Orthostatic hypotension-induced autonomic dysreflexia

Article abstract—Three patients with chronic traumatic cervical myelopathy had severe orthostatic hyperhidrosis. Orthostatic challenge revealed that hypotension preceded hyperhidrosis, hypertension, and chills, all manifestations of autonomic dysreflexia. Treatment of orthostatic hypotension with fludrocortisone acetate relieved these symptoms. Therefore, orthostatic hypotension may trigger autonomic dysreflexia and the usual way of managing such patients, propping them upright, may be counterproductive.

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Ramesh K. Khurana, MD

Cervical spinal cord transection in humans is frequently associated with immediate onset of orthostatic hypotension.[1,2] Autonomic dysreflexia, however, appears months or years later.[3] The stereotyped response follows sensory stimulation below the level of the lesion; there is hyperhidrosis, flushing or pallor of the skin, reflex change in heart rate, and a sudden rise in blood pressure. Hypotension induced by head-up tilt has been used therapeutically to counteract the hypertension.[2] We have studied three quadriplegic patients in whom hypotension itself precipitated or aggravated the symptoms of autonomic dysreflexia.

Case reports. Patient 1. A 41-year-old man was disabled for 1 month by drenching sweats. He had sustained a C6-7 fracture and quadriplegia after a diving injury 26 years earlier. Cervical laminectomy revealed a crushed spinal cord. Recurrent urinary tract infections led to ileal loop construction at age 41, followed by severe, painful spasms of the legs and abdominal muscles. These spasms were refractory to usual medical management and were treated with intercostal nerve blocks from T-8 to T-12. To minimize the afferent input, a longitudinal myelotomy was carried out from T-8 to T-12 and L-1 to L-3. This was followed by profuse sweating, chills, lightheadedness, and blood pressure fluctuations from 54/42 mm Hg to 266/124 mm Hg when he was supine. Use of a pillow or sitting in a chair aggravated the symptoms. Consequently, he was disabled.

Examination showed patulous anal sphincter, absent bulbocavernosus reflex, right Horner's syndrome, and paralysis below the C-6 level. There was hypalgesia at the C-6 level and analgesia distally. Routine chemistries, blood volume, ACTH stimulation test, and thyroid functions were normal. Continuous ECG recording and echocardiogram were normal. Cortical somatosensory evoked potentials (peroneal, median) were absent.

The patient developed dizziness followed by drenching sweat with head-up tilt of 15 to 20°. Upon sitting, the blood pressure dropped to 54/42 mm Hg. Within a few minutes he felt a burning sensation in the pelvic region followed by sweating and piloerection in the face, neck, upper extremities, and chest down to the lower margins of the rib cage. He shivered, had pounding occipital headache, and his blood pressure increased to 110/80 mm Hg. Treatment with fludrocortisone acetate, 0.3 mg/d, diminished his symptoms within 1 week. After 6 weeks, the patient was asymptomatic and employed full time. Two attempts at discontinuation of treatment, 12 and 18 months later, resulted in a return of his symptoms requiring reinstitution of treatment within 1 week. The symptoms improved within 4 days of reinstitution of treatment. The patient was successfully weaned off treatment after 2 years.

Patient 2. A 38-year-old woman presented with profuse sweating when upright. Ten years earlier, she had had spinal cord injury with complete paralysis below the fifth cervical level. Laminectomy, posterior wiring, anterior fusion, and prolonged rehabilitation resulted in some motor improvement of the right upper extremity. The episodes of sweating, hypertension, and headache, 1 year after her injury, responded to management of decubitus ulcers, bladder, or bowel dysfunction. One year before admission, the patient noted frequent episodes of sweating within a few minutes after sitting in a wheelchair that could not be attributed to the usual trigger factors. Sweating on the entire face and neck was most profuse along the hairline, the forehead, and the back of the neck. A towel was soaked wet in 1 hour. Sweating was accompanied by shaking, goose flesh, pallor, chattering of teeth, and agitation.

Examination revealed normal pupils with motor paralysis and analgesia below C-5 level. Routine blood studies, AM and PM cortisol, thyroid function tests, glucose tolerance test, and blood volume were normal. Echocardiogram was normal. A continuous ECG recording revealed heart rate varying between 61 to 149 beats per minute with occasional sinus tachycardia. Cranial CT was normal. Cortical somatosensory evoked potentials with stimulation of the median or peroneal nerves were absent.

The patient, when in sitting position, had orthostatic hypotension followed by rising blood pressure, profuse sweating, chattering of teeth, piloerection, blurred vision, and agitation (table 1). The sweating was profuse over the head, neck, and chest regions and moderate down to the umbilicus. She also manifested piloerection down to the lower margin of the rib cage. When supine, symptoms improved within 10 minutes. Within 1 week of treatment with fludrocortisone acetate, 0.3 mg/d, she had only shivering and mild chattering without sweating when upright. Three months later, the patient was asymptomatic and gainfully employed. Four years after the start of treatment, she is asymptomatic on fludrocortisone, 0.2 mg/d.

Patient 3. A 34-year-old man suffered cervical injury and quadriplegia in an auto accident 10 years earlier. Over a period of 4 months, he partially regained his strength in the upper limbs and breathed comfortably. Five years after the accident, while sitting, he would develop symptoms of dizziness, syncope, and sweating. Bowel and bladder management only partially relieved his symptoms, but the symptoms ceased after the administration of IV fluids for 9 days. Two years before admission, he reported increasing dizziness, sweating,

Table 1. Orthostatic challenge (patient 2)

Position	Time in minutes	Blood pressure (mm Hg)	Heart rate per minute	Symptoms
Supine	—	90/56	92	0
Sitting	1	80/68	110	0
	5	64/50	88	0
	7	80/58	104	Onset of sweating
	10	100/70	96	Profuse sweating head, neck, and chest Piloerection down to rib cage, chattering of teeth
	15	130/90	96	As above, blurred vision and agitation
	20	140/70	76	Same as above
Supine	5	110/66	76	Symptoms improving
	10	80/56	90	Symptoms abated

Table 2. Orthostatic challenge (patient 3)

Position	Time in minutes	Blood pressure (mm Hg)	Heart rate per minute	Symptoms
Before treatment				
Supine	—	96/60	60	0
Sitting	1	80/70	96	0
	5	70/54	96	0
	10	70/54	100	0
	30	54/40	86	Dizziness, "weak eyes," headache
	45	70/50	86	Same as above
	60	150/110	72	Nervous; sweating face, neck, and upper chest on the right with midline demarcation; right upper limb cold and clammy
After treatment with fludrocortisone acetate 0.1 mg/d × 7 days				
Supine	—	116/66	68	0
Sitting	1	104/64	96	0
	5	76/58	104	0
	10	76/58	104	0
	30	72/60	90	0
	45	80/60	92	0
	60	78/60	90	0

and even blackout while sitting in bed.

The examination revealed ptosis on the left. Motor strength was diminished distally in the fingers, wrists, and elbow extensors bilaterally, but was normal in the deltoid and biceps muscles. Both lower extremities were paralyzed except for some voluntary movements in the left toes. Sensation to pinprick was normal to C-6 level, diminished to T-8 level, and absent distally, but S-2, S-3, and S-4 segments were partially spared. Routine chemistries, glucose tolerance test, blood volume, and AM and PM cortisol values were normal. CSF fluid analysis was normal and somatosensory evoked potentials with stimulation of peroneal nerves produced no consistent cortical response.

Sweating appeared on the right side of the face when the patient was in a left lateral position and terminated when supine. Sitting produced dizziness, hypotension, and headache (table 2) and was followed by a feeling of nervousness, and sweating of the face, neck, and upper chest on the right with midline demarcation. His right upper extremity was cold and clammy. A 60-minute orthostatic challenge, done five times in 48 hours, induced these episodes three times. He was treated with fludrocortisone acetate, 0.1 mg/d, and after 1 week he was able to sit in the wheelchair in excess of 3 hours without developing symptoms. It did not improve right facial sweating in the left lateral position.

Autonomic investigations. These patients had sustained cervical spinal cord injury between segments C-5 and C-7, 10 to 26 years earlier. The lesions were clinically and electrophysiologically complete in the first two patients and clinically incomplete in the third patient. The patients were previously in a wheelchair much of the day until the onset of sweating disturbances. Autonomic evaluation was carried out after excluding the usual precipitating factors for autonomic dysreflexia. During autonomic assessment, bladder emptying was ensured.

Autonomic functions of pupils, sweat glands, heart, and blood vessels were assessed in all three patients (table 3). Hydroxyamphetamine test, sweat test, tilt table test, and norepinephrine infusion study were employed to assess sympathetic functions.[4-7] Sinus arrhythmia, cold face test, and atropine administration determined vagal activity.[8-10] Pupillary dilatation in response to the topical application of hydroxyamphetamine was abnormal in the first patient only. Thermal-induced sweating was abnormal in all three patients, but the pattern of distribution varied. It was absent in the third patient and was confined to the head and neck region in the second patient. The first patient had facial anhidrosis with preserved sweating over the neck, chest up to T-6 level, and over the ulnar aspects of both upper limbs. Since orthostatic challenge via tilt table resulted in marked drop in blood pressure with subnormal rise in heart rate and fainting, the study was carried out with patients seated in wheelchairs. All patients manifested a drop in blood pressure before the development of hyperhidrosis and rise in blood pressure. For example, the second patient had a drop in blood pressure from 90/56 mm Hg to 64/50 mm Hg for a few minutes before she developed hyperhidrosis accompanied by piloerection, chattering of teeth, blurred vision, agitation, and a progressive rise in blood pressure to 140/70 mm Hg. All symptoms abated within 10 minutes of lying down in bed. There were less severe changes over a longer period in patient 3 who had a partial lesion. His blood pressure dropped from 96/60 mm Hg to 54/40 mm Hg in 30 minutes. He complained of dizziness for another 30 minutes before sweating and nervousness ensued. His blood pressure at that time was 150/110 mm Hg. After 1 week of treatment with mineralocorticoid, all three patients showed improvement in posture-related symptoms. Hyperresponsiveness of

Table 3. Autonomic function tests

Organ	Test	Normal values	Results: Patient 1	Patient 2	Patient 3
Eyes	Hydroxyamphetamine test, 1%	Dilation of pupils	4→4.5 mm right 3→8 mm left	3→6 mm right and left	3.5→5 mm right 3.5→5.5 mm left
Skin	Sweat test	Generalized sweating	Sweating over neck, ulnar aspect of upper limbs and chest up to T-6	Sweating over forehead, face, and neck	No sweating
Heart & blood vessels	Tilt table test	Heart rate ↑20 beats/min Systolic BP ↓ 5-10 mm Hg	90/70 mm Hg 45° tilt ↓1 min unrecordable Heart rate ↑20 beats/min Lightheaded, dull hearing, and visual blackout	90/60 mm Hg 90° tilt ↓1 min unrecordable Heart rate ↑24 beats/min Cloudy sensorium, blurred vision, dim hearing & purple stars	84/56 mm Hg 30° tilt ↓2 min unrecordable Heart rate ↑22 beats/min Headache right side
	Norepinephrine infusion 0.1 μg/kg body wt/min	Systolic BP ↑ 22 mm Hg	Systolic BP ↑ 50 mm Hg	Systolic BP ↑ 35 mm Hg	Systolic BP ↑ 76 mm Hg
	Sinus arrhythmia	20-30 beats	14 beats	24 beats	24 beats
	Cold face test	Bradycardia 23 ± 10%	Tachycardia 6% BP ↑ 16/12 mm Hg	Tachycardia 12% BP ↑ 20/10 mm Hg	Bradycardia 10% BP ↑ 30/20 mm Hg
	Atropine test 0.03 mg/kg body wt IV	Heart rate ↑ 38 ± 5/min	Heart rate ↑ 8/min	Heart rate ↑ 40/min	Heart rate ↑ 42/min

blood vessels to norepinephrine infusion was documented in all patients. Sinus arrhythmia, cold face test, and atropine test were employed to assess vagal function. Abnormalities of vagal function were evident in the first patient.

Discussion. Severe hyperhidrosis, the presenting complaint in all three patients, has been well described by Head and Riddoch.[11] The pattern of thermoregulatory sweating in these patients was different from that produced in response to postural changes and was noted only in the regions where sympathetic innervation was preserved (table 3). Spinal reflex sweating associated with other manifestations of autonomic dysreflexia was evoked by orthostatic challenge in the first and second patients and affected the whole head, neck, and arms extending to the level of the umbilicus. This pattern of reflex sweating is well recognized in patients with lower cervical cord transections. In the third patient, lack of sweating over the left upper half of the body suggested possible additional injury to the cervical sympathetic chain.[12] In addition, stimuli from the bladder or bowel also evoked similar patterns of reflex sweating.

Orthostatic hypotension precipitated autonomic dysreflexia in these patients and treatment with mineralocorticoids relieved their posture-related symptoms. One can only speculate about the genesis of hypotension-induced autonomic dysreflexia. It has been previously postulated that hypotension may generate afferent impulses from the blood vessels which in turn produce a mass discharge of sympathetic neurons.[13] Animals with chronic cervical spinal cord transection showed a sympathoadrenal reaction to the hypotension produced by hemorrhage. Neither sectioning of dorsal roots to remove peripheral reflex mechanisms nor denervation and complete removal of the adrenals affected the compensatory ability of the spinal animals.[14] This study suggested that spinal cord may be directly affected by low blood pressure producing a temporary state of sympathetic nervous system hyperexcitability. Another possibility is that hypotension triggered sympathetic discharge as a compensatory mechanism analogous to that seen in subjects with shock. Even a relatively small amount of catecholamines released during this state coupled with adrenergic hyperresponsiveness may be responsible for clinical manifestations of autonomic dysreflexia.

Autonomic evaluation revealed some unusual findings. The first patient had minimal vagal activity as documented by sinus arrhythmia, cold face test, and atropine test. The other two patients had normal vagal function. All three patients demonstrated hyperresponsiveness to norepinephrine infusion, although to a variable degree. The patient with vagal hypoactivity had a moderate rise in blood pressure while the patient with good vagal function had a marked rise in blood pressure. It is believed that rise in blood pressure in response to norephinephrine infusion is affected by the denervation of adrenergic receptors and by the activity of the baroreflexes.[15] In quadriplegic patients, peripheral sympa-

thetic nerve endings and adrenoceptors are stated to be normal since isolated spinal cord is capable of reflex sympathetic activity. Therefore, decentralization supersensitivity has been attributed to defective baroreflexes. In our patients, the degree of blood pressure rise was not reciprocal to the degree of vagal activity. These data dispute the simple explanation about adrenergic hyperresponsiveness in quadriplegic patients.

In conclusion, three patients presented with severe orthostatic hyperhidrosis, a manifestation of autonomic dysreflexia. Orthostatic hypotension precipitated autonomic dysreflexia in these patients and treatment with fludrocortisone acetate relieved their posture-related symptoms. It is recommended that orthostatic hypotension should be looked for in patients with unexplained, posture-related dysreflexic symptoms, and in such patients propping upright may be counterproductive.

From the Department of Neurology, University of Maryland School of Medicine, Baltimore, MD.

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Address correspondence and reprint requests to Dr. Khurana, Department of Neurology, University of Maryland School of Medicine, Baltimore, MD 21201.

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Serum prolactins in the diagnosis of epilepsy: Sensitivity, specificity, and predictive value

Article abstract— Serum prolactin levels rise after generalized tonic-clonic and partial complex seizures, but not after pseudoepileptic seizures. The criteria for a significant elevation in serum prolactin vary with individual investigators. The prevalence of pseudoseizures in the population studied determines the predictive value of serum prolactin determinations. In populations where most patients have epilepsy, a rise in serum prolactin is highly predictive for true epilepsy, but no increase in serum prolactin is not predictive for pseudoseizures.

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M.S. Yerby, MD, MPH; G. van Belle, PhD; P.N. Friel, BS; and A.J. Wilensky, MD

Epilepsy, particularly partial complex epilepsy, can manifest itself in a variety of clinical forms. Changes in and disagreements over the International Classification are illustrative of this fact.[1] Patients with nonepileptic or pseudoseizures present a particularly difficult problem in differential diagnosis. Current clinical practice recommends the use of EEG telemetry with closed-circuit television (CCTV) monitoring as the "gold standard" for the diagnosis of epilepsy.[2] This technique, while accurate, is expensive and not readily available in most communities. The demonstration by Trimble[3] of elevations in serum prolactin (PRL) after epileptic but not after pseudoepileptic seizures provoked intense interest in this method as an alternative diagnostic test in epilepsy. Despite this test's clear economic advantages, it has limitations. In addition to deficiencies in sensitivity and specificity of PRL measures, the prevalence of pseudoseizures in the population studied profoundly affects the utility of this test in the diagnosis of epilepsy.

PRL is a polypeptide of approximately 200 amino acids secreted by the anterior pituitary. Its secretion is regulated by an inhibitory factor and occurs in a pulsed fashion throughout the day. There is a gradual rise during sleep, reaching a peak of 1.6 to 1.8 times mean levels, just prior to awakening. PRL can be measured in CSF, amniotic fluid, and plasma. It is elevated most