Myasthenia Gravis

PBL; Second case

KING SAUD UNIVERSITY

COLLEGE OF MEDICINE

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Definition:

A chronic disease marked by abnormal fatigability and weakness of selected muscles, which is relieved by rest. It is also known as **Goldflam disease**. The degree of fatigue is so extreme that these muscles are temporarily paralyzed. The muscles initially affected are those around the eyes, mouth, and throat, resulting in drooping of the upper eyelids (ptosis*), double vision, dysarthria*, and dysphagia*.

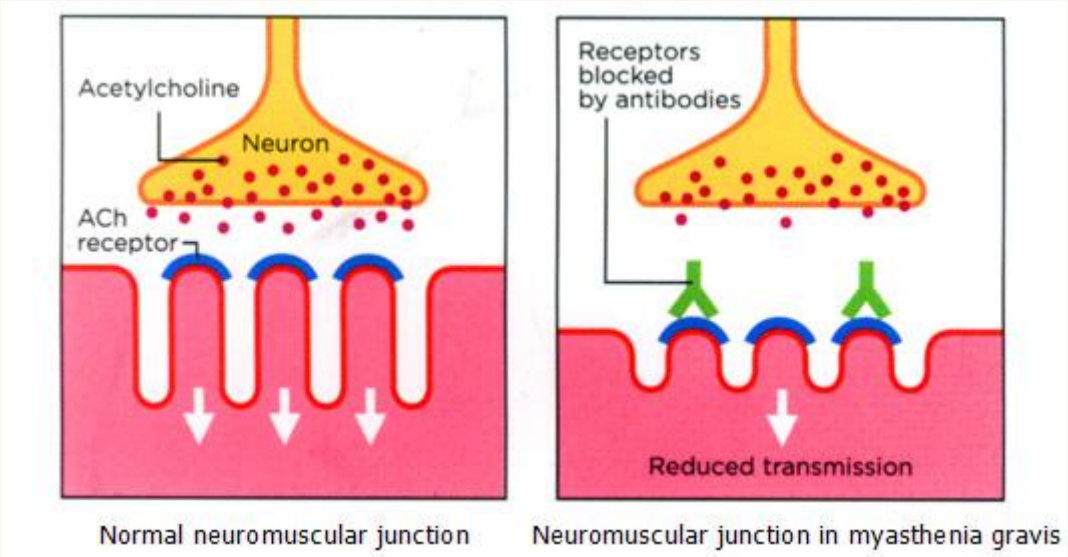
Pssst!

***Ptosis** (**Blepharoptosis**): drooping of the upper eyelid.

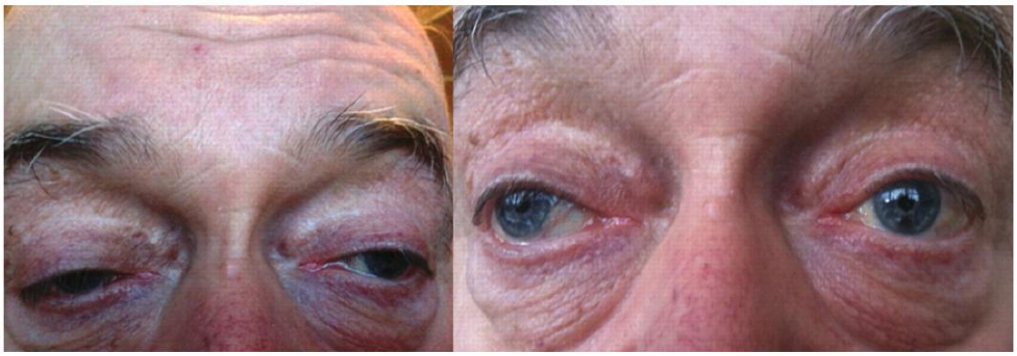
***Dysarthria:** a speech disorder in which the pronunciation is unclear although the language content and meaning are normal.

***Dysphagia:** a condition in which the action of swallowing is either difficult to perform or in which swallowed material seems to be held up in its passage to the stomach.

Pathophysiology of MG:



Myasthenia gravis is an **autoimmune disease** in which acetylcholine-receptor autoantibodies bind to cholinergic receptors on muscle cells, which impairs the ability of the neurotransmitter acetylcholine to induce muscular contraction. The concentration of ACh receptors on the muscle end-plate membrane is reduced, and antibodies are attached to the membrane. ACh is released normally, but its effect on the post-synaptic membrane is reduced. The post-junctional membrane is less sensitive to applied ACh, and the probability that any nerve impulse will cause a muscle action potential is reduced.



PTOSIS

Symptoms:

- Drooping of one or both eyelids (ptosis).
- Double vision (diplopia).
- Limited facial expressions.
- Difficulty swallowing.
- Altered speaking.
- Weakness in neck and limb muscles.
- Susceptibility to fatigue, especially during periods of activity.

Factors that make symptoms worse:

- Emotional/mental stress.
- Illness.
- Fatigue.
- Extreme heat.
- Some medications — such as **beta blockers**, **calcium channel blockers**, **quinine** and **some antibiotics**.

THE THYMUS IN MYASTHENIA GRAVIS:

Thymic abnormalities are clearly associated with myasthenia gravis but the nature of the association is uncertain. These are areas within lymphoid tissue where B-cells interact with helper T-cells to produce antibodies. Because the thymus is the central organ for immunological self-tolerance, it is reasonable to suspect that thymic abnormalities cause the breakdown in tolerance that causes an immune-mediated attack on AChR in myasthenia gravis. The thymus contains all the necessary elements for the pathogenesis of myasthenia gravis

Differential Diagnosis (Hypothesis):

- Botulism.
- Congenital myasthenic syndromes.
- Drug-induced myasthenia-like syndrome.
- Mitochondrial cytopathies.
- Mitochondrial myopathies, with or without external ophthalmoplegia.
- Senile ptosis.
- Polymyositis.
- Thyroid disorders.
- Multiple sclerosis.

Risk Factors:

- Family history for myasthenia gravis.
- Most common in **young women** and **older men**.
- Other autoimmune illness:
  i) Rheumatoid arthritis
  ii) Lupus.

Tests:

- The Edrophonium Chloride (Tensilon) test:
- *Edrophonium chloride (Tensilon, Reversol) or neostigmine (Prostigmin) is injected into a vein - the drug clocks the breakdown of acetylcholine by cholinesterase (cholinesterase inhibitors) and temporarily increases the levels of acetylcholine at the neuromuscular junction - put simply, edrophonium bocks an enzyme that breaks down acetylcholine, the chemical that transmits signals from the nerve ending to the muscle receptor sites. Some patients may experience a brief period in which muscle weakness is relieved.*
- Serum Anti-Ach receptor Antibodies.
- Electromyography (EMG).
- Single-fiber electromyography.
- Eye examination.
- CT or MRI scan may be performed to identify a thymoma;
  Because CT/MRI scans are better at detecting thymomas (tumor in the thymus gland) than X-rays.
- Pulmonary function test (spirometry);
  The aim here is to determine whether the patient is breathing adequately.

Questions to ask a mysthenic patient:

- When did the symptoms begin?
- Are you taking any medications currently?
- Are you able to swallow properly?
- Any history of Myasthenia Gravis in your family?

Treatment:

- Anticholinesterase drugs such as **Neostigmine** or **Pyridostigmine** to improve the communication between the nerves and the muscles.
- Surgical removal of the thymus in younger patients. (**Thymectomy**)
- Steroid therapy to suppress the immune system response. (e.g. **Prednisone**)
- Intravenous immunoglobulin treatment. (IVIG)
- Plasma exchange maybe used to treat the more severly affected patients.

NOTE THAT:

➔ Anticholinesterase drugs such as **Pyridostigmine** prolong acetylcholine activity by inhibiting cholinesterase enzyme.

➔ The management of this disease is via **symptomatic medication**, not disease medication.

Prevention:

- Avoid stress and heat exposure, which can make symptoms worse.
- Avoid strenuous, exhausting activities.
- Treat any infections promptly.

Complications:

- Myasthenic crisis. *(a life-threatening condition, which occurs when the muscles that control breathing become too weak to do their jobs)*
- Thymus tumors.
- Underactive or overactive thyroid.
- Pernicious anemia.

Learning Objectives:

- ✓ **Discuss** the structures involved in the neuromuscular junction and the process of signaling transduction in normal nerve and muscle.
- ✓ **Discuss** the different possible mechanisms by which interference may occur with the conduction from nerve fibers to muscle fibers.
- ✓ **Discuss** the mechanisms by which skeletal muscle fibers contract.
- ✓ **Understand** the role of investigations in confirming the diagnosis of neuromuscular junction dysfunction (myasthenia gravis).
  Discuss the pharmacology of drugs used in the management of myasthenia gravis.
- ✓ **Use** knowledge learnt from physiology and histology to interpret the patient's symptoms and signs.

Best of luck,

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Don't just read, open up your mind and think. If you have any suggestions for developing next PBL files, please feel free to contact me at: Shaikha.x@hotmail.com