SUNY Downstate Department of Ophthalmology

Grand Rounds
February 26, 2009
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medical knowledge

Case Presentation

- 39 year old female referred from Staten Island University Hospital to Coney Island Hospital
- Was unable to get her work up because of insurance reasons

Case Presentation

- Complains of an intermittent binocular vertical diplopia that started 8 months ago.
- 4 months prior to presentation noticed ptosis of the left lower lid.
- The ptosis has become more prominent in the past two weeks.

Past Medical History

- Denies other medical problems
- Denies medications
- Denies allergies
- Previous ocular history – upon questioning admitted to self-resolving similar incident 5 years ago, but otherwise no history or family history of glaucoma; no gtt's or glasses; no surgery or trauma.

Ocular Exam

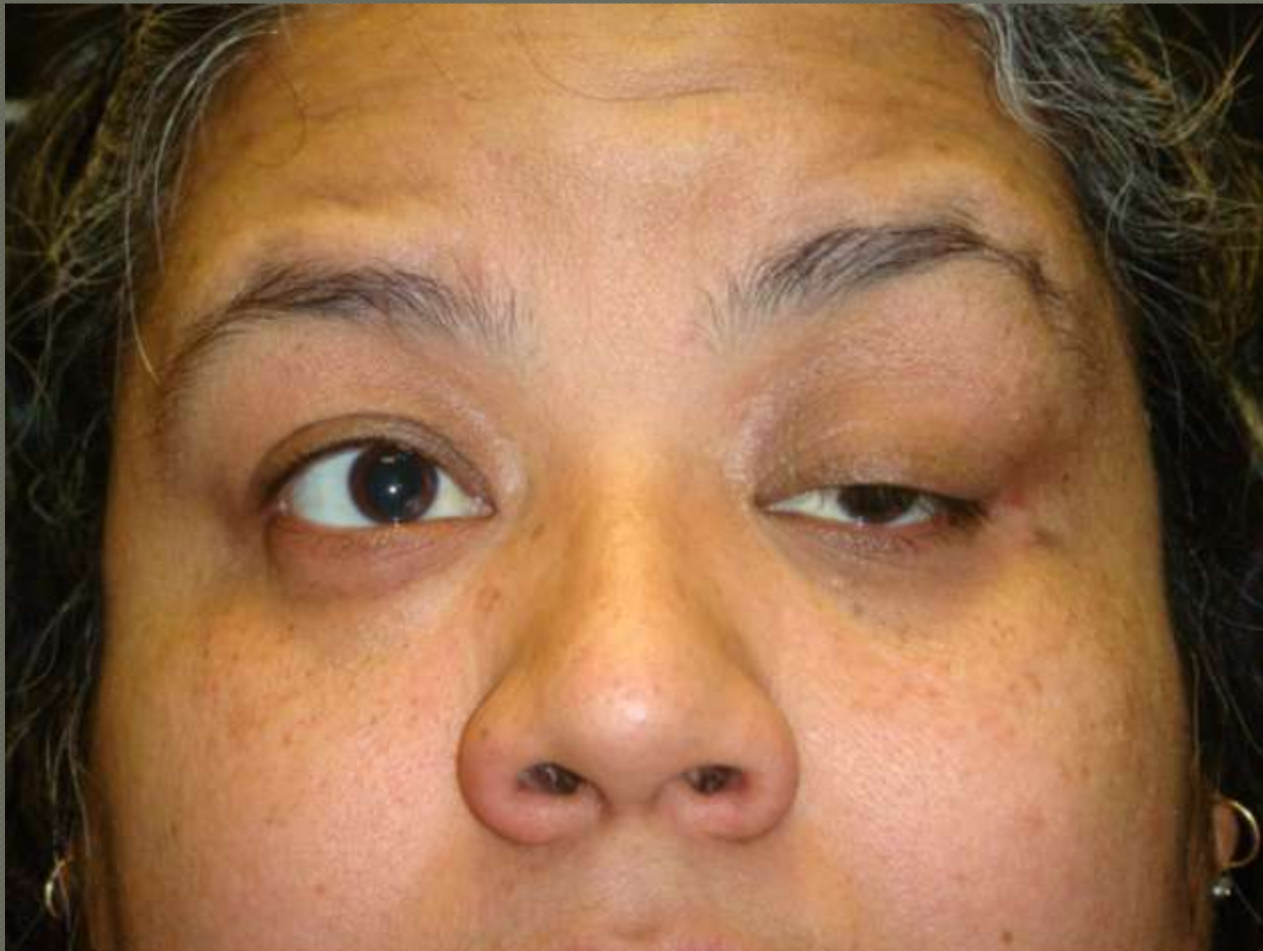
- Dvasc 20/20, 20/20
- Nvasc 20/20 ou
- P 4→2 ou no apd
- EOM -1 limitation of up and downgaze OD. Diplopia in extreme downgaze and in right and left gaze
- Ocular alignment see photos
- Ta 10 ou
- CVF full ou
- Color plates full ou

Ocular Exam

- LLA see picture
- CS wq ou
- K clear ou, pterygium OS
- AC dq ou
- IP rr ou. No apd
- Lens trace NS ou

- DFE
- Vitreous clear, C/D 0.2 sharp and pink
- M/V/P WNL ou

Without Frontalis Suspension



Differential Diagnosis

- Pupil Sparing 3rd nerve palsy
- Thyroid Eye Disease (lid retraction?)(incomitant strabismus)
- Internuclear Ophthalmoplegia
- Eaton-Lambert Myasthenic Syndrome
- Myasthenia Gravis
- Medication Induced Mysthenia Gravis (penicillamine/aminoglycosides)
- Chronic Progressive External Ophthalmoplegia/Kearns – Sayre Syndrome (neg tensilon test – no diurnal variation)
- Horners Syndrome
- Levator Dehiscence
- Orbital Inflammatory Pseudotumor (incomitant strabisumus)
- Myotonic Dystrophy
- Cavernous Sinus Process (unilateral)

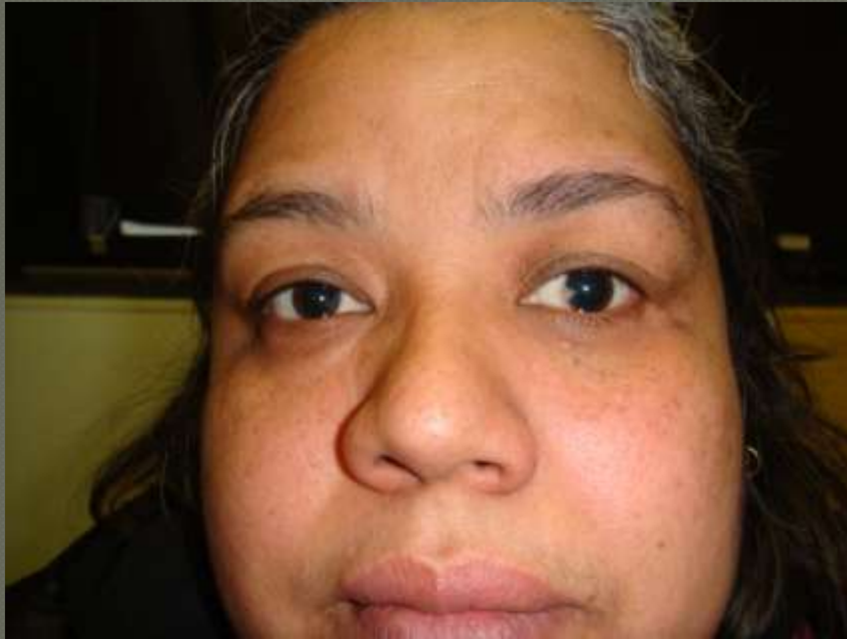
Any additional questions?

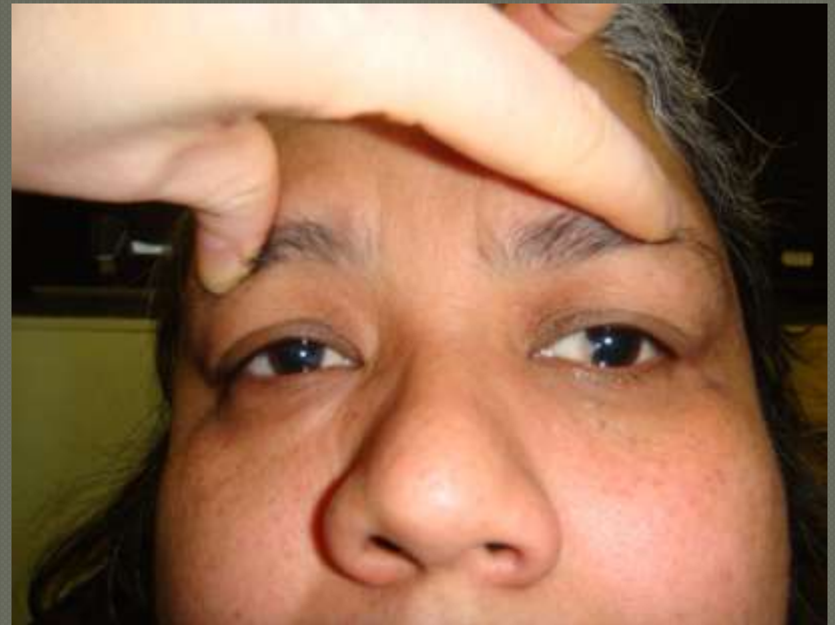
- Why did she wait so long to seek medical attention?
- Has this ever happened before?
- Worse in the morning or evening?
- Trouble breathing? Chewing? Other muscle weakness?

medical knowledge, practiced based learning and improvement, patient care

5 pm on a Friday….no Tensilon

Immediately After the Ice Pack Test





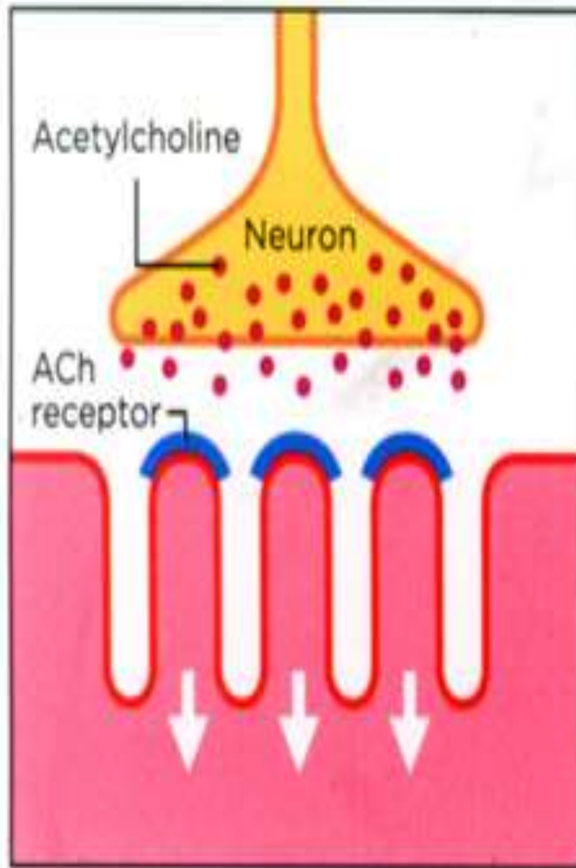
Myasthenia Gravis

- Incidence 15 per million
- Women 2x affected as men
- 2nd/3rd decade = women
- 6th/7th decade = men
- Some HLA associations (DR – 2,3, B-7,8)

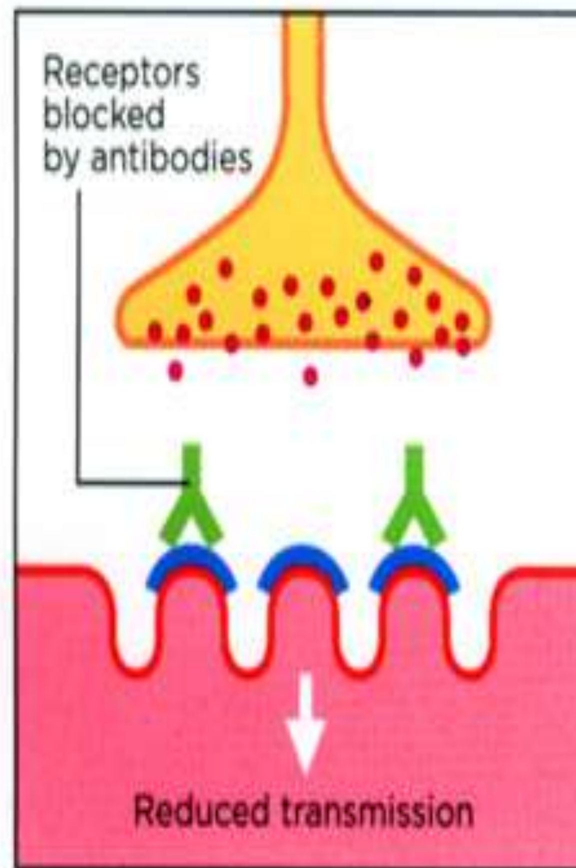
Myasthenia Gravis

- Most common of the disorders of the neuromuscular junction
- Caused by an antibody-mediated autoimmune attack on the Ach receptor at the NMJ.
- Muscle weakness worsening with exertion and improving with rest.
- Ptosis and diplopia are the most common ocular findings

NMJ



Normal neuromuscular junction



Neuromuscular junction in myasthenia gravis

1. Loss and Simplification of AchR in the post synaptic folds
2. Widened synaptic cleft

NMJ in MG

- New receptors that are synthesized are not incorporated into the post synaptic cleft (1/3 of normal receptors)

- Number of receptors correlated to severity of disease
- Antibody mediated process originating in the thymus gland
- 1. accelerate rate of degredation of AchR
- 2. block Ach binding sites
- B and T cell mediated

Ocular Manifestations

- Diurnal Variation of Ptosis and Diplopia (70-90%)
- Gaze Evoked Nystagmus 2/2 Fatigue
- Clinically normal pupils (anisocoria, sluggish, impaired accom)
- Hering's law of equal innervation "pseudo lid retraction"
- Cogan's Lid Twitch
- Fatigue with Prolonged upgaze
- Slowing of eye movements with repetitive saccades

Diagnosis

- Symptoms
- Ice pack test (2 min)
- Tensilon Test (15 min)
- Sleep/Rest Test (30 min)
- Serologic Work up: AbAchR (70% sensitive, 90% in generalized), anti MuSK (muscle specific kinase)
- Electrophysiologic Testing
  - repetitive supramaximal motor nerve stimulation (progressive decrease in response with decreasing frequency).
  - Single Fiber EMG shows "jitter" – variability of propagation time to individual muscle fibers supplied by a single motor neuron and "blocking" – failure of conduction at NMJ
  - Levator or Orbicularis as muscle of choice.

Tensilon (Edrophonium Chloride) Test

- Action in 30 seconds, duration 5 minutes
- Strict monitoring of vital signs in addition to ocular measurements
- Side effect profile: diaphoresis, abdominal cramping, nausea, vomiting, salivation, light headedness
- Serious complication: Heart Block (atropine available)
- Draw 10mg into tuberculin syringe
- Initial dose of 2mg IV, wait one minute, then 4mg IV if no response or adverse reaction. 4mg IV may be repeated.

Ice pack test

- Wills 2000
- 90% sensitive, 100% specific
- (rest is 50%, 100%)
- 1. Decreases cholinesterase activity
- 2. Promotes efficiency of Ach at the end plate of the NMJ

Additional Required Work up

- CT/MRI of the Chest – evaluate for Thymoma (15% of MG patients have a thymic tumor—fullness over 40yrs)
- Thyroid Studies – 5% coexistent thyroid disease
- CBC, ANA, ESR – evaluate for SLE, Pernicious Anemia
- DM, TB testing – if corticosteroids to be used.
- Neuroimaging – atypical, Ab negative cases.

Treatment

- Acetylcholinesterase Inhibitors
- Immunosuppressive Therapy
- Symptomatic Treatment of ocular manifestations
- Avoidance of Medications
- Thymectomy
- Plasmapheresis/IVIG

Acetylcholinesterase Inhibitors

- Prevent the degradation of Ach
- Increase the probability of transmission across the NMJ
- Mestinon (2-8 hrs duration): 60mg PO QID to 120mg PO Q3h. GI disturbances. Muscle twitching. OD: sialorrhea, blurred vision, worsening weakness
- Diplopia is difficult to treat with AchEI

Immunosuppressive Therapy

- Corticosteroids and Cytotoxic agents, ie Prednisone, Azathioprine, Cyclophosphamide, Cyclosporin
- Combination
- Monitor blood counts, liver, renal function. Risk of neoplasm.

Removal of Antibodies

- Plasmapheresis – rapid but transient effect
- IVIG – binds antibodies

- Reserved for patients in myasthenic crisis who are in pulmonary failure

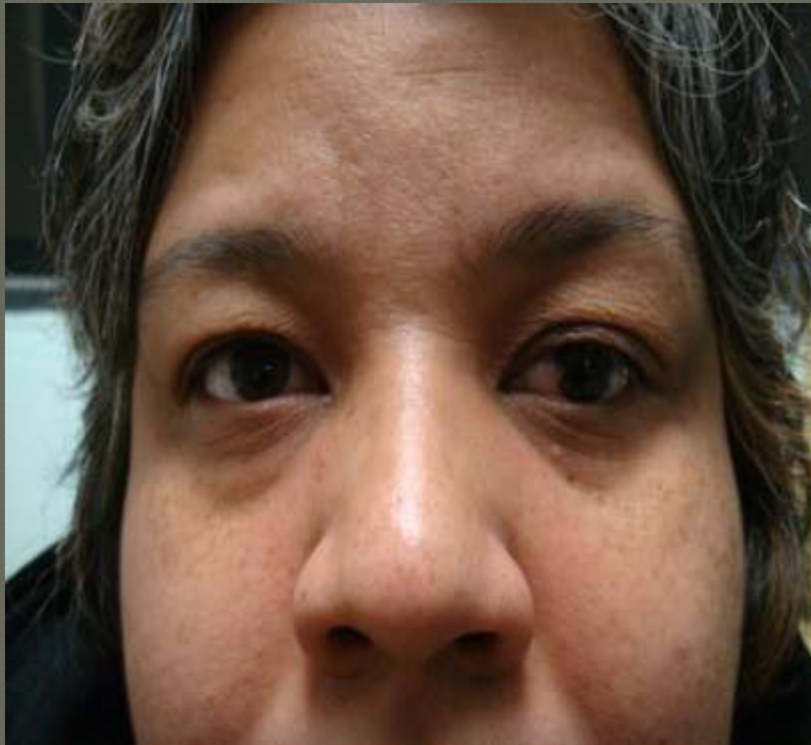
Medication Induced Myasthenia…

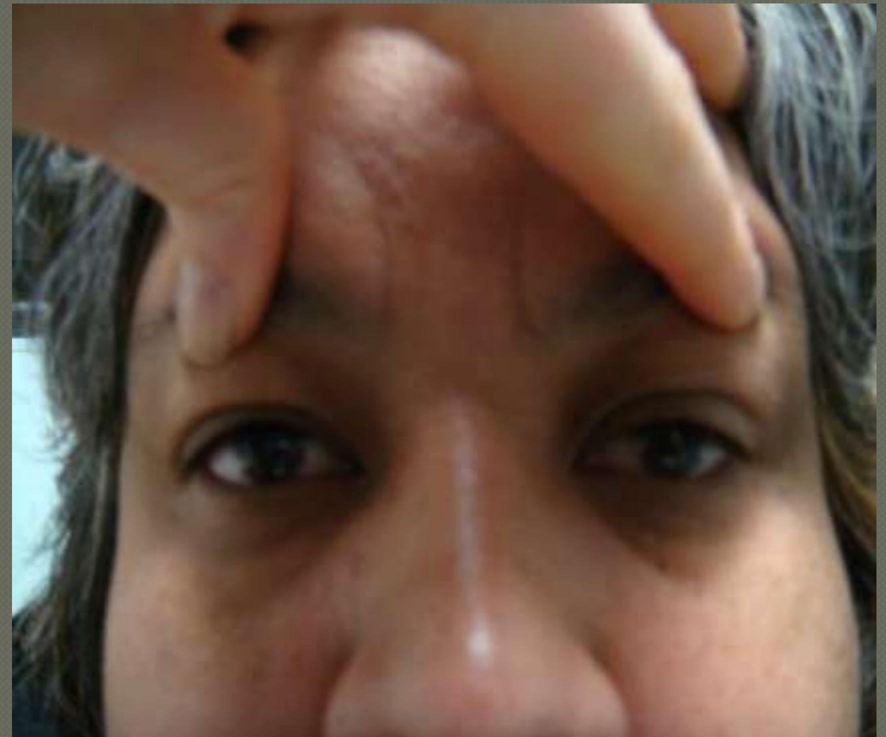
- Penicillamine
- Aminoglycosides
- Bacitracin
- Polymyxins
- Clindamycin
- Erythromycin (rare)
- Depolarizing agents (curare)
- Chloroquine
- Lithium
- Magnesium
- Procainamide
- Quinidine
- Phenytoin
- B Blockers
- Cisplatin
- Phenothiazines
- Tetracyclines

Our Patient

- AchR Ab Postive
- CT brain and orbits negative
- CT chest negative for thymoma
- TSH wnl
- Started on Mestinon 60mg PO QID
- RTC 2 weeks later:

2 Week Follow up





Motility and Alignment (thank you to Dr. Kumar)

- 20 PD RHT in primary gaze
- 25 PD RHT in right gaze
- 12 PD RHT in left gaze
- 16PD RHT in down gaze
- Ortho in up gaze
- 6 PD RHT in right head tilt
- 16-18 PD RHT in left head tilt

- Incomitant RHT worse in right gaze and left head tilt
- Right Inferior Rectus Palsy

Steroids or Pyridostigmine

- Kupersmith et al. 2005

- Compared Prednisone to Pyridostigmine
- Followed 89 patients for two years
- less than 10% of patients had ptosis only, less than 30% had diplopia only, while the majority (64%) had both diplopia and ptosis
- Combined horizontal and vertical ocular misalignment was most frequent (43.5%) but horizontal (34.1%) or vertical (22.4%) deviations alone occurred.

Results

- The prednisone group showed resolution in primary gaze diplopia, downgaze diplopia, unilateral ptosis, and bilateral ptosis in 73.5%, 75.5%, 85.7%, and 98%, respectively at 1 month. The benefit persisted at 3–6, 12, and 24 months
- The pyridostigmine group showed resolution in primary gaze diplopia, downgaze diplopia, unilateral ptosis, and bilateral ptosis in 6.9%, 17.2%, 50%, and 76.7% of patients after 1 month
- The prism cover results improved ($p = 0.003$) in the prednisone group only.
- In the prednisone group, four patients had no response to therapy.
- Among the 51 prednisone responsive patients, there were 33 recurrences in 26 patients.
- 12 patients, all prednisone treated, had remissions.

Our Patient

- Increased Mestinon to 90mg PO QID
- She has a follow up appointment in 2 weeks.
- No Diplopia in primary gaze, and able to read without diplopia’
- Happy with improvement
- Observe for now.

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Thank you

- Our patient
- Dr. Gopal
- Dr. Kumar
- Dr. Ahmad
- Dr. Frisbee
- Dr. Whitaker