Other Neuromuscular Transmission Disorders

**CONGENITAL MYASTHENIAS**

- **Incidence**: < incidence of MG.
- **not autoimmune!**

**PATHOGENETIC CLASSIFICATION** — see p. Mus1

**CLINICAL FEATURES**

- **Deficit** in both presynaptic and postsynaptic structures.
- **Lesions** may be congenital or acquired.

**MYASTHENIC SYMPTOMS after neonatal period** (*“floppy baby”*)

- **Family history** (autosomal recessive inheritance is most common)
- N.B. may present later in life and, in some cases, without family history — diagnosed as serologically-negative autoimmune myasthenia.
- difficulty with feeding, delayed motor milestones, persistent or sometimes progressive limb weakness.
- skeletal abnormalities can result from weakness.
- some syndromes lack ocular involvement!

**DIAGNOSIS**

- positive AChR antibody test excludes congenital myasthenia (negative test is less helpful).
- positive* edrophonium (Tensilon) test confirms myasthenic syndrome but does not differentiate congenital myasthenia from MG.
- *may be negative in deficiency of acetylcholinesterase.
- repetitive nerve stimulation** — decrement in CMAP. **at 10 Hz (vs. MG — at 3 Hz).
- single-fiber EMG — as in MG.

**Differential Diagnosis**

1. Indirect ophthalmoplegia
2. myasthenia gravis / neonatal myasthenia (passive placental transfer of AChR antibodies).

**TREATMENT**

- respiratory & bulbar supportive measures.
- some patients respond to anticholinesterases; if not — try 3,4-DIAMINOPYRIDINE.

**EATON-LAMBERT SYNDROME**

- **autoantibodies against voltage-gated Ca**2+**-channels in peripheral nerves** — reduced acetylcholine release* (at neuromuscular and autonomic synapses).

**Diagnosis**

- *number* of released ACh quanta.
- **Disorder of presynaptic cholinergic cell**
  - a) 66% paraneoplastic disorder (60% patients, esp. men, have small cell lung cancer) - antibodies arise in reaction to tumor.
  - Syndrome may predate tumor detection by up to 3 years!
  - b) 33% associated with other autoimmune disorders (thyroid disease, pernicious anemia, vitiligo, type I diabetes mellitus).

**Clinical Features**

- Skeletal muscles: proximal & limb girdle muscle weakness + hyporeflexia
- **Major**: chest X-ray, fiberoptic examination, nerve conduction studies
- **Minor**: xerostomia, loss of taste, impotence.
- **Autoimmune cholinergic (nicotinic & muscarinic) dysfunction**: xerostomia, loss of taste, impotence.
- **Orthostatic hypotension, sluggish pupillary responses, peripheral paresthesias are rare**.

**Diagnosis**

- **Negative** EDROPHONIUM test.
- **Abnormally small CMAP amplitude on EMG**.
- **Repetitive nerve stimulation**
  - at 2 Hz — CMAP increment (2 to 20 times original)!!! — that is the opposite of myasthenia gravis**.
  - *facilitates calcium accumulation in nerve terminal* at 2 Hz — CMAP decrement.
  - *search for malignancy*: chest X-ray, mammography, pelvic ultrasound.

**Treatment**

- **Acetylcholine receptor (AChR) agonist**
- **Ranitidine** (FDA approved (11/28/2018)).

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- **Anticholinesterase**
- **Pyridostigmine (Tensilon)**
- **EDROPHONIUM**
- **Choline esters**
- **Choline choride**
- **Acethalamine**
- **Baclofen**
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OTHER NEUROMUSCULAR TRANSMISSION DISORDERS

GUANIDINE - bone marrow depression, cerebellar syndrome.
4-AMINO PYRIDINE - convulsions.
- IVIG, plasmapheresis effects are transient.
- cytotoxic drugs should be used cautiously.
- optimal treatment of non-neoplastic cases - modest doses of alternate-day PREDNISONE.

BIBLIOGRAPHY for ch. “Neuromuscular, Muscular Disorders” → follow this LINK >>