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Abstract

Background/Objective: To report manifestation of autonomic dysreflexia (AD) in a man with multiple sclerosis (MS).

Design: Case report.

Findings: A young man presented with a history of several admissions to the emergency department with complaints of hypertensive attacks, palpitations, difficulty in breathing, headaches, and flushing. The attacks were attributed to a previously diagnosed anxiety disorder. Onset of numbness of the left leg numbness prompted a more thorough study, which showed evidence of MS. AD was suspected as the cause of his recurrent attacks of hypertension. Bladder distension was identified as the cause of AD, and his hypertensive attacks were controlled by management of neurogenic bladder.

Conclusions: This report emphasizes that AD can occur in MS. Somatic symptoms warrant thorough investigation before attributing them to psychosomatic causes.

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Key Words: Autonomic dysreflexia; Multiple sclerosis; Spinal cord injuries; Anxiety; Panic disorder; Hypertension

INTRODUCTION

Autonomic dysreflexia (AD) is an acute syndrome characterized by an unregulated massive sympathetic discharge that occurs in patients with spinal cord lesion as low as level T10 but typically at or above the sixth thoracic level (T6) (1,2). The significant signs are hypertension (HT), altered heart rate (usually reflex bradycardia), anxiety, visual changes, cardiac arrhythmia, and nasal congestion. Headache, flushing, and sweating usually occur above the level of injury (3). Any stimuli below the level of the spinal lesion can trigger AD. Urinary distension, urinary tract infection, bladder irrigation, fecal impaction, pressure ulcers, and surgery are the common stimuli of AD (4). Recognition of AD is important because inadequate management can have adverse consequences, including death (5). AD is a known syndrome in patients with traumatic spinal cord injury; however, there is less awareness of this syndrome in individuals with multiple sclerosis (MS) (6).

Psychiatric disturbance is frequently observed in MS, with depression (50%), cognitive impairment (40–65%), euphoria, anxiety disorders, and personality changes (7,8) being the most prevalent conditions. Some of the peripheral manifestations of anxiety such as HT, hyperhidrosis, and palpitations are similar to those of AD (9). Coexistence of an anxiety disorder and AD may lead to misdiagnosis of AD in MS. It is critical to increase awareness and question the etiology of the symptoms, because AD can be a life-threatening syndrome. This report shows the presentation of AD in a patient with MS and panic disorder.

CASE REPORT

A 21-year-old single man presented to the department of physical medicine and rehabilitation with complaints of numbness of the left leg after starting to exercise at a fitness center 2 weeks ago. He thought that he had injured his lower back or abdominal muscles.

His history showed a diagnosis of panic disorder 4 years earlier. He had had an episode of left hemihypoesthesia 1 month ago that had resolved within 24 hours. He had had 4 recent emergency admissions for suddenly increased blood pressure (BP) ranging from 160/90 to 220/110 mmHg. During 2 of these admissions, he had elevated heart rate (range, 86–131 beats/min). The patient claimed that his BP was usually ~120/60 mmHg. Headache, flushing, and sweating were

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Table 1. Laboratory Tests

Test	Units	Normal Range	Result
Fasting blood sugar	mg/dL	74–106	93
Blood urea nitrogen	mg/dL	<50	17
Creatinine	mg/dL	0.7–1.2	0.93
Alanine aminotransferase	U/L	<41	16
Aspartate aminotransferase	U/L	<38	15
Sodium	mmol/L	136–145	140
Potassium	mmol/L	3.5–5.1	4.1
Calcium	mg/dL	8.8–10.2	9.6
Hemoglobin	g/dL	13.2–17.3	16.4
Hematocrit	%	39–49	47.3
White blood count	10 ³ /μL	4.5–13	5.98
Platelet	10 ³ /μL	150–400	162
Erythrocyte sedimentation rate	mm/h	<15	2
Total protein	g/dL	6.4–8.3	7.8
Albumin	g/dL	3.4–4.8	4.7
Vanillylmandelic acid	mg/24 h	<6.5	2.5
Total protein, CSF	mg/dL	15–45	28
Glucose, CSF	mg/dL	40–70	69
Chloride, CSF	mmol/L	118–132	125
Albumin, –CSF	mg/dL	10–30	22.4
Immunoglobulin IgG, CSF	mg/L	<55	45.4
IgG index, CSF		<0.7	0.82
Oligoclonal band, CSF			Positive
Free T4	ng/dL	0.93–1.7	1.67
Free T3	pg/mL	2–4.4	3.22
Thyroid-stimulating hormone	mIU/L	0.27–4.2	1.49
Anti-thyroglobulin	IU/mL	<115	<10.00
Anticardiolipin IgG	GPL	<20	7.8
Anticardiolipin IgM	GPL	<20	2.7
ANA (indirect immunofluorescence technique)			Negative
Anti dsDNA			Negative
ANCA			Negative
Anti SS-A antibodies			Negative
<i>Borrelia burgdorferi</i>			Negative
Human immunodeficiency virus			Negative
HBs antigen			Negative
Hepatitis C virus			Negative
Somatosensory evoked potential			Increased latency of left posterior tibial nerve (56.3 ms, 31.5% increased compared with right side)

ANCA, anti-neutrophilic cytoplasmic antibodies; GPL, 1 GLP unit = 1 μg of affinity purified IgG ACA from an index sample.

reported during each admission. Cardiology and internal medicine consults were requested to study the etiology of these attacks of HT. Renal Doppler ultrasonography, abdominal ultrasonography, renal artery magnetic resonance (MR) angiography, funduscopy examination, echocardiography, and cardiac examination were unremarkable. A neurologic examination was not done. His vanillylmandelic acid level was in the normal range (2.5 mg/24 h; range, < 6.5 mg/24 h). His whole blood count, biochemistry, and urine analysis were normal (Table 1). Captopril 25 mg and labetalol 25 mg/d were

prescribed for hypertension, but he continued to have labile HT.

The hypertensive attacks were attributed to his history of panic disorder. The diagnosis of panic disorder was confirmed by the psychiatry department of our hospital according to Diagnostic Manual of Mental Disorders IV criteria (10). However, when questioned in detail, he reported that the panic attacks were characterized by palpitations, difficulty breathing, fear of dying, nausea, feelings of derealization, and numbness of the feet and hands but not elevated BP, diaphoresis, or facial flushing. Cranial MR imaging

Figure 1. T2-weighted axial images of cranial MRI show lesions in corpus callosum body, left corona radiata, and left temporal lobe.

(MRI) 3 years ago had shown no abnormality. The panic attacks responded well to psychopharmacotherapy. He had not received any psychiatric pharmacotherapy for the previous 3 years.

He had no low back pain with movement and no limited range of motion. He had global hypoesthesia of the left leg. He did not have hypoesthesia of the left arm (tested by light touch). No motor deficit was observed. Deep tendon reflexes were hyperactive bilaterally in the lower extremities and had bilateral Achilles clonus. He had no pain with deep palpation of abdominal muscles, but hypoesthesia of this region was detected. When a neurologic examination was done in detail, loss of sensation was observed below the level of T4. Cutaneous abdominal reflexes were absent on the left side. No gait abnormality was observed. Questions about his urinary and bowel function revealed occasional urinary hesitancy (he sensed the need to urinate but had difficulty in starting to void). He did not report any abnormality in

sexual function such as decreased libido or erectile or ejaculatory dysfunction.

Cranial MRI showed sclerotic plaques on the left temporal lobe, corpus callosum body, and left corona radiata (Figure 1). MRI of the dorsal and cervical spine showed a sclerotic plaque of the spinal cord at C2 (Figure 2A). Decreased thickness of the spinal cord was observed between T2 and T4 (Figure 3). Based on these findings, a diagnosis of MS was made, and he was referred to the neurology department.

Ten days later, he developed a disturbed gait pattern characterized by slow walking velocity, wide step width, and decreased stride length. He had poor balance while turning and rapid alternating movements. These symptoms suggested a new MS attack; therefore, new cranial and cervical MRIs were done. The new cranial MRI (10 days later) showed a new-onset millimetric plaque on the left anterior portion of the medulla oblongata (Figure 4). The new cervical MRI showed a 4-mm craniocaudal expansion of the plaque at C2 level (Figure 2B). The

Figure 2. (A) Sagittal T2-weighted image shows a hyperintense intramedullary lesion at the level of C2. (B) Sagittal T2-weighted image shows the craniocaudal height of the lesion increased in 10 days from 14 to 18 mm.

patient now met the McDonald diagnostic criteria for MS (2 known attacks, 2 or more MRI lesions consistent with MS, and positive cerebral spinal fluid [CSF] findings) (11) (Table 1). The patient was diagnosed with the relapsing-

remitting form of MS based on the recent, brief attack of left hemihypoesthesia 1 month ago and the new attack with disturbed gait pattern. This exacerbation of MS was treated by methylprednisolone infusion for 10 days followed by glatiramer acetate (Copaxone) injections once daily.

One month later, the hypertensive attacks (accompanied with tachycardia, flushing, and diaphoresis) recurred several times but without difficulty in breathing or fear of dying. These symptoms and signs were attributed to AD. He was hospitalized again to document AD and identify the responsible noxious stimulus. Bladder distension caused by neurogenic bladder was thought to be the noxious stimulus, and a urodynamic evaluation was planned. During his hospital stay, AD was observed. BP was 230/120 mmHg, and his heart rate was 120 beats/min. Flushing and diaphoresis of his face were prominent, and he complained of headache and anxiety. Bladder distension was confirmed by catheterization, which yielded 1,200 mL of urine. After catheterization, his BP immediately decreased to 112/73 mmHg, and his heart rate dropped to 79 beats/min. Headache, anxiety, diaphoresis, and flushing also resolved. A urine sample was sent to rule out urinary tract infection. Urine culture was negative. The urodynamic evaluation showed a compliant but hypocontractile bladder. Clean intermittent catheterization was resumed with a frequency of 4 times daily. Two months later, bladder dysfunction was being managed well with this program, and the patient's BP remained stable. His panic disorder was controlled with escitalopram 20 mg/d and alprazolam 0.25 mg twice daily.

Figure 3. T2-weighted sagittal images of the spine MRI show the decrease of thickness of the spinal cord between T2 and T4 level.

Figure 4. (A) Axial FLAIR W image shows no lesion on medulla oblongata. (B) Axial FLAIR W image performed 10 days later shows a new onset plaque on the left anterior portion of the medulla oblongata.

DISCUSSION

This case shows that AD can occur in individuals with MS who have plaques or lesions on the spinal cord at or above the sixth thoracic level. Moreover, it can be the initial or predominant sign of primary disease. Furthermore, this case showed delayed diagnosis of AD caused by the coexistence of an anxiety disorder with similar symptomatology.

AD is caused by spinal reflex mechanisms that remain intact despite the patient's injury/dysfunction of the spinal cord. The sympathetic nervous system supplies blood vessels throughout the body with vasoconstrictor axons that control local blood flow and contribute to total peripheral resistance. Signals arising in the central nervous system send specific controls to different tissues according to the functional response for each organ by means of reflexes and patterned regulation from higher centers. The sympathetic outflow arises in the thoracolumbar cord, being damaged directly if the lesion involves regions between T1 and L3 or the ventral roots at these levels and being disconnected from the higher control centers by injuries to descending pathways in the cervical cord. The degree of disordered visceral and vascular function that ensues depends on the level and the severity of trauma in each individual (12).

A noxious stimulus below the level of the lesion produces an afferent impulse that generates a generalized sympathetic response, which results in vasoconstriction below the neurologic lesion (13). With lesions at or above the T6 level, the splanchnic vascular bed becomes involved, which provides the critical mass of blood vessels required to cause elevation of the BP. The brain detects HT crisis through intact baroreceptors and stimulates parasympathetic nervous system in an attempt to lower BP. However, these inhibitory signals are blocked in the injured spinal cord and only affect vessels above the level of injury, which is characterized by headache, diaphoresis,

and vasodilatation with skin flushing (14). In this patient, the noxious stimulus was bladder distension. Almost all signs and symptoms of AD were present. He had headache, flushing, and diaphoresis of the face, tachycardia and anxiety, and a tendency toward tachycardia. Although it is often suggested that bradycardia is a common finding, the response varies among people at risk for AD. Although the expected physiological baroreceptor response to the abnormal HT is an increase in parasympathetic activity and a drop in heart rate, this is not always the case. Tachycardia is not an uncommon finding, especially in patients with cervical lesions (15,16), as in this case.

Hypertension is a relatively common manifestation of AD. In this case, HT was the dominant manifestation of the AD. Possible etiologic factors that may cause HT in a young man were studied in the emergency department. However, AD was not considered because his MS and spinal cord atrophy had not been diagnosed. Although he had no neurologic complaints at the time of admissions to the emergency unit, he might have neurologic signs. Failing to question and examine the patient for any neurologic symptoms and signs the attribution of the symptoms to his psychiatric problems led to delayed diagnosis of the primary disease (MS), and consequently, the diagnosis of the complication of AD. As seen in this case, manifestation of AD by severe HT before the diagnosis of primary disease has been previously reported (17).

Most clinicians are less familiar with AD because they see few patients with spinal cord injury. Clinician awareness is important in preventing the deadly consequences of this syndrome. Only 1 study in the recent literature discussed AD in MS (6). In the same study, it is mentioned that clinicians who are familiar with MS have little or no knowledge of AD.

The previous diagnosis of panic disorder in this patient presented a challenge because some of the symptoms of AD were closely related to those of an anxiety syndrome, such as palpitations, hyperhidrosis, headache, and HT. Furthermore, no other etiologic factor was identified to explain HT. Because this patient had been diagnosed with panic disorder 4 years ago in another hospital, we did not have access to the details of the previous examination. The patient reported that he had palpitations, difficulty in breathing, fear of dying, nausea, feelings of derealization, and numbness of the feet and hands, but no HT at that time. He also informed us that the cranial MRI at that time showed no abnormality but that a spinal MRI was not performed (which would have shown any existing spinal cord lesions). With psychotropic medication, his complaints had resolved, indicating that the symptoms of this early event were not caused by AD. Also, at that time, he had no symptoms of AD such as hypertensive attacks, diaphoresis, or flushing.

CONCLUSION

Although uncommon, AD can occur in individuals with MS who have plaques or lesions of the spinal cord at or above T6. A complete physical and neurologic examination is essential to establishing the diagnosis of MS, as well as for diagnosing and preventing AD in these patients. Furthermore, clinicians should be careful about attributing somatic symptoms to psychological problems. Patients with known psychological conditions should be studied in detail because their symptoms may be indicative of another disorder.

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