Autonomic NS Disorders (SPECIFIC)

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PURE AUTONOMIC FAILURE (PAF), s. CHRONIC POSTGANGLIONIC AUTONOMIC INSUFFICIENCY, BRADBURY-EGGLESTON SYNDROME

- idiopathic, sporadic, degenerative disorder of autonomic nervous system.

- pathology - **neuron loss in autonomic ganglia**, as well as pre-ganglionic cells in medulla and spinal cord.
- begins insidiously in middle age or late adult life.
- initial complaint is often **ORTHOSTATIC HYPOTENSION** (develops gradually).
  Primary involvement of *postganglionic sympathetic neurons*!
  - low supine plasma NE levels;
  - reduced NE response to tyramine;
  - decreased neuronal uptake of NE;
  - widespread ***denervation supersensitivity*** - abnormally accentuated blood pressure response to intravenous norepinephrine.
- ***no motor manifestations*** (vs. multiple system atrophy, Parkinson's disease), no peripheral neuropathy (EMG, nerve conduction velocities, sural nerve biopsy, and CSF may be normal).
- slowly progressive, does not appear to shorten life span (prognosis better than MSA).

DOPAMINE-β-HYDROXYLASE DEFICIENCY

- hereditary disease - inability to convert DA to NE.

- severe orthostatic hypotension, ptosis, ejaculatory failure, nocturia, nasal congestion, hyperextensible joints.

DIAGNOSIS

- abnormal adrenergic innervation tests.
- thermoregulatory sweat test normal.
- serum NE/DA ratio is 0.1 (normal 10); decreases further with maneuvers that increase sympathetic neural discharge.

TREATMENT

3,4-DIHYDROXYPHENYLSERINE (DOPS) - synthetic amino acid.

- decarboxylated by *L-amino acid decarboxylase* to NOREPINEPHRINE (bypassing dopamine-β-hydroxylase step of catecholamine synthesis!).

IDIOPATHIC ORTHOSTATIC HYPOTENSION

- orthostatic hypotension of neurologic origin without evidence of other neurologic disorder.

- defect in ***postganglionic sympathetic neurons*** (vs. Shy-Drager syndrome - pre-ganglionic sympathetic neurons).
- no clinical involvement of CNS (vs. Shy-Drager syndrome).
- **basal plasma [NE]** is low (vs. Shy-Drager syndrome – normal).
- supine plasma [NE] *fails to rise* adequately when patient stands (as in Shy-Drager syndrome).
- ***denervation supersensitivity*** to IV NOREPINEPHRINE - abnormal rise in BP (vs. Shy-Drager syndrome - normal response).
- TYRAMINE (indirectly acting sympathomimetic agent that releases norepinephrine) causes blunted response (vs. Shy-Drager syndrome - normal response).

HYPOTHALAMIC SYNDROMES

Hypothalamus is most important area for integration of ***behavior*** with ***autonomic*** responses and with ***neuroendocrine*** control of anterior and posterior pituitary glands

1. **Neurologic defects**
   1) **thermoregulation** disorders (hyperthermia / hypothermia, poikilothermia)
      - ***chronic*** expanding lesions cause hypothermia, whereas ***acute*** lesions may cause hypothermia or hyperthermia.
   2) **emotional** disorders (rage responses)
   3) **arousal** disorders (hypersomnolence)
   4) **pyramidal** / **extrapyramidal** signs
   5) **eye** signs
   6) headache, vomiting, convulsions

2. **Endocrine changes** - **pituitary** dysfunction (e.g. hyper- / hypo-gonadism)
   N.B. possibility of hypothalamic pathology should be kept in mind in evaluating all patients with pituitary dysfunction (esp. isolated deficiencies of single pituitary tropic hormones)

3. **Metabolic abnormalities**:
   1) **feeding** disorders (hyperphagia / hypophagia), obesity
   2) **electrolyte** / **osmotic** disorders (hyponatremia / hypernatremia, diabetes insipidus)

Region	Normally Regulates	Disorders
PREOPTIC	Blood volume, pressure, and electrolytes	Paroxysmal hyponatremia Essential hypernatremia
	Thermoregulation	Paroxysmal hypothermia
TUBERAL	Gastrointestinal tract and feeding	Hyperphagia (ventromedial lesions) Hypophagia (lateral lesions; must be bilateral!)
	Reproduction	Hypogonadism
	Emotions	Rage responses
POSTERIOR	Arousal	Hypersomnolence
	Descending autonomic and motor pathways	Poikilothermia

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