

Postural orthostatic tachycardia syndrome following Lyme disease

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Abstract

Background: *A subgroup of patients suffering from Lyme disease (LD) may initially respond to antibiotics only to later develop a syndrome of fatigue, joint pain and cognitive dysfunction referred to as 'post treatment LD syndrome'. We report on a series of patients who developed autonomic dysfunction in the form of postural orthostatic tachycardia syndrome (POTS).*

Methods: *All of the patients in this report had suffered from LD in the past and were successfully treated with antibiotics. All patients were apparently well, until years later when they presented with fatigue, cognitive dysfunction and orthostatic intolerance. These patients were diagnosed with POTS on the basis of clinical features and results of the tilt table (HUTT) testing.*

Results: *Five patients (all women), aged 22–44 years, were identified for inclusion in this study. These patients developed symptoms of fatigue, cognitive dysfunction, orthostatic palpitations and either near syncope or frank syncope. The debilitating nature of these symptoms had resulted in lost of the employment or inability to attend school. Three patients were also suffering from migraine, two from anxiety and depression and one from hypertension. All patients demonstrated a good response to the employed treatment. Four of the five were able to engage in their activities of daily living and either resumed employment or returned to school.*

Conclusions: *In an appropriate clinical setting, evaluation for POTS in patients suffering from post LD syndrome may lead to early recognition and treatment, with subsequent improvement in symptoms of orthostatic intolerance. (Cardiol J 2011; 18, x: xx–xx)*

Key words: postural tachycardia, orthostatic intolerance, Lyme disease

Introduction

Lyme disease (LD), a tick-borne illness caused by the spirochete *Borrelia burgdorferi*, is the multi-system disorder that begins with erythema migrans and may later be followed by widespread complications which may involve the nervous system, cardiovascular system and musculoskeletal system [1, 2]. While most of these manifestations usually respond to antibiotic treatment, there is a subgroup of patients who later develop a syndrome of fatigue, joint

pains and cognitive dysfunction known as 'post treatment LD syndrome' [3–5]. The post treatment LD syndrome has been reported to result in a substantial decline in the quality of life in affected patients [5]. We present a series of patients who suffered from LD and were successfully treated initially with antibiotics, but who later developed a syndrome of fatigue, cognitive dysfunction and symptoms of orthostatic intolerance (OI). Further investigation revealed that each of these patients was suffering from postural orthostatic tachycardia syndrome (POTS).

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Methods

This was a single center report on a series of five patients who followed our clinic for orthostatic intolerance. This study was approved by our local Institutional Review Board. All of these patients had suffered from LD in the past and were successfully treated with antibiotics. All of these patients were apparently well, until years later when they started with fatigue, cognitive dysfunction and OI. In a retrospective chart review, we collected data including demographic information, presenting symptoms, laboratory data, tilt-table response, and treatment outcomes. OI refers to a heterogeneous group of disorders of hemodynamic regulation characterized by insufficient cerebral perfusion resulting in symptoms during upright posture relieved by recumbency. Symptoms included syncope, near syncope, fatigue, palpitations, exercise intolerance, lightheadedness, diminished concentration, and headache [6].

Head up tilt test (HUTT) protocol

The protocol used for tilt table testing has been described elsewhere, but basically consisted of a 70-degree baseline upright tilt for a period of 30 min, during which time heart rate and blood pressure were monitored continually [7]. If symptomatic hypotension and bradycardia occurred, reproducing the patient's symptoms, the test was ended. If no symptoms occurred, the patient was lowered to the supine position and an intravenous infusion of isoproterenol started with a dose sufficient to raise the heart rate to 20–25% above the resting value. Upright tilt was then repeated for a period of 15 min.

Criterion for diagnosing postural orthostatic tachycardia syndrome

POTS was defined as symptoms of OI (of greater than six months' duration) accompanied by a heart rate increase of at least 30 bpm (or a rate that exceeds 120 bpm) observed in the first ten minutes of upright posture or HUTT occurring in the absence of other chronic debilitating disorders [6, 7].

Treatment protocols

The treatment protocols employed were based on our previous experiences with orthostatic disorders and are described in detail elsewhere [6–11]. Briefly, a sequence of therapies is employed that included physical counter maneuvers as well as increased dietary fluids and sodium. If these were ineffective, pharmacotherapy was initiated in a sequence generally consisting of fludrocortisone, midodrine, methylphenidate, selective serotonin re-

uptake inhibitors, pyridostigmine, and erythropoietin, either alone or in combination. The rationale for this sequence and the doses employed are described in detail elsewhere. A treatment was considered successful if it provided symptomatic relief. Not all drugs were used in every patient.

Results

Five patients (all women), aged 22–44 years, were identified for inclusion in this study. All these patients had suffered from LD and were apparently cured with antibiotics and were asymptomatic for periods ranging from two to 12 years. Table 1 summarizes the clinical features of these patients.

Diagnosis of Lyme disease

LD was diagnosed in each patient based on the combined clinical criteria and immunological responses seen against *Borrelia burgdorferi*. Each patient had an acute episode of LD. None presented with any cardiac complications. The acute episode presented mainly as skin rash with a prior history of tick bite. All these patients had suffered from LD and were apparently cured with antibiotics and were asymptomatic for periods ranging from two to 12 years (Table 1).

Symptoms of orthostatic intolerance

After the quiescent period of two to 12 years following their initial infection with LD, all these patients developed symptoms of fatigue, cognitive dysfunction, orthostatic palpitations and either near syncope or frank syncope. These symptoms had resulted in substantial limitation of activities of daily living, to such an extent that each patient either lost their employment or became unable to attend school. The fear of passing out upon standing had resulted in substantial limitation and all these patients had initially become housebound.

Tilt testing

All five patients were evaluated by a head up tilt table testing. All demonstrated a tilt pattern consistent with POTS (the criteria have been discussed in the methods section above). Three patients had a tilt table response seen within the ten minutes; the other two patients had to be started on an isoproterenol infusion before the test was repeated.

Comorbidity

Three patients complained of recurrent migraines, two of anxiety and depression, and one of hypertension. The patient who was suffering from hypertension had wide fluctuations in her blood

Table 1. Clinical characteristics of the postural orthostatic tachycardia syndrome patients with pre-existing post Lyme disease syndrome.

Patient #	1	2	3	4	5
Age (years)	44	33	31	23	21
Onset after Lyme disease (years)	3	12	5	4	4
Fatigue	+	+	+	+	+
Orthostatic palpitations	+	+	+	+	+
Near syncope	+	+	+	+	+
Syncope	+	+	+	+	+
Cognitive dysfunction	+	+	+	+	+
Anxiety	+	-	-	+	-
Depression	+	+	-	-	-
Migraine	+	-	+	-	+
Hypertension	-	+	-	-	-

pressure, with episodes of very high blood pressure followed by episodes of hypotension.

Medications

The commonly used medications in this group of patients were fludrocortisone (in two) and pyridostigmine (in three). Bupropion, erythropoietin and clonidine were used in one patient each (Table 2).

Response to treatment

All patients demonstrated a good response to the employed treatment. The orthostatic symptoms (especially fatigue) improved in all of them. In three patients, their syncope was completely abolished, while two patients have continued to have syncope but at a much lesser frequency than before starting treatment. All except one patient were able to engage in their daily activities and either resume employment or return to school.

Discussion

A subgroup of patients diagnosed with chronic LD may in fact have post LD syndrome. These patients usually improve initially with the antibiotics and have resolution of physical symptoms and signs of LD. However, after a quiescent period, they again develop symptoms of fatigue, pain and cognitive dysfunction. Interestingly, these symptoms usually develop within six months following a successful treatment with antibiotics. The exact etiology of this syndrome remains elusive. Randomized trials have failed to show any benefit of continued antibiotic use in patients suffering from post LD syndrome, as this syndrome is not thought to be due to persistence of spirochete infection in this group

Table 2. Various treatments employed in the study group.

Fludrocortisone	+	-	-	+	-
Pyridostigmine	-	+	+	+	+
Bupropion	+	-	-	-	-
Clonidine	-	+	-	-	-
Erythropoietin	-	-	+	-	-

of patients [13–15]. In a recent report by Chandra et al. [16] anti-neural antibody reactivity was found to be significantly higher in the patients suffering from post LD syndrome (49%) as compared to post Lyme healthy individuals (18.5%) or healthy individuals without a history of LD (15%) with a $p < 0.01$. It has been postulated that LD can trigger ‘auto antibodies’ that can bind or block post-synaptic acetylcholine receptors in the autonomic ganglia. However, due to the retrospective nature of the current study, we did not check for synaptic antibodies.

All our patients demonstrated a good response to pyridostigmine. Pyridostigmine augments the availability of acetylcholine at the synaptic cleft by inhibiting acetylcholine esterase, an enzyme that causes hydrolysis of acetylcholine. Pyridostigmine has been shown to improve symptoms in patients suffering from POTS or OI [17, 18]. Clinical symptoms of post LD syndrome are debilitating and have been reported to impair quality of life [5]. In our patients, symptoms of fatigue, orthostatic palpitations, cognitive dysfunction and syncope had resulted in substantial impairment of the quality of life in each patient. After diagnosis and initiation of the treatment, all but one patient reported a marked

improvement in their symptoms and quality of life. While there is no proven therapy for symptom control in patients suffering from post-treatment LD syndrome, it is possible that some of these patients might have OI as a contributor to their symptoms. Recognition of orthostatic intolerance in this subset of patients may lead to the initiation of appropriate treatment earlier, with subsequent improvement in their symptoms and quality of life. Physicians need to have a high index of suspicion for OI in patients suffering from post-treatment LD syndrome.

Limitations of the study

This was a retrospective report on a relatively small number of patients. Because of the retrospective nature and small number we could not estimate any incidence of POTS in patients suffering from post LD syndrome. Also, some questions such as why only a few patients with post LD develop POTS remain unanswered from this report. A high index of suspicion for POTS may allow for its early recognition and treatment in patients suffering from post LD syndrome.

Conclusions

In an appropriate clinical setting, evaluation for POTS in patients suffering from post LD syndrome may lead to earlier recognition and treatment, with subsequent improvement in symptoms of OI.

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