CASE REPORT

Postural orthostatic tachycardia syndrome (POTS)

Bharat Sidhu,¹ Nonyelum Obiechina,² Noman Rattu,² Shanta Mitra³¹Department of General Medicine, NHS, Birmingham, West Midlands, UK²Department of Elderly Care & General Medicine, Queens Hospital Burton, Birmingham, UK³Department of General Medicine, Queens Hospital Burton, Birmingham, UK**Correspondence to**
Dr Bharat Sidhu,
b.sidhu2@hotmail.com**SUMMARY**

Postural orthostatic tachycardia syndrome (POTS) is a heterogeneous group of conditions characterised by autonomic dysfunction and an exaggerated sympathetic response to assuming an upright position. Up till recently, it was largely under-recognised as a clinical entity. There is now consensus about the definition of POTS as a greater than 30/min heart rate increase on standing from a supine position (greater than 40/min increase in 12–19-year-old patients) or an absolute heart rate of greater than 120/min within 10 min of standing from a supine position and in the absence of hypotension, arrhythmias, sympathomimetic drugs or other conditions that cause tachycardia. We present two cases of POTS, followed by a discussion of its pathogenesis, pathophysiology, epidemiology and management.

BACKGROUND

Its diagnosis requires a high index of suspicion in patients in the relevant age group (15–50-year-old patients) particularly female patients who present with these symptoms.¹ More health professionals need to be aware that this is now a well-recognised clinical entity with a general consensus as to its diagnostic criteria.^{1–3}

CASE PRESENTATION**Case 1**

A 37-year-old lady was admitted twice in 1 week with symptoms of tiredness, palpitations and breathlessness. In addition, she presented with symptoms of right-sided facial numbness and a headache during her first admission. She was investigated, initially, with a CT head scan and, subsequently, an MRI head scan to rule out intracranial pathology. Both investigations revealed no significant abnormalities.

While in hospital, she presented with symptoms of palpitations which came on fairly frequently on standing. She had observed a similar pattern prior to admission. She had also been able to note that when she used a pulse oxymeter at work, her heart rate increased to 160/min on standing up and walking. She had a head-up tilt table test. This showed a blood pressure of 125/91 and a heart rate of 73/min at rest in the supine position; her blood pressure remained stable but her heart rate went up to 120/min on standing. A diagnosis of postural orthostatic tachycardia syndrome (POTS) was made. As she had a family history of cardiomyopathy, she was referred to the cardiology team for further investigations. She had a stress echocardiogram which was, essentially, normal. She was initially treated with propranolol 40 mg twice daily

and sertraline 50 mg once daily with good symptomatic control. However, there were times she felt very tired on the propranolol and she was changed to midodrine. Her symptoms have been much better controlled since and she has been able to care for her children and hold down a job while undertaking a postgraduate degree.

Case 2

This 33-year-old lady who had had recurrent blackouts and palpitations over the years presented to the accident and emergency (A&E) department with further episodes of loss of consciousness. They tended to occur when she had been standing for a little while. The episodes of blackouts first began a few years previously when she had been pregnant. Following the birth of her daughter, they continued and she was seen by a consultant neurologist. He reassured her that these were not seizures but were likely to be stress-related blackouts. Unfortunately they continued to occur though less frequently as time went on. However, they resurfaced about a year ago with much greater frequency and became much more disruptive to her day-to-day life, culminating in her presenting to the A&E department. Her clinical examination, routine blood tests as well as her ECG and cardiac enzymes were normal. She had a 24 h ECG which was also normal. Her head-up tilt test showed sinus tachycardia at rest but this worsened on being tilted at an angle of 60° to the horizontal and her heart rate went up to 140/min within 10 min of being tilted. She felt unwell with it and had a presyncopal episode. Following this, she had some chest pain. She was seen the same day in A&E and, again, her ECG, cardiac enzymes and D-dimers were normal. A diagnosis of POTS was made and she was referred to the cardiology clinic and she is currently awaiting review. In the meantime, she was advised to avoid triggers such as prolonged standing and to keep well-hydrated.

DISCUSSION

POTS was first described by Low and colleagues at the Mayo clinic in 1993⁴ although the condition was recognised as early as 1940.⁵

Its prevalence is largely unknown because it is frequently under-diagnosed and patients with the condition are more likely to be labelled as having anxiety, stress-related blackouts, vasovagal syncope or depression.⁶

Nonetheless, it is thought that there are more than 500 000 people living with the condition in the USA alone.⁵ It is commonest in patients aged 15–50 years and has a 5:1 female preponderance.^{3 5 6}

To cite: Sidhu B, Obiechina N, Rattu N, et al. *BMJ Case Rep* Published online: [please include Day Month Year] doi:10.1136/bcr-2013-201244

Pathogenesis/pathophysiology

It is currently unclear exactly what triggers POTS in patients but various conditions have been linked to its onset. These include viral infections, for example, with Epstein-Barr virus, pregnancy, certain medications, surgery or trauma, and autoimmunity as with paraneoplastic conditions in small cell lung and pancreatic cancers as well as with autoimmune autonomic neuropathy.^{1 7}

In addition POTS has been found to overlap with or occur in certain conditions such as chronic fatigue syndrome (CFS), inappropriate tachycardia syndrome and some other forms of orthostatic intolerance such as neurocardiogenic syncope.¹ Amyloidosis, Sjogren's syndrome, multiple sclerosis, mast cell activation disorders and hypermobility syndrome (Ehlers-Danlos syndrome type III) are other diseases associated with or thought to cause POTS.^{1 7} Some researchers⁸ have suggested that there is a neuropathic basis underlying at least half of patients with POTS and found that about 1:7 of patients studied had ganglionic acetylcholine receptor antibodies suggesting an autoimmune aetiology for this proportion of patients with POTS.

POTS is seen as a form of orthostatic intolerance just like postural hypotension.¹⁻³ In physiological conditions, assuming an upright posture immediately leads to descent of about 300–800 mL of blood from the thorax to the more dependent abdominal, pelvic and leg veins (capacitance vessels).⁹ This leads to reduced venous return to the heart and a transient reduction in blood pressure. Reduced activation of the baroreceptor sensors results in a reflex increase in sympathetic outflow with a tachycardia that rarely ever exceeds 100/min and increased vasoconstriction resulting in the effective circulating volume and, thus, blood pressure being maintained in the upper body.⁹

The pathophysiology of POTS is thought to be due to an excessive sympathetic response to pooling of blood on assuming an upright position.¹⁰ Proposed mechanisms underlying this include α -1 receptor hyposensitivity and denervation insensitivity of the capacitance vessels, β -receptor hypersensitivity with vasodilation and reflex tachycardia, increased capillary permeability with fluid loss from the intravascular to the interstitial space.^{9 10} Other hypotheses suggest impaired baroreceptor functioning at different levels including its ability to maintain blood pressure when there is reduced venous return to the heart.^{5 11} Some researchers have postulated that the excessive tachycardia is the trade off for attempts by the neurovascular machinery to maintain a normal blood pressure in the face of excessive pooling and inadequate physiological compensatory mechanisms.¹²

Diagnosis

The diagnosis of POTS involves a combination of the haemodynamic criteria that comprise the syndrome, exclusion of other conditions that can cause tachycardia and identifying conditions that may coexist with it.⁵

The symptoms of POTS are many and varied reflecting the heterogeneous nature of the disorder and can range from mild symptoms to severely disabling symptoms that interfere with day-to-day functioning. They include recurrent light-headedness, lethargy, palpitations, chest pain, tremulousness and syncope on standing.¹⁻⁶ Others include abdominal pain, neck pain, insomnia and dyspnoea¹ although the list is not exhaustive.

The mainstay of diagnosis is a rise in heart rate of greater than 30/min compared to supine heart rate or an absolute heart rate of greater than 120/min following a head up tilt at an angle

of about 60–70° to the horizontal within 10 min of the patient being tilted.^{1-5 7 9}

Alternatively, a free standing test where a patient is left free standing for about 10 min after being supine can be performed. The haemodynamic diagnostic criteria is as for the head up tilt test.⁵

Some centres measure norepinephrine levels in the supine and upright position after 15 min each. A rise in norepinephrine in the upright position compared to the supine levels identifies a hyperadrenergic subgroup of patients.⁵ These patients tend to have orthostatic hypertension with systolic blood pressures that can be greater than 200 mm Hg in the standing position in addition to the tachycardia that is the hallmark of the condition.⁵

Treatment

The evidence base for treatment strategies in POTS is limited but data from small studies and case series are emerging.¹³⁻²² What evidence there is suggests that different treatment modalities can help control the symptoms although they are not curative.^{14 15 16-22} They consist of non-pharmacological and pharmacological measures which can be used in different combinations.^{1-3 13-22} In addition to managing the symptoms of POTS, the conditions that may be associated with it, for example, CFS need to be identified when present and treated in their own right wherever possible.¹⁻⁵

Non-pharmacological measures

These include countermeasures such as avoidance of precipitants¹⁻⁶ like prolonged standing, dehydration and certain medications, for example, ACE inhibitors, Angiotensin-II (A-II) antagonists, diuretics and α -blockers.

Increased fluid intake of at least 2–3 L/day and increased salt intake (not recommended in the hyperadrenergic subgroup) may also help.¹⁻⁶

Graduated exercises including recumbent rowing with rowing machines and cycling and swimming in the reclined position have been suggested as helpful in improving orthostatic tolerance particularly in patients with deconditioning.^{5 13 14}

Bolus drinks of water, for example, 500 mL at each given time as well as squeezing the leg muscles periodically particularly when upright have also been suggested as having some benefit.^{3 5 6}

Other measures that have been suggested include thigh length compression hosiery and abdominal bands^{3 5 13} although there does not appear to be much evidence as to their benefit in this condition.

Pharmacological measures

Fludrocortisone is a synthetic mineralocorticoid which acts by increasing salt and water retention. It also sensitises the α -1 receptors to circulating norepinephrine.¹⁵ It works in POTS by expanding plasma volume, mitigating against the effects of excessive pooling.⁵

β -Blockers such as propranolol and bisoprolol have been used successfully in some cases to treat POTS.^{16 17} They act by reducing the excess sympathetic response to standing.^{16 17} However, because they can also lower renin levels, they can be counterproductive in patients with low circulating volume.^{1 5} In the hyperadrenergic subgroup where patients can also have high blood pressure recordings during standing, β -blockers can cause unopposed α -1 adrenoceptor activity with worsening in their

symptoms.¹ In that case labetalol may be a preferable option as it has both β and α -1 receptor blockade.¹

A small study¹⁸ comparing low dose propranolol 20 mg once daily to placebo showed a modest benefit in reducing heart rate and improving orthostatic tolerance.

Ivabradine is a selective I_f channel blocker¹⁹ (where f stands for 'funny') of the sinoatrial node which is the main pacemaker of the heart. The channel has been described as 'funny' because at the time of its discovery it was thought by the researchers to have unusual properties compared to other ion channels in that it enables the inward current flow of both Na^+ and K^+ ions.¹⁹ Blocking of these channels by Ivabradine leads to a slowing of the heart rate without some of the adverse side effects like negative inotropic effects usually seen with β and calcium channel blockers.¹⁹ It has been used with varying degrees of success for treating patients with POTS in the UK.²⁰

A retrospective case series conducted by McDonald *et al*²⁰ showed that Ivabradine was effective in improving symptoms in 60% of patients with POTS that were studied. The study limitations, however, include its small sample size, retrospective nature of the study and lack of randomisation.²⁰

Midodrine is an α -1 agonist.²¹ It is a prodrug that is converted by the liver to desglymidodrine, the active metabolite. It acts by causing vasoconstriction and increasing peripheral resistance, thereby reducing pooling and the ensuing reflex tachycardia. Chen *et al*²¹ found that Midodrine was effective in treating POTS in adolescents.

Pyridostigmine which is an acetylcholinesterase inhibitor has been used successfully in some patients with POTS. Raj *et al*²² in a small, crossover, randomised, controlled study showed that pyridostigmine significantly attenuated tachycardia in some patients with POTS.

Others treatments include selective serotonin reuptake inhibitors (SSRIs) such as sertraline and duloxetine.^{1 5}

α -2 agonists, such as clonidine, which act centrally to reduce sympathetic outflow, have been used in some patients with the hyperadrenergic subtype of POTS with variable degrees of success.¹

Erythropoietin has been tried but concerns about its safety in this context and its great expense limit its use.⁵

Obviously, to help guide best practice in the future, larger, better designed, prospective, randomised controlled trials are needed. The problem with the current evidence base for treatment of POTS is the fact that a lot of the study samples are small, many of the data are retrospective and there is a general lack of randomisation. It is hoped that with the consensus definition of POTS and clarification of its diagnostic criteria, as well as better understanding of the pathophysiological mechanisms that underlie this heterogeneous condition, the gathering of more robust evidence regarding treatment efficacy will become more feasible.

It is worth noting that none of the above treatments are currently licensed for treatment of POTS although this may well change in the future as more evidence becomes available. Some of them such as fludrocortisone and midodrine are licensed for treatment of other forms of orthostatic intolerance such as postural hypotension and vasodepressor forms of neurally-mediated syncope.

Prognosis

There is a paucity of long-term longitudinal data for this condition but different researchers suggest that where the condition arises during adolescence, most patients recover from it.^{1 13} Other patients have a variable course with some improvement

in symptoms.¹³ For a few patients, their lives continue to be crippled by the condition.^{1 13}

Learning points

- Postural orthostatic tachycardia syndrome is a heterogeneous condition whose diversity of symptoms and non-specificity of presentation sometimes leads to its under-diagnosis or to a misdiagnosis of other conditions that can present with similar symptoms such as anxiety and stress-related syncope.
- It is also a condition that can be disruptive to day-to-day functioning of the patients afflicted with it and the importance of identifying it and putting patients on appropriate treatment tailored to their needs cannot be overstated.
- However, it is a syndrome that is only just becoming increasingly understood and robust evidence for its different treatment options is, currently, limited.
- Its diagnosis requires a high index of suspicion in patients in the relevant age group (15–50-year-old patients) particularly female patients who present with these symptoms. More health professionals need to be aware that this is now a well recognised clinical entity with a general consensus as to its diagnostic criteria.

Contributors NO was involved in conception, literature review and decision to submit article for review. BS was involved in article design, patient consent, patient summaries, proof read and edit of article NR and SM were involved in patient summaries and proofreading of the article.

Competing interests None.

Patient consent Obtained.

Provenance and peer review Not commissioned; externally peer reviewed.

REFERENCES

- 1 Grubb BP. Postural tachycardia syndrome. *Circulation* 2008;117:2814–18.
- 2 Freeman R, Wieling W, Axelrod FB, *et al*. Consensus statement on the definition of orthostatic hypotension, neurally mediated syncope and the postural tachycardia syndrome. *Auton Neurosci* 2011;161:46–8.
- 3 National Institute Of Neurological Disorders and Stroke (NINDS). *Postural Tachycardia Syndrome Information Page*. http://www.ninds.nih.gov/disorders/postural_tachycardia_syndrome/postural_tachycardia_syndrome.htm (accessed Jul 2013).
- 4 Schondorf R, Low PA. Idiopathic postural tachycardia syndrome: an attenuated form of acute pandysautonomia? *Neurology* 1993;69:790–8.
- 5 Abed H, Ball PA, Wang L. Diagnosis and management of postural orthostatic tachycardia syndrome: a brief review. *J of Geriatr Cardiol* 2012;9:61–7.
- 6 Agrawal AK, Gang R, Ritch A, *et al*. Postural orthostatic tachycardia syndrome. *Postgrad Med J* 2007;83:478–80.
- 7 Mathias CJ, Low DA, Iodice V, *et al*. Postural tachycardia syndrome—current experience and concepts. *Nat Rev Neurology* 2012;8:22–34.
- 8 Thieben MJ, Sandroni P, Sletton DM, *et al*. Postural orthostatic tachycardia syndrome: the Mayo clinic experience. *Mayo Clin Proc* 2007;82:308–13.
- 9 Raj SR. The postural tachycardia syndrome (POTS): pathophysiology, diagnosis and management. *Indian Pacing Electrophysiol J* 2006;6:84–99.
- 10 Bush VE, Wight VL, Brown CM, *et al*. Vascular responses to orthostatic stress in patients with postural tachycardia syndrome (POTS) in patients with low orthostatic tolerance in asymptomatic controls. *Clin Auton Res Soc* 2000;10:279–85.
- 11 Meunter Swift N, Charkoudian N, Dotson RM, *et al*. Baroreflex control of muscle sympathetic nerve activity in postural orthostatic tachycardia syndrome. *Am J Physiol Heart Circ Physiol* 2005;289:H1226–33.
- 12 Diehl RR. Continuous progression of orthostatic tachycardia as a further feature of the postural tachycardia syndrome. *Pacing Clin Electrophysiol* 2005;28:975–9.
- 13 Low PA, Sandroni P, Joyner M, *et al*. Postural tachycardia syndrome (POTS). *J Cardiovasc Electrophysiol* 2009;20:352–8.
- 14 Winker R, Barth A, Bidman D, *et al*. Endurance exercise training in orthostatic intolerance: a randomized, controlled trial. *Hypertension* 2005;45:391–8.

- 15 Davies B, Banrester R, Server P, *et al.* The pressor actions of noradrenaline, angiotensin II and saralasin in chronic autonomic failure treated with fludrocortisone. *Br J Clin Pharmacol* 1979;8:253–60.
- 16 Freitas J, Santos R, Azevedo E, *et al.* Clinical improvements in patients orthostatic intolerance after treatment with bisoprolol and Fludrocortisone. *Clin Auton Res* 2000;10:293–9.
- 17 Gordon VM, Opfer-Gehrking TL, Novak V, *et al.* Haemodynamic and symptomatic effects of acute interventions on tilt in patients with postural tachycardia syndrome. *Clin Auton Res* 2000;10:29–33.
- 18 Raj SR, Black BK, Biaggioni I, *et al.* Propranolol decreases tachycardia and improves symptoms in the postural tachycardia syndrome (POTS): less is more. *Circulation* 2009;120:725–34.
- 19 Sulfi S, Timmis AD. Ivabradine—the first selective sinus node I_f channel inhibitor in the treatment of stable angina. *Intern J Clin Pract* 2006;60:222–8.
- 20 McDonald C, Firth J, Newton JL. Single centre experience of Ivabradine in postural orthostatic tachycardia syndrome. *Europace* 2011;13:427–30.
- 21 Chen L, Wang L, Sun J, *et al.* Midodrine hydrochloride is effective in the treatment of children with postural orthostatic tachycardia syndrome. *Circulation* 2011;75:927–31.
- 22 Raj SR, Black BK, Biaggioni I, *et al.* Acetyl cholinesterase inhibition improves tachycardia in postural tachycardia syndrome. *Circulation* 2005;111:2734–40.

Copyright 2013 BMJ Publishing Group. All rights reserved. For permission to reuse any of this content visit <http://group.bmj.com/group/rights-licensing/permissions>.
BMJ Case Report Fellows may re-use this article for personal use and teaching without any further permission.

Become a Fellow of BMJ Case Reports today and you can:

- Submit as many cases as you like
- Enjoy fast sympathetic peer review and rapid publication of accepted articles
- Access all the published articles
- Re-use any of the published material for personal use and teaching without further permission

For information on Institutional Fellowships contact consortiasales@bmjgroup.com

Visit casereports.bmj.com for more articles like this and to become a Fellow