heat)
- Elastic support hose (waist high)
- Exercise (recumbent) (IIa)
- IVF (emergency therapy) (IIa)
- Salt (10-12 g / day) (IIb)
- Hydration (8-10 cups of water daily) (IIb)
Beneficial effects of exercise

Which drug is NOT recommended in POTS?

A. Propranolol  
B. Ritalin  
C. Methyldopa  
D. Pyridostigmine

Pharmacologic therapy (off label, mostly IIb)

- Fludrocortisone (aldosterone analog)  
- Midodrine (vasoconstrictor)  
- DDAVP (for special events)  
- Low-dose propranolol, ivraboradine  
- Pyridostigmine (acetylcholinesterase inhibitor)  
- Clonidine, methyldopa (hyperadrenergic form)  
- Modafinil (stimulant)  

Sheldon RS and colleagues, Heart Rhythm, 2015
Propranolol – go low!

Low dose / placebo

Low / High dose

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Raj SR and colleagues, Circulation, 2005
**POTS - Summary**

- Orthostatic symptoms and tachycardia
- Lightheadedness, exercise intolerance, palpitations, occasionally syncope
- Incapacitating but not malignant
- Etiology multifactorial: peripheral autonomic denervation, hypovolemia, hyperadrenergic, deconditioning
- Exclude reversible causes (meds)
- Tx: reconditioning, hydration, salt
- Rx: volume expansion, vasoconstriction, HR control, neuromodulators

**INAPPROPRIATE SINUS TACHYCARDIA**

**Diagnosis**

- Elevated resting HR
  - Daytime > 100 bpm
  - Mean 24 hour HR >90 bpm
  - Exaggerated response to exertion
  - P wave consistent with sinus mechanism
  - No physiologic basis for tachycardia

**Which Holter is from a patient with IST?**

A.

B.

C.

Castellanos A and colleagues, American Journal of Cardiology 1998

Brady PA and colleagues, PACE 2005
Which Holter is from a patient with IST?

A.  
B.  
C.  

All!

Brady PA and colleagues, PACE 2005

Clinical manifestations

- Asymptomatic -> incapacitating sx’s
- Palpitations
- Lightheadedness, syncope
- Fatigue
- Exercise intolerance
- Chest pain, shortness of breath

Epidemiology

- Primarily young women
- Often hypertensive
- Healthcare professionals?
- 1.2% of (middle-aged) population
- Often hypertensive
- No gender difference

Still AM and colleagues, Europace 2005
In favor of localized autonomic dysfunction

- High intrinsic heart rate (125% predicted)
- β-adrenergic hypersensitivity
- Impaired vagal response
- Normal sympathovagal balance

In favor of primary sinus node abnormality

- Generally benign
- Aggravation of symptoms rare
  Yet
- Concern persists for effect on mortality
Exclude secondary causes

- Anemia
- Infection / Fever
- Diabetic neuropathy
- Hyperthyroidism
- Cushing’s disease
- Pheochromocytoma
- Carcinoid
- Structural heart disease

Evaluation

- Complete History and Physical (I)
- ECG (I)
- CBC and TFTs (IIa)
- 24 hour Holter monitor (IIb)
- Exercise stress testing (IIb)
- Urine/serum drug screening (IIb)
- Autonomic testing (IIb)

What is the primary goal of IST treatment?

A. Heart rate reduction
B. Decrease in mortality
C. Improvement in palpitations
D. Reduction in heart failure risk

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**Conventional Treatment**

- Engagement of the patient
  - Multidisciplinary team
- Regular exercise
- Avoidance of stimulants
- Good sleep hygiene
- Beta-blockers
- Verapamil

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**Ivabradine**

- Mean HR
- Max HR
- Min HR

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*Calo L and colleagues, Heart Rhythm 2010*
Ivabradine

Calo L and colleagues, Heart Rhythm 2010

RCT

Cappato R and colleagues, JACC 2012

Treatment

- Seek and treat reversible causes (I)
- Ivabradine (IIa)
- Sinus node modification (III)
- Surgical ablation (III)
- Sympathetic denervation (III)

Sheldon RS and colleagues, Heart Rhythm 2005

Ptaszynski P and colleagues, Europace 2013

Ptaszynski P and colleagues, Europace 2013
**Ablation**

- Lee RJ and colleagues, *Circulation* 1995

**Better HR control**

- Lee RJ and colleagues, *Circulation* 1995

**Yet**

- Persistent cardiac and extracardiac symptoms
- Need for pacemaker
- Other procedural complications
  - Phrenic nerve injury
  - Superior vena cava obstruction
  - Pericarditis
IST - Summary
- Tachycardia out of proportion to demand
- Asymptomatic -> debilitating
- Intrinsic HR elevation likely exacerbated by autonomic dysfunction
- Benign prognosis
- Exclude secondary causes
- Ivabradine now available!
- Integrated management may be helpful

Differentiating IST and POTS
- POTS – greater postural change in HR
- IST – higher resting HR, more increase with exertion
- IST treatments may worsen orthostatic intolerance in POTS patients
- POTS treatments likely useless for IST patients

Happy Holidays!