DIAGNOSTIC APPROACH TO THE PATIENT WITH DYSAUTONOMIA

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I. Introduction

Disorders of the autonomic nervous system encompass a diverse set of common, relatively benign entities, as well as rare forms of disabling autonomic failure. Both are often misunderstood. As for the evaluation of any neurologic condition, an organized approach is needed, beginning with listening to and observing the patient, and then proceeding through a series of detailed questions and a physical examination informed by autonomic physiology.

I wish to stress that "dysautonomia" is not a specific diagnosis, but rather a broad category comprising many diverse clinical conditions. A parallel term is "weakness," which in a given patient might reflect a disorder of muscle, neuromuscular junction, motor neuron, anterior horn cell, corticospinal tract, or motor cortex – or it might not reflect a neurologic disorder at all. It would be improper and a matter of diagnostic indolence to consider "weakness" to be a specific diagnosis. Even worse would be to recommend one treatment approach for all patients with weakness. And yet the term "dysautonomia" is sometimes applied in that way. Patients who have benign forms of dysautonomia or, in some cases, are incorrectly labeled with dysautonomia, feeling bewildered, may turn to the Internet to find information about autonomic disorders and mistakenly think that they have a serious or life-threatening disease. Clarity, therefore, is needed. At the same time, it can be helpful to validate the patient's symptoms by offering an explanation of how the autonomic nervous system is involved.

II. Types of Dysautonomia

The first question to explore is whether the patient has or does not have a disorder of the autonomic nervous system. If the answer is yes, then the second question to explore is whether the lesion can be localized and whether collateral signs and symptoms coalesce around a recognizable diagnostic pattern. Several categories may be distinguished:

A. *Generalized autonomic failure*
A number of rare disorders cause widespread impairment of autonomic responses. Examples include:

i. Multiple system atrophy
ii. Pure autonomic failure
iii. Autoimmune autonomic ganglionopathy or neuropathy
iv. Autonomic neuropathies (e.g., amyloid, vincristine, diabetic, hereditary).

Signs of parkinsonism, cerebellar ataxia, or distal sensory peripheral neuropathy may coexist, leading to a specific neurologic diagnosis.

The most disabling feature of autonomic failure is typically orthostatic hypotension, defined by a sustained reduction on standing of >20 mmHg systolic or >10 mmHg diastolic blood pressure, with or without symptoms,[1] although the drop in blood pressure in autonomic failure is often much greater and can severely limit standing activities.

B. *Selective system autonomic failure*
Some patients will present with autonomic failure restricted to one or several organ systems. Examples include:

i. Adrenergic failure presenting as isolated orthostatic hypotension, often also with supine hypertension
ii. Cholinergic failure presenting with colonic intertia and anhidrosis
iii. Thermoregulatory sudomotor failure presenting with anhidrosis and heat intolerance
iv. Neurogenic bladder due to cauda equina or conus medullaris lesion
v. Harlequin syndrome with oculosympathetic paresis and hemifacial flushing

C. *Medical conditions or pharmacologic effects mimicking a primary autonomic disorder*
The patient with an intact autonomic nervous system may present with secondary autonomic signs or symptoms. Examples include:

i. Non-neurogenic, reversible orthostatic hypotension caused by diuretics or antihypertensive medication
ii. Anhidrosis caused by anticholinergic or carbonic anhydrase-inhibiting medication
iii. Urinary bladder retension caused by anticholinergic medication
iv. Opioid-induced constipation or urinary retension
v. Neuroleptic malignant syndrome
vi. Serotonin syndrome
vii. Flushing in a patient taking niacin or in a perimenopausal woman
viii. Night sweats in a patient with tuberculosis or lymphoma
ix. Tachycardia in a patient taking a stimulant or anticholinergic

D. *Intermittent or paroxysmal autonomic hyperactivity*
In contrast to autonomic failure, which is a form of autonomic hypofunction, disorders of autonomic hyperfunction are also encountered. Examples include:

i. Baroreflex failure following bilateral carotid sinus denervation, with markedly labile blood pressure
ii. Pheochromocytoma causing autonomic storms: hypertension, sweating, headache
Pseudopheochromocytoma, which is idiopathic, is far more common
iii. Autonomic dysreflexia caused by spinal cord lesion above T5
iv. Diencephalic syndrome with autonomic storms caused by acute axonal injury or hydrocephalus
v. Familial dysautonomia with baroreflex afferent failure
vi. Palmoplantar hyperhidrosis
vii. Frey syndrome caused by aberrent innervation of facial sweat glands by salivary fibers following damage to the auriculotemporal nerve
viii. Postural orthostatic tachycardia syndrome

E. *Functional dysautonomia*
Dysautonomias involving lesions of the central or peripheral nervous system are sometimes referred to as structural dysautonomias. A functional dysautonomia is “a medical condition that impairs normal autonomic function in some way but in the absence of a known structural neurologic deficit. Examples include neurally mediated syncope, irritable bowel syndrome, and some forms of orthostatic intolerance and pain, the molecular basis of which await discovery.”[2] Whether all functional dysautomias are truly disorders or simply physiologic variations of normal can be a matter of controversy.[3] Cool fingers in an anxious person, for example, may be physiologically normal and not an example of abnormal vasoconstriction. Vasomotor changes in a painful limb may occur from disuse or guarding and do not always indicate a complex regional pain syndrome.

F. *Psychiatric symptoms manifest through the autonomic nervous system*
As the sympathetic nervous system is responsible for the “fight or flight” response, emotional states, such as anxiety, frequently trigger a cascade of autonomic responses. These patients do not have a primary disorder of the autonomic nervous system, although their symptoms may be manifest by way of activation of autonomic responses. Examples include:

i. Panic disorder
ii. Phobic disorder
iii. Post-traumatic stress disorder
iv. Somatic symptom disorder
v. Psychogenic pseudosyncope

III. Diagnostic Approach

Neurologic evaluation begins with a detailed review of autonomic symptoms, inquiring as to when and under what conditions they occur, what makes them better or worse, and how they limit the patient’s ability to engage in daily activities.[4] The patient with orthostatic hypotension or orthostatic intolerance may experience difficulty standing up for more than a few seconds or minutes. One should ask about symptoms that occur immediately upon standing or after standing for some time and whether they are immediately relieved by sitting or lying down. Orthostatic symptoms are most likely to occur when rising from bed, standing at the sink to perform morning hygiene, taking a shower, standing in the kitchen to cook, or standing outdoors in hot weather. Similarly, one may, depending on the clinical concern, inquire about patterns of sweating, flushing, urinary bladder control, gastrointestinal motility, or sexual function. Medication lists should be carefully scrutinized.

Physical examination should, depending on the concern, correlate objective blood pressure and heart rate measurements with symptoms and assess skin and oral cavity moisture, pupillary reactivity, distal sensation, focusing on potentially autonomic signs as part of a complete neurologic examination. Orthostatic blood pressure measurements are best taken with a sphygmomenometer and upper arm inflatable cuff, listening with a stethoscope, rather than relying on automated devices. Supine blood pressure measurements should be taken after the patient has been supine at rest for several minutes. Standing blood pressure measurements are best taken one minute after standing and may need to be repeated to assess the trend over several minutes.

IV. Clinical Testing

Formal autonomic is often helpful to establish whether autonomic failure is present. Valid autonomic testing is performed under carefully controlled conditions and assesses autonomic responses to a standardized stimulus. Adrenergic function is best evaluated by assessing beat-to-beat changes in blood pressure and heart rate in response to a Valsalva maneuver or head-up tilt. Sudomotor function may be evaluated by warming the body to induce a generalized thermoregulatory response, or stimulating specific skin areas with acetylcholine to produce localized sweating responses. Cardiovagal function may be evaluated by analysis of beat-to-beat heart rate changes in response to sinusoidal deep breathing, the Valsalva ratio, or spectral analysis of electrocardiogram R-R interval variability.

Each of these tests requires interpretation by a physician knowledgeable about autonomic physiology. Neurologists should beware, as some compact commercial devices that claim to evaluate autonomic function rapidly and automatically are of unproven scientific validity, may omit essential aspects of autonomic testing (such as blood pressure), and can generate incorrect or misleading results.

V. Principles of Treatment

Treatment of dysautonomia begins with educating patients so that they can understand what their symptoms mean (without panicking unnecessarily) and how to manage them to improve function and quality of life.

Specific lifestyle modifications, such as oral hydration, physical exercise, and adequate sleep can achieve a great deal, depending on the type of dysautonomia. Sometimes the best treatment is discontinuation of a medication causing autonomic symptoms rather than adding a new medication to the list.[5,6] Managing heat and cold stress is important in patients with impaired thermoregulation.[7]

Pharmacologic interventions should target the specific physiological deficit. A variety of medications are available for treating neurogenic orthostatic hypotension.[8]

References

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