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Rare disease

A 69-year-old man with excessive sweating of the right hemithorax

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Summary

The pure autonomic failure is a rare entity, with only a few cases reported in the literature. The authors describe a case with compensatory excessive sweating of the right hemithorax as an initial manifestation of a pure autonomic failure, and the authors review the clinical characteristics of this disease. A 69-year-old man presented excessive sweating of the right hemithorax. Physical examination revealed orthostatic hypotension. No other neurological features were present. The autonomic study showed a low heart rate response to the Valsalva maneuver and reduced supine plasma norepinephrine levels. A pure autonomic failure was diagnosed. Treatment did not improve patient's symptoms. Anhidrosis with asymmetrical compensatory hyperhidrosis can be the only symptom of a pure autonomic failure. The authors highlight an unusual form of presentation of a rare disease, difficult to diagnose if it is not taken into consideration.

BACKGROUND

The pure autonomic failure or Bradbury Eggelston syndrome is a rare entity, with very few cases reported in the literature. It is included within the chronic primary dysautonomias. By consensus, three forms of primary chronic autonomic failure have been recognised: pure autonomic failure, multiple-system atrophy and Parkinson's disease with orthostatic hypotension.[1] Characteristically, these features cannot be explained neither by medication side effects nor by other disorders. We present a 69-year-old man's case with excessive sweating of the right hemithorax being finally diagnosed as a pure autonomic failure.

CASE PRESENTATION

A 69-year-old man was referred to internal medicine consultation due to excessive sweating of the right hemithorax. His antecedents were 'low blood pressure', appendectomy, transurethral resection for benign prostatic hyperplasia, ex-smoker of two packs a day for 20 years and ex-weekend-drinker. The patient complained of excessive sweating in the right hemithorax and armpit for about 1 year. The systematic anamnesis discovered the presence of dizziness when standing up quickly since 10 years ago, impotence after transurethral resection and unquantified weight loss. Physical examination revealed a severe orthostatic hypotension when adopting orthostatism with a decrease in 25 mm Hg of systolic and diastolic blood pressure, neither showing presyncopal symptoms nor compensatory tachycardia. Complete cardiopulmonary, abdominal and neurological examinations were normal.

INVESTIGATIONS

The laboratory studies including complete blood count, erythrocyte sedimentation rate, coagulation, serum immunofixation electrophoresis test, serum immunoglobulins, tumour markers (carcinoembryonic antigen, cancer antigen 19.9, squamous cell carcinoma antigen) and urinalysis were normal. The autoimmune study including antinuclear antibodies, antineutrophil cytoplasmic antibodies and anticardiolipin antibodies was negative. Anti-Yo and anti-Hu antibodies were negative. Serology for hepatitis B virus, hepatitis C virus and syphilis was negative too. Chest radiography, chest and abdominal CT scan, cranial CT scan, cranial MRI and Doppler ultrasonography of the supra-aortic arteries were performed without finding significant changes. In the cervical MRI severe degenerative changes from C3 to C6 were observed, with channel reduction, without displacing the spinal cord. After these tests, a study of the autonomic function was requested (table 1), showing a compromised cardiac parasympathetic function and sympathetic function with plasma catecholamine levels below-normal in both decubitus and supine position, with no increase in the concentrations when standing. A pure autonomic failure was diagnosed.

DIFFERENTIAL DIAGNOSIS

At the beginning, a differential diagnosis with diseases associated with excessive sweating was made, including both primary and secondary hyperhidrosis[2–4]:

Idiopathic unilateral circumscribed hyperhidrosis occurs mainly on the face and upper extremities, with profuse sweating precipitated by heat. Axillary hyperhidrosis is confined to the armpits and responds to heat and emotional stimuli. Palmoplantar hyperhidrosis is associated only with stress. Ross' syndrome is characterised by the triad of unilateral tonic pupil, hyporreflexia and progressive hypohidrosis with or without compensatory segmental hyperhidrosis.

In Frey's syndrome, unilateral redness appears, accompanied by local heat sensation and sometimes sweating and pain, located in the cutaneous response distribution area of the auriculotemporal nerve, in response to gustatory and exceptionally tactile stimuli. This is due to damage to this nerve's parasympathetic fibers. Localised hyperhidrosis

Table 1 Autonomic tests performed

Autonomic tests	Patient		Normal values
Parasympathetic function			
E:I ratio*	3.87		>10
Valsalva ratio*	1.23		>1.5
30:15 ratio*	0.88		>1.1
Sympathetic function†			
Epinephrine (pg/ml)	Decubitus: 14		20–60
	Orthostatism:	10′: 18 15′: 14 20′: 23 30′: 12	20–60
Norepinephrine (pg/ml)	Decubitus: 13		135–300
	Orthostatism:	10′: 18 15′: 14 20′: 23 30′: 12	300–650
Dopamine (pg/ml)	Decubitus: 22		10–150
	Orthostatism:	10′: 9 15′: 21 20′: 32 30′: 46	10–150

E:I ratio: To perform the test, the subject remains supine and breathes deeply at the rate of one breath per 10 s (ie, six breaths/min) for 1 min while being monitored by ECG. The E:I is the ratio of the mean of the longest R-R intervals during deep expirations to the mean of the shortest R-R intervals during deep inspirations.
Valsalva ratio: Evaluates the heart rate response to Valsalva maneuver. It is determined from the ECG tracings by calculating the ratio of the longest R-R interval after the maneuver to the shortest R-R interval during the maneuver.
30:15 ratio: This test evaluates the heart rate response to standing. The patient stands up and the R-R variation during the first 30 beats is measured. The ratio is calculated dividing the longest R-R interval near the 30th beat between the shortest R-R interval before the 15th beat.
*Variation in beats per minute.
†Catecholamine levels while supine were tested at 10, 15, 20 and 30 min.

associated with skin diseases can occur at the periphery of glomus tumours and POEMS (polyneuropathy, organomegaly, endocrinopathy, monoclonal gammopathy and skin changes) syndrome. Harlequin syndrome consists in sudden facial redness and unilateral facial sweating. Pachydermoperiostosis is characterised by a thickening of the skin on the scalp, forehead and eyelids. There is overactivity of the sebaceous glands of the face and scalp with hyperhidrosis of hands and feet. Granulosis rubra nasi presents erythematous papules and hyperhidrosis on the tip of the nose.

Our patient did not meet criteria of any of these conditions. Since the patient had orthostatic hypotension as an expression of autonomic nervous system dysfunction; at first, it had to be ruled out autonomic dysfunction associated with peripheral nervous system disorders and spinal injuries,[5] including diabetic neuropathy,[6] autonomic dysfunction associated with amyloidosis,[7] hereditary,[8] toxic-metabolic and infectious diseases, dysautonomias associated with connective tissue disorders, paraneoplastic diseases[9] and chronic inflammatory polyneuropathies. In the second place, we ruled out autonomic dysfunction associated with central nervous system disorders such as brain tumours, hydrocephalus, multiple sclerosis, myelopathy and amyotrophic lateral sclerosis. We also excluded the use of drugs that may cause autonomic dysfunction.

Once the secondary dysautonomias was discarded, differential diagnosis was made with other primary dysautonomias,[10 11] such as multiple-system atrophy and Parkinson's disease, in which neurological symptoms appear. In multiple-system atrophy, autonomic dysfunction, parkinsonism and ataxia in any combination appear progressively. But it is important to consider that during the early stages of multiple-system atrophy, autonomic deficits may be the sole clinical manifestation[12]; therefore, the disease may resemble pure autonomic failure.[13] Nevertheless, our patient was followed-up for 7 years and no other neurological symptoms appeared. Besides, in the multiple-system atrophy, neuropathological analysis indicates predominantly central lesions, with preservation of sympathetic ganglia; this finding is consistent with the normal basal serum norepinephrine concentrations in affected patients, unlike the frequently low values in patients with pure autonomic failure as showed in our patient.[14] Parkinson's disease may involve autonomic nervous system failure in addition to the typical symptoms of the disease. However, pure autonomic failure or Bradbury Eggleston syndrome symptomatology refers exclusively to the one derived from the alteration of the autonomic nervous system with no other subsequent neurological symptoms such as those occurred in our patient.

TREATMENT

Elastic stockings, fludrocortisone and midodrine treatments were tested with no significant improvement. It is interesting to note that the patient learnt to use physical measures spontaneously, such as crossing the legs or squatting, to counteract the symptoms. These physical exercises increase blood pressure by increasing venous return.[15]

OUTCOME AND FOLLOW-UP

After a 7-year follow-up, orthostatic hypotension became important in the patient's symptoms without the development of other neurological symptoms. Despite the established treatment, the patient did not detect clinical improvement.

DISCUSSION

The pure autonomic failure or Bradbury Eggelston syndrome is an idiopathic sporadic disorder included in the chronic primary dysautonomias. It is characterised by signs and symptoms arising from the autonomic involvement, being orthostatic hypotension the most disabling of them all and a frequent reason for consultation. It is usually accompanied by dizziness, visual disturbances and changes in the sweating pattern with anhidrosis and asymmetrical compensatory hyperhidrosis. Digestive symptoms like nausea, constipation and diarrhoea may appear, as well as bladder disorders like nocturia, urinary retention and sexual dysfunction. No other neurological features are present. In this case, the patient was referred due to increased sweating at the right side of the body. At first, differential diagnosis of the pathologies accompanied by excessive sweating was made, delaying final diagnosis. In fact, a delay of years to reach the diagnosis of this disease has been reported.[16] As a matter of fact, the patient suffered from left hemithorax anhidrosis with compensatory sweating of the right hemithorax. Nevertheless, orthostatic hypotension, which initially hardly caused any symptoms, allowed reaching the final diagnosis. This is explained by the widespread loss of postganglionic sympathetic neurons and therefore decreased levels of plasma norepinephrine in supine,[17] as it has been proved in this case. The baseline norepinephrine

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levels were very low and did not increase when standing up despite the significant blood pressure drop. Sweating disturbances are due to neurons loss in the intermediolateral cell column of the spinal cord.[18] Secondary disautonomias must be dismissed, and then differential diagnosis must be done with the other primary forms, like multiple system atrophy and Parkinson's disease.[13] The treatment is based on hygienic measures and vasopressors,[19 20] although they were little use in our patient. In conclusion, we highlight an unusual form of presentation of a rare disease, difficult to diagnose if it is not taken into consideration.

Learning points

- The pure autonomic failure or Bradbury Eggleston syndrome is a rare disease.
- It is characterised by symptoms of autonomic nervous system failure without other neurological involvement.
- Orthostatic hypotension and hemicorporal anhidrosis may be the presentation form of this disease, and it should be included in the differential diagnosis of orthostatic hypotension. Excessive compensatory sweating may mislead the clinician.
- To confirm the diagnosis, slow cardiac response to Valsalva maneuver and decreased plasma norepinephrine levels must be demonstrated.
- The treatment is based on hygienic measures and vasopressors, however, it is not always effective.

Competing interests None.

Patient consent Obtained.

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