ORIGINAL ARTICLE

Postural Orthostatic Tachycardia Syndrome: The Mayo Clinic Experience

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OBJECTIVE: **To evaluate the prevalence and pathogenetic mechanisms of postural orthostatic tachycardia syndrome (POTS).**

PATIENTS AND METHODS: **We reviewed the medical records of patients with POTS seen at the Mayo Clinic in Rochester, Minn, from January 1, 1993, through December 31, 2003. All patients were required to have had a full autonomic reflex screen. The results of the following additional tests were evaluated: thermoregulatory sweat test, plasma catecholamine measurement, serum ganglionic (α3) acetylcholine receptor antibody detection, and 24-hour urinary sodium measurement.**

RESULTS: **We identified 152 patients (86.8% female; mean ± SD age, 30.2±10.3 years) with a mean duration of symptoms of 4.1 years. The mean orthostatic heart rate increment was 44 beats/min. Half the patients had sudomotor abnormalities (apparent on both the quantitative sudomotor axon reflex test and thermoregulatory sweat test), and 34.9% had significant adrenergic impairment, indicating that at least half of the patients had a neuropathic pattern of POTS. In 13.8% of patients, onset was subacute, and ganglionic acetylcholine receptor antibody was detected in 14.6%, suggesting an autoimmune origin in at least 1 in 7 patients. Hyperadrenergic status was documented in 29.0% of patients (standing plasma norepinephrine level ≥600 pg/mL), and at least 28.9% were presumably hypovolemic (24-hour urinary sodium level <100 mEq/24h). The lack of correlation between urinary sodium and standing norepinephrine levels suggests that mechanisms other than hypovolemia accounted for the hyperadrenergic state.**

CONCLUSION: **Our findings suggest a neuropathic basis for at least half the cases of POTS and that a substantial percentage of cases may be autoimmune. Hyperadrenergic and hypovolemic correlates are likely compensatory or exacerbating.**

***Mayo Clin Proc.* 2007;82(3):308-313**

AChR = acetylcholine receptor; CASS = composite autonomic severity score; IQR = interquartile range; POTS = postural orthostatic tachycardia syndrome; QSART = quantitative sudomotor axon reflex test

Postural orthostatic tachycardia syndrome (POTS) is the most common form of orthostatic intolerance without associated orthostatic hypotension.[1] Numerous causes and mechanisms have been proposed.[2] In addition to orthostatic intolerance and other autonomic features, such as sudomotor changes, patients commonly experience fatigue, abnormalities of sleep, and migraine headache.

The pathophysiology of POTS is complex and heterogeneous. In some patients, the standing norepinephrine concentration is elevated, suggesting a hyperadrenergic state.[1,3] Other studies have suggested hypovolemia and peripheral pooling of blood as causes of POTS. Hypovolemia has been demonstrated in some patients,[3] and relative hypovolemia can occur, possibly attributable to pooling of blood in the legs[1,4,5] or abdomen.[6] This pooling could be related to peripheral denervation[1,4,7,8] or to abnormal activation of the renin-angiotensin system.[3] In a preliminary study, we found ganglionic (α3) acetylcholine receptor (AChR) antibody in 10% of patients with POTS, suggesting that some cases represent a limited form of autoimmune autonomic neuropathy.[9]

We reviewed the experiences of a large unselected population of patients with POTS to determine the frequency of different subtypes of the condition and to gain better insight into its pathogenesis. The aims of our study were to (1) document the clinical features of and results of autonomic function tests in a large cohort of patients with POTS; (2) determine what percentage of patients had evidence of peripheral denervation based on sudomotor testing and thermoregulatory sweat testing; (3) examine the frequency of patients with a standing norepinephrine level of 600 pg/mL or higher and determine whether this group had different symptoms or a better response to β-blocker medications; (4) evaluate the percentage of patients with presumed hypovolemia; (5) investigate how plasma volume might correlate with standing plasma catecholamine concentrations; and (6) determine the percentage of patients in whom ganglionic AChR antibody is detectable.

PATIENTS AND METHODS

We undertook a retrospective study of patients who presented to the Mayo Clinic in Rochester, Minn, with POTS during an 11-year period (January 1, 1993, through December 31, 2003). To ensure uniformity of data, we restricted

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This work was supported in part by the National Institutes of Health (NS32352, NS44233, NS43364, DK068055, and MO1 RR00858) and Mayo Foundation.

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the study to patients evaluated clinically by 2 of the authors (P.S., P.A.L.). Symptoms of orthostatic intolerance, aggravating factors, antecedent illness, tempo of onset, medications, and response to medications were abstracted from the medical record. Recorded investigations included supine and standing plasma catecholamine levels and 24-hour urinary sodium excretion.

Inclusion criteria were as follows: (1) baseline sinus rhythm with no evidence of arrhythmia or cardiac disease, (2) sustained heart rate increment of 30 beats/min or greater in response to 10 minutes of head-up tilt, and (3) symptoms of orthostatic intolerance such as light-headedness, weakness, palpitations, blurred vision, breathing difficulties, nausea, or headache developing on standing or after head-up tilt and resolving with recumbency. These symptoms had to be present for more than 3 months.

Exclusion criteria were as follows: (1) orthostatic hypotension defined as a decline of 30 mm Hg or more in systolic blood pressure or 20 mm Hg or more in mean blood pressure within 3 minutes of standing or head-up tilt; (2) pregnancy or lactation; (3) presence of another cause of autonomic failure; or (4) presence of failure of other organ system or systemic illness affecting autonomic function or the patient's ability to cooperate (dementia, pheochromocytoma, congestive heart failure, hypertension, renal or hepatic disease, severe anemia, alcoholism, malignant neoplasm, diabetes, hypothyroidism, sympathectomy, or cerebrovascular accident).

Autonomic Function Tests

Cardiovagal, adrenergic, and postganglionic sudomotor functions were assessed as follows.[10] The quantitative sudomotor axon reflex test (QSART) evaluates the postganglionic sympathetic sudomotor axon[11] and is performed at 4 sites (forearm, proximal lateral aspect of the leg, medial distal aspect of the leg, and proximal foot). Acetylcholine is iontophoresed as a stimulus, and responses are recorded in a single compartment of a multicompartmental sweat cell separate from the stimulus compartment. The axon reflex is mediated by postganglionic sympathetic sudomotor fibers. Three hundred fifty-seven healthy subjects aged 10 to 83 years were used to determine control values.[12] Healthy subjects for this and other autonomic function tests were population based. Subjects from this and other autonomic tests were drawn from the same population.

Cardiovagal function is assessed on the basis of heart rate response to deep breathing and the Valsalva ratio.[12] The heart rate response to deep breathing is the range of heart rate with the subject supine and breathing 6 times per minute. This technique assesses the degree of sinus arrhythmia. Three hundred seventy-six healthy subjects aged 10 to 83 years were used to determine the heart rate deep breathing control values.[12] To test the Valsalva maneuver, the subject was recumbent and asked to maintain a column of mercury at 40 mm Hg for 15 seconds. The ratio of the maximal to minimal heart rate defines the Valsalva ratio. Four hundred twenty-five healthy subjects aged 10 to 83 years were used to determine the control values for the Valsalva ratio.[12]

Adrenergic function is assessed by the blood pressure and heart rate responses to the Valsalva maneuver and head-up tilt. Beat-to-beat blood pressure was monitored continuously (Finapres Monitor, Ohmeda, Englewood, Colo), and a computer console continuously displayed systolic, diastolic, and mean blood pressure.[10] Manual measurement of the blood pressure using a sphygmomanometer cuff and mercury manometer was used to assess the accuracy of beat-to-beat blood pressure. Two hundred seventy healthy subjects aged 10 to 83 years were used to determine head-up tilt control values.[12]

The composite autonomic severity score (CASS) is a semiquantitative score from 0 (no deficit) to 10 (maximal deficit) that combines the results of 3 subsets of autonomic tests and corrects for the effects of age and sex: sudomotor (range, 0-3), cardiovagal (range, 0-3), and adrenergic (range, 0-4).[13] The severity and distribution of autonomic failure are reflected in the total and subset scores.

The thermoregulatory sweat test is performed in a cabinet with a hot and humid environment (45°-50°C air temperature; 35%-40% relative humidity). The mean skin temperature was kept at 39.0°C. Oral temperature increased at least 1.0°C or to 38.0°C (whichever was higher). Maximal sweating was achieved in 30 to 65 minutes. An indicator powder was used to demonstrate sweating, and the percentage of anhidrosis on the anterior body surface was calculated from images created from digital photographs of the sweat distribution.[14]

Statistical Analyses

Descriptive statistics are presented as percentages, mean ± SD, or median (interquartile range [IQR]). The χ^2 tests examined associations among categorical variables, and the Spearman ρ tested correlations among continuous variables. All tests were 2-tailed. $P<.05$ was considered statistically significant. All statistical analyses were performed using SPSS statistical software, version 14 for Windows (SPSS Inc, Chicago, Ill).

RESULTS

Demographics

We identified 152 patients with POTS (Table 1). They were predominantly female (86.8%) and relatively young (mean ± SD age, 30.2±10.3 years). Most patients had experienced symptoms for several years before diagnosis

TABLE 1. **Characteristics and Ancillary Test Results of Patients With Postural Orthostatic Tachycardia Syndrome***

Feature	Finding	No. (%) of patients (N=152)
Mean ± SD age (y)		
Female	30.8±9.7	132 (86.8)
Male	26.3±13.3	20 (13.2)
Total	30.2±10.3	152 (100)
Mean ± SD symptom duration (y)		
Female	4.1±5.0	128 (86.5)
Male	4.0±4.2	20 (13.5)
Total	4.1±4.9	148 (97.4)
Mean ± SD heart rate increase to head-up tilt (beats/min)	44.2±13.3	152 (100)
Mean ± SD TST percent anhidrosis	8.2±18.1	78 (51.3)
Median supine norepinephrine level (pg/mL) (IQR)	219.5 (154.3-309.0)	98 (64.5)
No. with supine norepinephrine level >100 pg/mL	8	98 (8.2)
Median standing norepinephrine level (pg/mL) (IQR)	486.0 (339.0-654.0)	93 (61.2)
No. with standing norepinephrine level >600 pg/mL	27	93 (29.0)
Mean ± SD 24-hour urinary sodium level (mEq/24h)	143.6±74.3	104 (68.4)
No. with 24-hour urinary sodium level <100 mEq/24h	30	104 (28.9)
No. with 24-hour urinary sodium level <150 mEq/24h	69	104 (66.4)
No. with ganglionic AChR antibody detected	6	41 (14.3)

*AChR = acetylcholine receptor; IQR = interquartile range; TST = thermoregulatory sweat test.

(mean, 4.1 years). A remote history of orthostatic intolerance or syncope before onset of persistent symptoms was common (41.4% of patients) (Table 2), and 12.5% had a family history of orthostatic intolerance.

Mode of Onset

Onset was subacute (maximal between 1-3 months) in 13.8% of patients, insidious in 5.9%, and acute in 12.5% (Table 2). Of patients with a preceding illness, 90.5% of patient reports suggested an antecedent viral infection, and 9.5% of patients presented postoperatively.

Clinical Features

Commonly reported symptoms related to standing are detailed in Table 3. Symptoms presumed to be related to cerebral hypoperfusion included the following: lightheadedness, 77.6%; presyncope, 60.5%; and weakness, 50.0%. Symptoms presumed to be associated with autonomic overactivity included the following: palpitations, 75.0%; tremulousness, 37.5%; shortness of breath, 27.6%; and chest wall pain, 24.3%. Sudomotor symptoms also were noted: loss of sweating, 5.3%; and hyperhidrosis, 9.2%. Several of the chronic symptoms reported may reflect dysautonomia: gastrointestinal complaints, including bloating, 23.7%; nausea, 38.8%; vomiting, 8.6%; abdominal pain, 15.1%; constipation, 15.1%; diarrhea, 17.8%; bladder dysfunction, 9.2%; and pupillary dysfunction, 3.3% (complained of excessive glare or problems with light).

Generalized complaints also were common: 48.0% experienced fatigue, 31.6% experienced pronounced sleep disturbance, 27.6% had migraine headache, and 15.8% had myofascial pain.

Precipitating and Aggravating Factors

Several precipitants caused a worsening of symptoms: exercise or heat exacerbated symptoms in 53.3% of patients each. A less common precipitant of symptoms was the postprandial state (23.7% of patients). In 14.5% of premenopausal female patients, worsening of symptoms was related to menses.

TABLE 2. **History of Patients With Postural Orthostatic Tachycardia Syndrome**

History	No. (%) of patients (N=152)
Remote history of orthostatic intolerance or syncope	
Yes	63 (41.4)
No	77 (50.7)
Unknown	12 (7.9)
Total	152 (100)
Family history of orthostatic intolerance	
Yes	19 (12.5)
No	71 (46.7)
Unknown	62 (40.8)
Total	152 (100)
Symptom onset	
Acute (<1 mo)	19 (12.5)
Subacute (1-3 mo)	21 (13.8)
Insidious (>3 mo)	9 (5.9)
Unknown	103 (67.8)
Total	152 (100)
History of preceding illness	
Yes	42 (27.6)
Preceding illness type	
Viral, gastrointestinal	5 (11.9)
Viral, upper respiratory tract	6 (14.3)
Viral, unspecified	27 (64.3)
Postoperative	4 (9.5)
Total	42 (100)
No	109 (71.7)
Total	151 (99.3)

TABLE 3. **Orthostatic and Nonorthostatic Symptoms in Patients With Postural Orthostatic Tachycardia Syndrome**

Symptoms	No. (%) of patients (N=152)
Orthostatic	
Light-headedness or dizziness	118 (77.6)
Presyncope	92 (60.5)
Weakness	76 (50.0)
Palpitations	114 (75.0)
Tremulousness	57 (37.5)
Shortness of breath	42 (27.6)
Chest pain	37 (24.3)
Loss of sweating	8 (5.3)
Hyperhidrosis	14 (9.2)
Exacerbation by heat	81 (53.3)
Exacerbation by exercise	81 (53.3)
Exacerbation by meals	36 (23.7)
Exacerbation associated with menses	22 (14.5)
Nonorthostatic	
Bloating	36 (23.7)
Nausea	59 (38.8)
Vomiting	13 (8.6)
Abdominal pain	23 (15.1)
Constipation	23 (15.1)
Diarrhea	27 (17.8)
Bladder dysfunction	14 (9.2)
Pupillary dysfunction	5 (3.3)
Generalized associated	
Fatigue	73 (48.0)
Sleep disturbance	48 (31.6)
Migraine headache	42 (27.6)
Myofascial pain	24 (15.8)
Neuropathic pain	3 (2.0)

TABLE 4. **Autonomic Function in Patients With Postural Orthostatic Tachycardia Syndrome***

Test	No. (%) of patients
CASS (N=152)	
Cardiovagal score	
0	137 (90.1)
1	13 (8.6)
2	2 (1.3)
Adrenergic score	
0	16 (10.5)
1	83 (54.6)
2	51 (33.6)
3	2 (1.3)
Sudomotor score	
0	64 (42.1)
1	60 (39.5)
2	19 (12.5)
3	9 (5.9)
Total CASS score (≤3)	138 (90.8)
Thermoregulatory sweat test (n=78)	
Distal pattern	20 (25.6)
Global pattern	2 (2.6)
Regional pattern	3 (3.8)
Mixed pattern	13 (16.7)
Other	4 (5.1)
Normal	36 (46.2)

*CASS = composite autonomic severity score.

Neurological Examination

Results of the motor neurological examination were abnormal in only 1.3% of patients, and results of the sensory examination were normal in all. A total of 1.3% of patients had pupillary dysfunction, and 1.4% had symptoms or signs consistent with peripheral neuropathy.

Autonomic Function Tests

Autonomic Reflex Screen and CASS. During head-up tilt, the mean ± SD heart rate increase was 44±13 beats/min. The CASS adrenergic score was 1 or less in 65.1% of patients, indicating minimal adrenergic failure. In the other 34.9%, the adrenergic score was 2 to 3, indicating mild to moderate adrenergic dysfunction.

The most common sudomotor abnormality was a distal loss of QSART responses, occurring in 42.8% of patients. The CASS sudomotor score was 0 in 42.1%, 1 in 39.5%, 2 in 12.5%, and 3 in 5.9% of patients (Table 4).

Cardiovagal function was abnormal in only 9.9% of patients. In 90.8% of patients, the total CASS score was 3 or less, indicating only mild autonomic dysfunction.

Thermoregulatory Sweat Test. Thermoregulatory sweat testing was performed in 51.3% of patients, 53.8% of whom had an abnormal result. Of this group, 25.6% had a distal pattern of sweat loss, 16.7% showed a mixed pattern, and the remainder had a regional, global, or other pattern of sweat loss. The mean ± SD amount of total body anhidrosis was 8.2%±18.1%.

Ganglionic AChR Antibody. Of 42 patients tested, 6 (14.3%) had low positive values (range, 0.07-0.28 nmol/L; reference range, <0.05 nmol/L).

Plasma Norepinephrine. Supine and standing catecholamine levels were measured in 64.5% and 61.2% of patients, respectively. The median supine norepinephrine level was 219.5 pg/mL (IQR, 154.3-309.0 pg/mL) (reference range, 49-1140 pg/mL). Eight patients had a supine norepinephrine level less than 100 pg/mL, but all 8 had robust orthostatic increments (from 49 to 316 pg/mL, from 80 to 257 pg/mL, from 97 to 291 pg/mL, from 78 to 245 pg/mL, from 82 to 170 pg/mL, from 72 to 132 pg/mL, from 63 to 120 pg/mL, and from 63 to 171 pg/mL). The median standing norepinephrine level was 486 pg/mL (IQR, 339-654 pg/mL), with a reference range of 120 to 1565 pg/mL. The standing norepinephrine level was greater than 600 pg/mL in 29.0% of patients tested.

Urinary Sodium Excretion. Twenty-four-hour urinary sodium excretion was measured in 68.4% of patients as a surrogate index of plasma volume.[15] Of those, 28.9% excreted less than 100 mEq in 24 hours and 66.4% excreted less than 150 mEq in 24 hours.

Associations Among Measurements. A significant association was found between the response to β-blockers

TABLE 5. **Treatments Reported by Patients With Postural Orthostatic Tachycardia Syndrome**

Treatment	No. (%) of patients
Volume expansion (n=147)	136 (92.5)
β-Blockers (n=150)	115 (76.7)
Fludrocortisone (n=152)	60 (39.5)
Midodrine (n=152)	48 (31.6)
Selective serotonin reuptake inhibitor (n=147)	76 (51.7)
Phenobarbitone (n=119)	19 (16.0)
Acetazolamide (n=119)	5 (4.2)
Clonidine (n=119)	14 (11.8)
Pyridostigmine (n=150)	8 (5.3)
Resistance training (n=145)	103 (71.0)
Pressure stockings (n=150)	16 (10.7)

and the standing plasma norepinephrine level (P=.02, χ^2 test). Patients with a higher standing plasma norepinephrine level (>600 pg/mL; 29.2%) had a better response to β-blockers compared with patients with a lower standing plasma norepinephrine level (<600 pg/mL; 22.9%). The correlation between CASS sudomotor score and percentage anhidrosis, according to the thermoregulatory sweat test, was statistically significant (P<.001, Spearman ρ).

No statistically significant correlation was found between CASS sudomotor score and standing norepinephrine level (P=.99, Spearman ρ). No statistically significant association was found between peripheral denervation (defined as a CASS sudomotor score of ≥1) and standing norepinephrine level (≤600 or >600 pg/mL) (P=.64, χ^2 test). No statistically significant difference was found in the symptoms of patients with standing norepinephrine levels of 600 pg/mL or less compared with those with standing norepinephrine levels of more than 600 pg/mL (all P>.07), except for loss of sweating (P<.001) and hyperhidrosis (P=.03), which were more common in patients with higher norepinephrine levels. No statistically significant association was found between a standing norepinephrine level of more than 600 pg/mL and syncope (P=.97, χ^2 test). The heart rate increment to head-up tilt was not statistically significantly related to standing norepinephrine level (P=.40, Spearman ρ) or norepinephrine increment on standing (P=.19, Spearman ρ). No statistically significant correlation was found between 24-hour sodium excretion and norepinephrine increment on standing (P=.73, Spearman ρ). No statistically significant association was found between level of urinary sodium (<100, 100-149, ≥150 mEq/24 h) and level of plasma norepinephrine (≤600, >600 pg/mL) (P=.21, χ^2 test).

TREATMENTS

The selection of treatment (percentage of patients who selected; Table 5) for volume expansion, β-blockers, fludrocortisone, midodrine, select serotonin reuptake inhibitors, and phenobarbitone varied widely; 40% to 60% of patients exhibited a positive response.

DISCUSSION

This study consisted of a large composite group of patients whose POTS symptoms were evaluated in a relatively uniform manner. The results support our initially postulated concept that POTS is a limited autonomic neuropathy.[1] Approximately 50% of patients had evidence of peripheral sudomotor denervation. Results of thermoregulatory sweat testing and QSART sudomotor function were significantly correlated, which supports a peripheral postganglionic sympathetic denervation in the legs. Loss of vasomotor tone and pooling of blood in the legs would be an anticipated outcome of sympathetic denervation and might contribute significantly to symptoms in patients with POTS. The detection of ganglionic AChR antibody in 14% of patients adds further support for functional sympathetic denervation. A study by Jacob et al[4] additionally implicates peripheral adrenergic denervation in a group of patients with POTS who had impaired sympathetic nerve function in the lower limbs and elevated standing norepinephrine levels. Our finding of an increase in the CASS adrenergic score (presumed to reflect impaired baroreflex-mediated vasoconstriction to the Valsalva maneuver or head-up tilt) is also consistent with this report. Impaired limb arteriolar vasoconstriction and increased venous compliance have been reported,[16] although the opposite finding of reduced venous compliance has also been reported.[17] The lack of correlation between peripheral denervation and high norepinephrine levels on standing is not surprising. The excessive norepinephrine response has several underlying mechanisms, including hypovolemia, peripheral denervation, and an unstable adrenergic nervous system. The lack of correlation indicates that the excessive norepinephrine response should not be used as a surrogate marker of peripheral denervation.

Elevation of plasma norepinephrine level on standing (>600 pg/mL) is commonly recognized in patients with POTS and was documented in 29.0% of patients tested in the current study. This finding defines a significant, but minority, subset of patients with POTS. However, the mean standing norepinephrine level was relatively high (531 pg/mL). The relationship between elevated plasma norepinephrine and symptoms of sympathetic overactivity is uncertain. We observed no statistically significantly greater frequency of hyperadrenergic symptoms on standing, such as tachycardia, tremulousness, chest pain, or shortness of breath, in patients with a standing norepinephrine level of 600 pg/mL or higher. However, patients with elevated standing levels of norepinephrine had a significantly more beneficial response to treatment with β-blocker medications.

An important first step in the assessment and treatment of patients with POTS is to determine their volume status and institute salt and fluid replacement in those with hypovolemia. El Sayed and Hainsworth[15] reported that 24-hour urinary sodium excretion correlated significantly with plasma volume as measured with Evans blue dye. In our study, 28.9% of patients excreted less than 100 mEq of sodium in 24 hours, consistent with hypovolemic status. One mechanism of hypovolemia is capillary leakage on standing.[18] We found no relationship between hypovolemia (reflected by low urinary excretion of sodium) and elevated standing norepinephrine level. This unanticipated observation suggests that this group of patients lacked the normal physiological stimulation of norepinephrine release in response to hypovolemia and supports the findings of Jacob et al[3] that plasma renin activity was low in a hypovolemic group of patients with orthostatic intolerance. Those authors proposed that renal denervation may be responsible for their observation.

Our study found no differences in the symptomatic response of different patient subgroups to drugs commonly used to treat POTS. By patient reporting, β-blockers, fludrocortisone, midodrine, and selective serotonin reuptake inhibitors all provided partial relief of symptoms in 40% to 60% of patients. These findings are at variance with our earlier reported study,[19] a prospective study that compared the short-term effects of various interventions on hemodynamic indices and symptom scores in 21 patients who met criteria for POTS diagnosis. Patients were studied with a 5-minute head-up tilt protocol, electrocardiographic monitoring, and noninvasive beat-to-beat blood pressure monitoring, both before and after administration of intravenous saline, midodrine, propranolol, clonidine, or phenobarbital. We concluded from the results that midodrine and intravenous saline, when given in the short term, are effective in decreasing symptoms on tilt in patients with POTS.

Fatigue is often a major complaint of patients with POTS. Some patients have an extended period of exhaustion after a bout of symptoms. This period may last from hours to days. In some patients, overwhelming fatigue is a chronic and persistent symptom. These patients describe a low energy level. Some authors have stressed an overlap between chronic fatigue syndrome and POTS.[20,21] A similar magnitude of increase in sympathetic tone at rest and during head-up tilt and impairment of baroreflex transfer was reported for patients with POTS and patients with chronic fatigue syndrome.[21] There is evidence of an increase in sympathetic activation as an early finding in POTS.[22] These patients experience symptoms of orthostatic intolerance before any alteration in cerebral perfusion is detected.[23] Cerebral hypoperfusion occurs with prolonged standing and is attributed to hypocapnia, secondary to hyperventilation.[7]

CONCLUSION

POTS is a relatively common condition. At least half of patients with POTS have neuropathic features, 1 in 3 has hyperadrenergic features, and 1 in 7 has serological evidence of an autoimmune pathogenesis. Hyperadrenergic and hypovolemic correlates are likely compensatory or exacerbating.

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