

Postural orthostatic tachycardia syndrome in a patient with relapsing-remitting optic-spinal multiple sclerosis: A case report and discussion of possible mechanism

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Abstract

Postural orthostatic tachycardia syndrome (POTS) is characterized by orthostatic intolerance, a presentation of autonomic dysfunction which is frequently observed in the patients with multiple sclerosis (MS). Nevertheless, to date, there have been a few studies focusing on POTS in MS patients and the underlying pathomechanism. We present a 28-year-old woman with relapsing-remitting optic-spinal multiple sclerosis who also suffered POTS and discuss the possible pathomechanism of POTS in MS.

INTRODUCTION

Postural orthostatic tachycardia syndrome (POTS) with the typical symptoms of orthostatic intolerance is a presentation of autonomic dysfunction and is presumed the result of peripheral sympathetic nerve dysfunction.^{1,2} Multiple sclerosis (MS) is a central nervous system demyelinating disorder with autonomic dysfunction being commonly observed. Despite the fact that orthostatic intolerance and dizziness were observed in approximately half of MS patients, there have been only few reports on POTS in MS.^{3,4} We present here a case of relapsing remitting MS with POTS, and discuss the possible mechanism of POTS in MS.

CASE REPORT

A 28-year-old woman was diagnosed with MS after two distinct episodes of neurologic deficits, one involved the left optic nerve and the other the 2nd to 5th cervical spinal cord seven years earlier.⁵ Her symptoms and signs fully recovered after being given intravenous steroids. Since then, she experienced multiple relapses, predominantly involving periventricular white matter and thoracic spinal cord.

In early 2010, she complained of intermittent dizziness, fatigue accompanied with palpitations. The symptoms progressed with increased

frequency of palpitations and occasional chest tightness precipitated by prolonged standing. This persisted over the next six months. On examination, her height was 170 cm and weight 58 kg. She had a baseline heart rate of 88 beats per minute and supine blood pressure of 111/71 mmHg. Her left lower extremity sensation was preserved to vibration and joint position but significantly impaired for pin-prick and crude touch. She did not have motor deficit or gait abnormality. There were exaggerated deep tendon reflexes in both lower extremities and right Babinski sign was observed. The routine laboratory tests (complete blood count, electrolytes, kidney and liver function tests), inflammatory markers (C-reactive protein, erythrocyte sedimentation rate), analysis for rheumatic diseases (antinuclear antibody, rheumatoid factor, anti-Ro/SSA and La/SSB antibodies, anti-double stranded DNA antibody) and thyroid function tests were all normal. A series of cardiac tests including 24-hour Holter electrocardiographic recording and transthoracic echocardiography were unremarkable.

The diagnosis of POTS was confirmed by a head-up tilt testing demonstrating heart rate increment from 88 beats per-minute supine to 125 beats per-minute within 10 minutes of 70° head up tilt without orthostatic hypotension, and accompanied by symptoms of orthostatic intolerance such as dizziness and nausea. Her

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baseline ratio of low and high frequency powers of heart rate variability (LF/HF) was low (0.4).⁶ Low thoracic fluid content (18 L/k Ohm), reflecting the low totally fluid volume in the chest cavity related to postural tachycardia, was observed by transthoracic electrical bioimpedance method.^{7,8} During tilt, the total peripheral resistance increased from 730 to 1161 dyn.s/cm⁵, the cardiac output decreased from 8.1 to 5.31 L/min and the baroreflex sensitivity reduced from 13.7 to 7.5. Skin discoloration was observed in her legs after the tilt table test. In contrast to the nerve conduction studies of the lower extremity which showed no peripheral sensorimotor neuropathy, the prolongation of sympathetic skin response (SSR) latency (2450 milliseconds) in legs demonstrated peripheral autonomic denervation.

Repeat cranial MRI showed multiple abnormal high signal white matter lesions in bilateral corona radiata, periventricular region and callosal-septal interface without brainstem involvement (Figure 1). Spinal cord MRI showed persistent hyperintense changes of the 2nd to 7th thoracic cord with slight atrophy (Figure 2). In addition to increasing salt and fluid intake, she was treated with midodrine and propranolol. Her symptoms of orthostatic intolerance and orthostatic tachycardia markedly improved.

DISCUSSION

It has been reported that orthostatic dizziness may develop in equivalent to 50% of MS patients.^{3,4} However, the occurrence of POTS in MS has

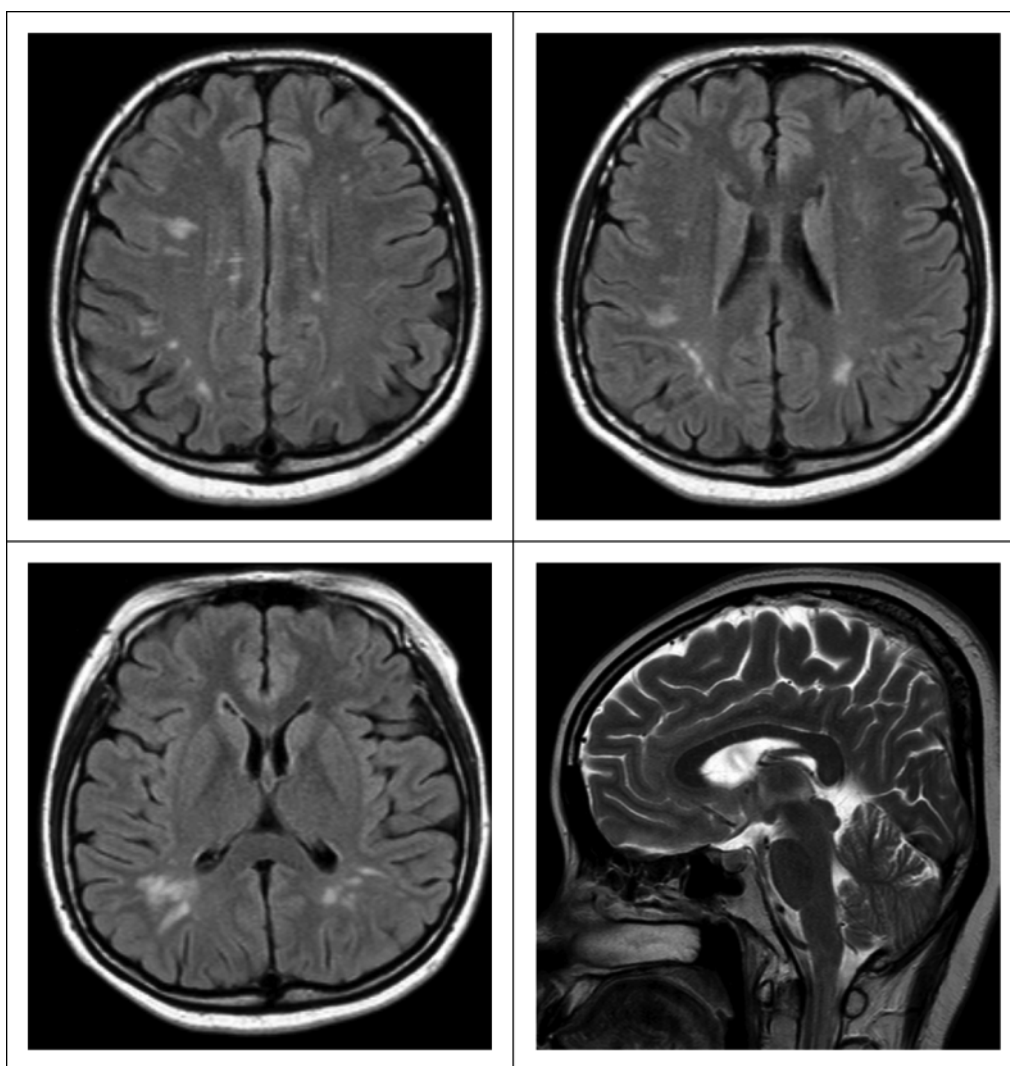


Figure 1. T2-weighted images of the cranial MRI reveal multiple abnormal high signals of white matter in bilateral corona radiata, periventricular regions and callosal-septal interface.



Figure 2. T2-weighted sagittal image of the spine MRI shows hyperintense changes of the 2nd to 7th thoracic cord with slight atrophy

rarely been reported. Grubb *et al.* reported a series of 9 MS patients with POTS.³ The patients were all Caucasians, age around 50 years and mostly females (89%) with co-morbidities of hyperlipidemia, migraine, coronary artery disease and diabetes mellitus. In contrast, our patient is ethnic Chinese, a young adult, and without systemic diseases.

The pathophysiology of POTS in MS patients remains unclear. The autonomic abnormalities in MS patients may possibly be caused by demyelination of autonomic regulatory areas and network involving the insular cortex, amygdale, cingulate, ventromedial prefrontal cortex, and paraventricular nucleus of hypothalamus. Plaques of the brainstem may also interfere with the descending pathways of autonomic nervous system.⁴ However, MRI studies did not demonstrate demyelination of central regulatory area as well as brainstem in our patient. Thus, other pathophysiology mechanisms are probably responsible for the POTS in our patient.

There are studies that proposed peripheral autonomic disorders to be involved in POTS. POTS occurs when there is excessive lower extremity venous pooling with standing. Autonomic denervation of the legs may thus result in the orthostatic intolerance and POTS.^{1,2}

Abnormalities of sympathetic skin response (SSR) have been found in more than 50% of patients with MS. This was thought to be due to lesion of the central sympathetic pathways.⁹ However cranial MRI studies in this patient did not demonstrate demyelination of central sympathetic pathways. Previous MRI studies in

MS patients also did not show any significant correlation between cardiovascular dysautonomia and demyelination in brain.^{10,11} Thus, at least a part of the lesions responsible for cardiovascular dysautonomia in MS are located outside the brainstem, i.e. in supramedullary reflex pathways or in the spinal cord.

In a study involving 75 MS patients, autonomic dysfunction correlated with spinal cord cross-sectional area reduction but not with spinal cord hyperintensities, suggesting that autonomic dysfunction are related to axonal loss rather than demyelinating lesions.¹² The study also showed that 30-48% of MS patients had abnormal SSR. The efferent part of SSR reflex arch consists of myelinated sympathetic fibers of neurons from intermediolateral nucleus in first thoracic to second lumbar segments of the spinal cord that terminate in paravertebral sympathetic ganglia. Prolonged SSR latency as well as hyperintense changes of the second to seventh thoracic cord segments with slight atrophy in our patient suggests the involvement of thoracic autonomic nucleus in the pathophysiology of her POTS.

In conclusion, we propose that peripheral autonomic denervation of legs from thoracic spinal cord atrophy and demyelination in our patient may be the pathophysiology of her POTS. Since autonomic dysfunction such as orthostatic intolerance is common in MS patients, we hope this report will help clinicians who cared for these patients. Comprehensive cohort study should also be done to investigate other probable causes and prognosis of POTS in MS patients.

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