Family Medicine & Medical Science Research

Kincaid, et al., Fam Med Med Sci Res 2015, 4:1
http://dx.doi.org/10.4172/2327-4972.1000153

Case Report Open Access

Manifestations of Anxiety? Explaining Tachycardia and Hypertension in a Patient with POTS

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Rec date: Nov 21, 2014; **Acc date:** Jan 09, 2015; **Pub date:** Jan 11, 2015

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Abstract

Background: Postural orthostatic tachycardia syndrome (POTS) is characterized by autonomic dysfunction causing orthostatic intolerance. Psychiatrists should be aware of POTS because the symptoms exhibited by patients, such as tachycardia, tremulousness, fatigue, and abdominal pain, may be misinterpreted as a primary anxiety disorder, in particular panic disorder, or even as one of the somatoform disorders.

Objective: The authors review literature on POTS and highlight a case of a 23-year-old female with hyperadrenergic POTS, admitted for a recurrent tachycardiac and hypertensive crisis.

Method: The authors present a case report of history, diagnosis, and treatment. After being treated in the medical intensive care unit, the patient was referred to the internal medicine psychiatry service (med-psych) for management because members of her medical team hoped her symptoms would be better treated by managing her anxiety.

Results: The patient had a history of multiple referrals for anxiety in spite of a known diagnosis of POTS. She also had serum catecholamines showing a normal norepinephrine while supine and comfortable, but highly elevated during a tachycardiac and hypertensive crisis.

Conclusion: This case highlights the need for a broader understanding of POTS. Patients with this syndrome have a primary autonomic dysfunction driving their symptoms, though anxiety can be a component. In addition, serum catecholamines drawn while supine and comfortable may lead to inaccurate judgments as to the etiology of the patients' tachycardia and should only be interpreted in conjunction with catecholamines drawn while upright or during an orthostatic crisis.

Keywords: Postural orthostatic tachycardia syndrome; Anxiety; Norepinephrine, autonomic dysfunction

Introduction

Postural orthostatic tachycardia syndrome (POTS) is a condition of autonomic dysfunction characterized by orthostatic intolerance without orthostatic hypotension. Patients with this condition can exhibit a variety of signs and symptoms, but the classic definition of POTS is an increase in heart rate greater than 30 beats per minute in the absence of hypotension within five minutes of assuming an upright position in a symptomatic patient [1-3]. In addition to tachycardia or palpitations, people with POTS can exhibit headaches, weakness, abdominal pain, dizziness, fatigue, sweating, tremulousness, and anxiety [2,3]. The symptoms associated with POTS are of particular importance for psychiatrists to be aware of because providers may overlook the overall symptom complex and focus only on the anxiety. This may cause patients to be mislabeled as having a primary anxiety disorder. This review begins with a case of a woman with POTS who, due to her clinical presentation, was repeatedly referred to psychiatry for management of her symptoms.

Case

Ms. X is a 23-year-old Caucasian female with a history of autonomic dysfunction, diagnosed as POTS. She has a history of multiple emergency department visits and hospital admissions since the age of 19 for symptoms associated with POTS, primarily episodes of profound hypertension and tachycardia. She was taking tizanidine, metoprolol, methyldopa, buccal fentanyl, and gabapentin as an outpatient for management of hypertension, tachycardia, extremity pain, and headache. She was also taking trazodone for insomnia, ferrous sulfate for iron-deficiency anemia, and oral contraceptive pills. Ms. X presented to the emergency department from a scheduled cardiology visit after having a severe headache, flushing, palpitations, burning leg pain, tachycardia with a heart rate in the 160s, and a systolic blood pressure of 170. She was admitted to the medical Intensive Care Unit (ICU), primarily for management of her hypertension and tachycardia, and was placed on a labetolol continuous infusion with intravenous (IV) hydromorphone as needed for pain. While in the ICU, she had several episodes of tachycardia and hypertension. During these episodes, Ms. X also complained of intense burning pain in her extremities, usually her legs. She appeared restless and anxious, and she was tremulous, writhing in the hospital bed due to pain. Ms. X complained of hot flashes, and she would usually be

flushed and sweating. Her episodes also had a diurnal variation, usually having no symptoms in the morning with the episodes primarily occurring in the late afternoon and evenings.

By hospital day number two, the patient's hypertension, tachycardia, and other symptoms resolved, and she was titrated off of the labetolol infusion. Ms. X was deemed ready for transfer to a general medicine bed. When deciding upon the accepting medicine team, the combined medicine-psychiatry service was contacted to see if they would accept the patient. Several physicians in the ICU were concerned about Ms. X's behavior, especially the restlessness and writhing movements during the episodes. In fact, they felt some of the behavior was inappropriate and extreme and hypothesized her symptoms could be secondary to a primary anxiety disorder. They felt that the med-psych service would be able to address her psychiatric issues while continuing to manage any further hypertension or tachycardia. Ms. X was transferred to the med-psych service in the afternoon of hospital day two. In the evening on that same day, the patient was sitting up in her room and again developed an episode of tachycardia with hypertension and pain. She was treated with oral and IV pushes of beta-blockers for blood pressure and heart rate control, but her symptoms remained refractory to these methods. She was transferred back to the medical ICU for management of hypertension and tachycardia with labetolol infusion. Ms. X remained in the ICU for three more days and was again titrated off of the infusion. On hospital day six, she was stable without symptoms and discharged on her home medications with the exceptions of scheduled propranolol for hypertension, metoprolol only as needed for tachycardia, and methadone for long-acting pain control. In addition, the patient's methyldopa was stopped due to ineffectiveness in controlling blood pressure and to worsened mood.

When further examining Ms. X's medical record and history during the previous admissions, there was often debate between the medical teams taking care of her and the psychiatry consult service or the med-psych service as to the underlying etiology of Ms. X's clinical presentation. The medical teams would see her behavior and often insist that the patient was primarily anxious and that treating the anxiety more effectively would improve her condition. The psychiatry service would evaluate the patient and would acknowledge that she appeared anxious during the episodes. However, they felt that the extreme hypertension and tachycardia and overall symptom complex could better be explained by POTS. Indeed, the diagnosis of POTS itself was questioned by some medical teams because of certain negative laboratory findings. Ms. X had an extensive workup in the months prior, which included negative laboratory and imaging studies for pheochromocytoma, carcinoid syndrome, hyperthyroidism, Cushing's disease, adrenal adenomas, or cardiac arrhythmias. She also had an otherwise negative medical history. In order to diagnose POTS as the cause of her episodes, fractionated catecholamines were drawn. In fact, they were drawn on several occasions and varied widely. On one occasion, Ms. X's catecholamines were normal, and several people on the medical teams cited this as evidence that the patient had no hormonal or autonomic component involved in her presentation. Thus, she must have a primary psychiatric illness rather than POTS.

Table 1 shows Ms. X's fractionated catecholamines drawn on three different occasions. During Times 1 and 3, the patient was in an acute episode when the labs were drawn.

Time	Symptoms/vital signs	Norepinephrine pg/mL (pmol/L)	Epinephrine pg/mL (pmol/L)	Dopamine pg/mL (pmol/L)
Time 1: 5 pm	Burning leg pain, flushed, HR* 170, SBP** 180	1258 (7436)	222 (1212)	32 (209)
Time 2: 10 am (8 months after time 1)	No symptoms; vital signs normal	81 (479)	<10	<10
Time 3: 5 pm (4 days after Time 2)	Burning leg pain, flushed, tremulous, HR* 180, SBP** 250	1618 (9564)	529 (2888)	40 (261)

Table 1: Fractionated plasma catecholamines in patient with POTS (*HR = heart rate **SBP = systolic blood pressure)

Literature Review and Case Discussion

Postural orthostatic tachycardia syndrome is a condition that is not easy to diagnose, as patients have varying symptom presentations. In general, POTS is characterized by functional hypovolemia when sitting upright due to dysfunction of autonomic homeostatic blood pressure control with changes in position [3]. Mainstays of treatment of most patients with POTS are to increase salt and fluid intake to minimize orthostatic decreases in venous return, encourage resistance exercises, and offer medications. Fludrocortisone is often added to further increase blood pressure and counteract the positional hypovolemia. Beta-blockers are commonly used to control heart rate, and alpha-1-agonists, like midodrine, are also utilized to increase vascular tone [2,3]. Additional medications, which have been variously used for this condition, include pyridostigmine, clonidine, methyldopa, Phenobarbital, and erythropoietin. The exact pathophysiology of POTS is not fully understood, but several subtypes of POTS (deconditioned POTS, neuropathic POTS, and hyperadrenergic POTS) have been described based on proposed mechanisms [2]. All three subtypes are characterized by orthostatic intolerance, but they vary as to other signs. Although patients may exhibit signs of one or more of these subtypes, each subtype has slightly different treatment strategies [2,3].

In many cases, patients with POTS reduce their physical activity in an effort to reduce symptoms. This can lead to deconditioning and cause a cycle in which they become increasingly intolerant of exercise or activity, leading to more and more severe symptoms with mild

activity or positional changes [2]. This is known as deconditioned POTS. In addition to the above treatments, a tailored and specific exercise and rehabilitation program should be included in the management strategy of this subtype.

Neuropathic POTS is characterized by a restricted autonomic neuropathy involving those post-ganglionic sympathetic neurons having the longest axons (innervating the splanchnic bed and extremities), the so-called length-dependent type. These patients occasionally have antibodies to the ganglionic acetylcholine receptor and will exhibit peripheral adrenergic failure due to denervation [2,3]. Patients with neuropathic POTS often respond to fludrocortisone and an alpha-1-agonist like midodrine to increase vessel tone in addition to volume expansion [2]. Acetylcholinesterase inhibitors like pyridostigmine have been utilized in these patients, as well.

Hyperadrenergic POTS is a condition in which there is an excessive release of norepinephrine with upright positional change. It is characterized by blood pressure increases >10 mmHg and orthostatic increases of plasma norepinephrine>600 pg/mL^2 , or greater than three times the supine level. Along with increased heart rate and blood pressure, these patients have other signs of sympathetic activation including tremulousness and anxiety. They may respond to abdominal binders to reduce venous capacitance and non-selective beta-antagonists like propranolol [2,4]. Acetylcholinesterase inhibitors may also work in this group by increasing parasympathetic tone, thereby mitigating the sympathetic over-activation. Alpha-2-agonists, like clonidine, are commonly used for pressure control [3].

Overall, there are some interesting aspects of Ms. X's case that warrant further discussion. Given her increases in blood pressure and serum catecholamines, it is most likely that she has the hyperadrenergic subtype of POTS. As mentioned above, patients with this type of POTS often have anxiety, a sign of sympathetic activation. The interesting part of her case was the multiple discussions between the psychiatric and medical services over several admissions about the cause of her symptoms and the treatment required. Multiple internists firmly held that anxiety or panic was driving the tachycardic and hypertensive episodes. The psychiatric and med-psych teams insisted that the patient had an autonomic dysfunction that was driving her symptoms and that methods solely targeted to reduce anxiety would have little benefit for her. They insisted that a more comprehensive treatment for POTS would better treat her illness. Unfortunately, patients with POTS are overly characterized as being anxious, and their anxiety is viewed as the driving force rather than one component of the overall illness [2,5]. Several studies have examined anxiety in patients with POTS.

Masuki et al. sought to better understand the relationship between POTS and anxiety [5]. In a group of fourteen patients with POTS and ten healthy controls, all subjects underwent heart rate monitoring during lower-body negative pressure (LBNP), simulating an orthostatic increase in lower extremity venous pooling, and mental arithmetic tests to represent an anxiety-provoking stimulus. Patients with POTS had significantly higher heart rates with LBNP than controls. However, there were no differences in heart rates between groups during mental arithmetic tests, supporting the point that physiologic changes in patients with POTS are not solely caused by anxiety.

In another study, Raj et al. had patients with POTS complete numerous questionnaires for psychiatric disorders, including the Beck Depression Inventory, Beck Anxiety Inventory, and Anxiety Severity Index, and also undergo the Structured Clinical Interview for DSM-IV axis-I disorders (SCID) [6]. They found that patients with POTS had no difference in prevalence of anxiety or depressive disorders compared to the general population.

The above studies support the view that the tachycardia, hypertension, and other symptoms in POTS are due to a diffuse and peripheral autonomic dysfunction rather than solely on anxiety. As in the case with Ms. X, POTS can be confused with anxiety or panic attacks, but the primary team should be aware of the diagnosis so that effective treatment is initiated, including agents like alpha-1 agonists or fludrocortisone, instead of focusing only on anxiolytics. Furthermore, understanding that the patient's problem is orthostatic intolerance rather than primary anxiety may help physicians to quickly start a more comprehensive treatment regimen that includes beta-blockers, which improve symptoms and decrease orthostatic changes in heart rate in patients with POTS [4]. Recognizing the distinctions between primary panic attacks/anxiety and POTS may also help psychiatrists on consult services when asked to see a patient with unexplained tachycardia, hypertension, tremulousness, and anxiety. The severity of tachycardia and hypertension in addition to an association with postural changes can suggest POTS within the differential diagnosis.

The second notable aspect of Ms. X's case is the debate regarding her serum catecholamines. She had fractionated catecholamines drawn on several occasions, and on one occasion they were normal. Several members of her multiple treating teams used the normal values to support their view of a psychiatric diagnosis. However, the normal values were observed when the patient was supine and asymptomatic. This highlights the important point that fractionated catecholamines should be drawn in patients with POTS in the setting of an orthostatic positional change, or during an acute tachycardic episode. In fact, this is one of the recommendations for diagnosing POTS [1,2]. Although seeing a normal plasma norepinephrine while the patient is supine, and not symptomatic, is important, this value can be misinterpreted if not taken in the context of another plasma norepinephrine drawn at the time of an orthostatic crisis. An elevated norepinephrine level suggests, though is not diagnostic of, POTS, as it represents neuronal spill over. A disproportionate elevation of epinephrine, which was not observed in this patient, represents an adrenal secretory phenomenon, as would more likely be evident with primary anxiety. Thus, providers should be careful of the context in which they are drawing these laboratory values. A broader understanding of the diagnostic criteria for POTS can eliminate much confusion for both the physicians and the patients.

Conclusion

This review focuses on postural orthostatic tachycardia syndrome by highlighting the case of a 23-year-old female diagnosed with POTS who presented to the emergency department with an episode of tachycardia, hypertension, headache, tremulousness, and anxiety. She required several days of IV labetolol for pressure control and was eventually discharged home with two beta-blockers for blood pressure and heart rate control in addition to tizanidine, gabapentin, methadone, and as-needed fentanyl. Her case was notable for a history of multiple referrals to psychiatry and the med-psych service for management of anxiety in spite of her diagnosis of POTS. This case highlights the importance for a broader understanding of POTS and some of the frustrations and labels that patients with this disorder face. Moreover, the diagnostic criteria for POTS based on plasma

catecholamines should be more widely publicized. It is imperative that norepinephrine be drawn both supine and after standing to look for orthostatic changes. Recognizing the symptoms and diagnosis of POTS may help decrease confusion between physicians regarding the etiology of symptoms in this patient population.

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