SUNY Downstate Department of Ophthalmology

Grand Rounds
February 26, 2009
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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

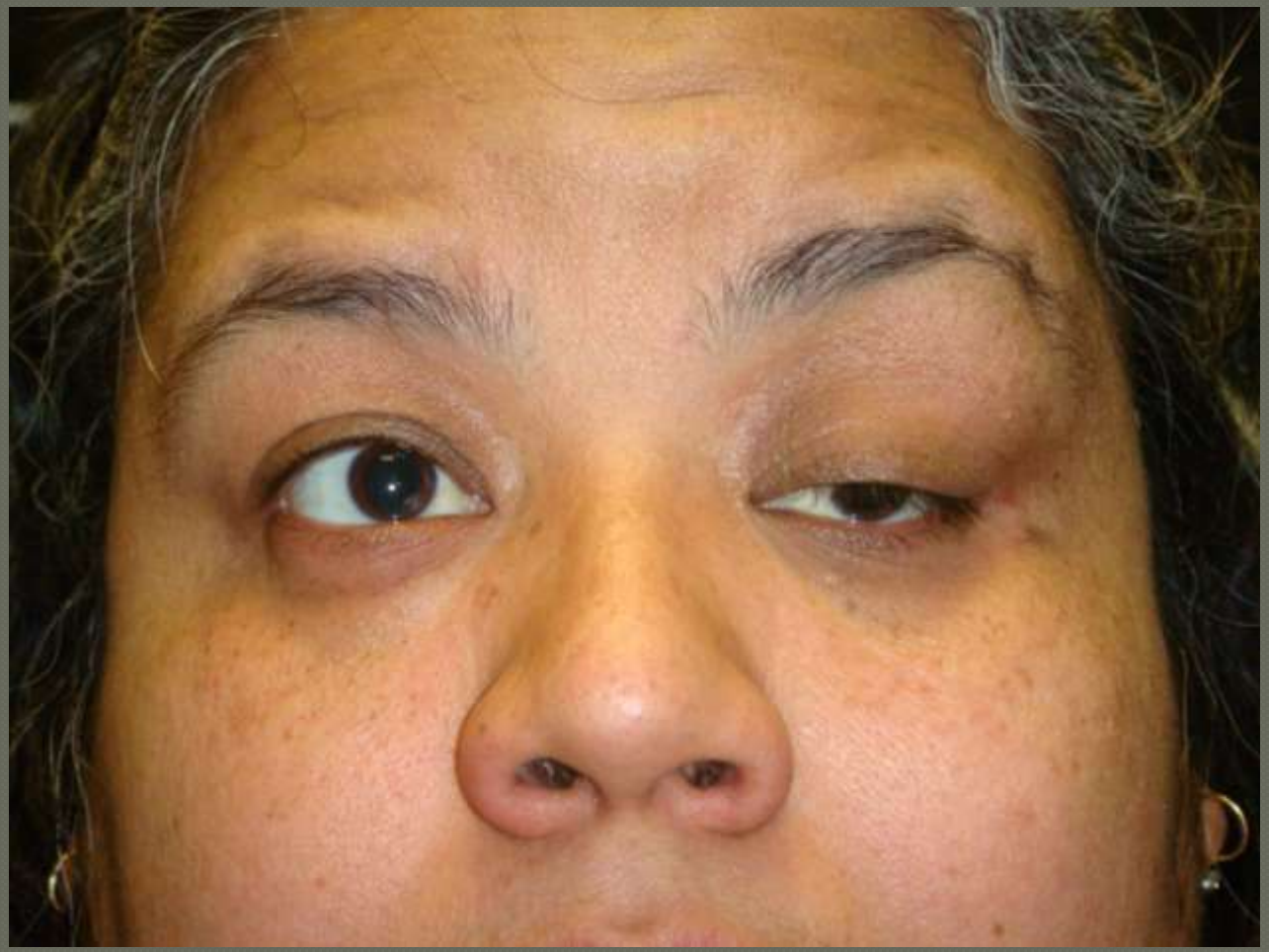
- Dvasc 20/20, 20/20
- Nvasc 20/20 ou
- P 4→2 ou no apd
- EOM -1 limitation of up and downgaze OD. Diplopia in extreme downgaze and in right and left gaze
- Ocular alignment see photos
- Ta 10 ou
- CVF full ou
- Color plates full ou

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

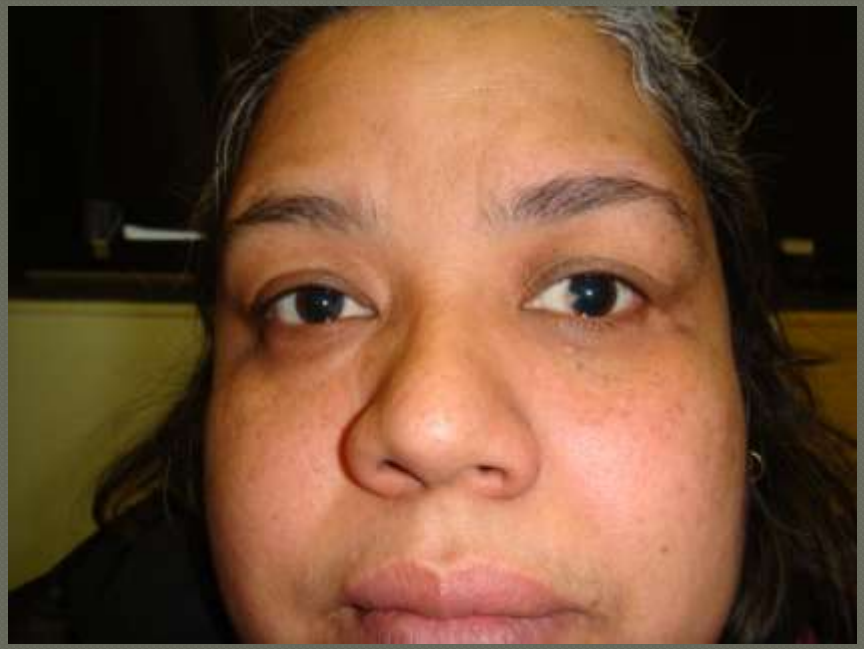
- Pupil Sparing 3rd nerve palsy
- Thyroid Eye Disease (lid retraction?)(incomitant strabismus)
- Internuclear Ophthalmoplegia
- Eaton-Lambert Myasthenic Syndrome
- Myasthenia Gravis
- Medication Induced Mysthenia Gravis (penicillamine/aminoglycosides)
- Chronic Progressive External Ophthalmoplegia/Kearns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

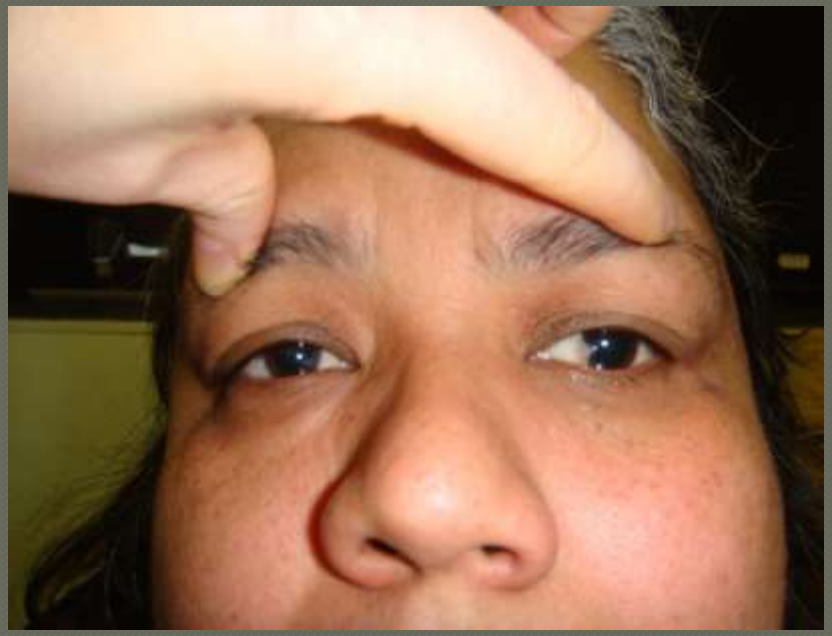
Any additional questions?

- 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?

5 pm on a Friday….no Tensilon

Immediately After the Ice Pack Test





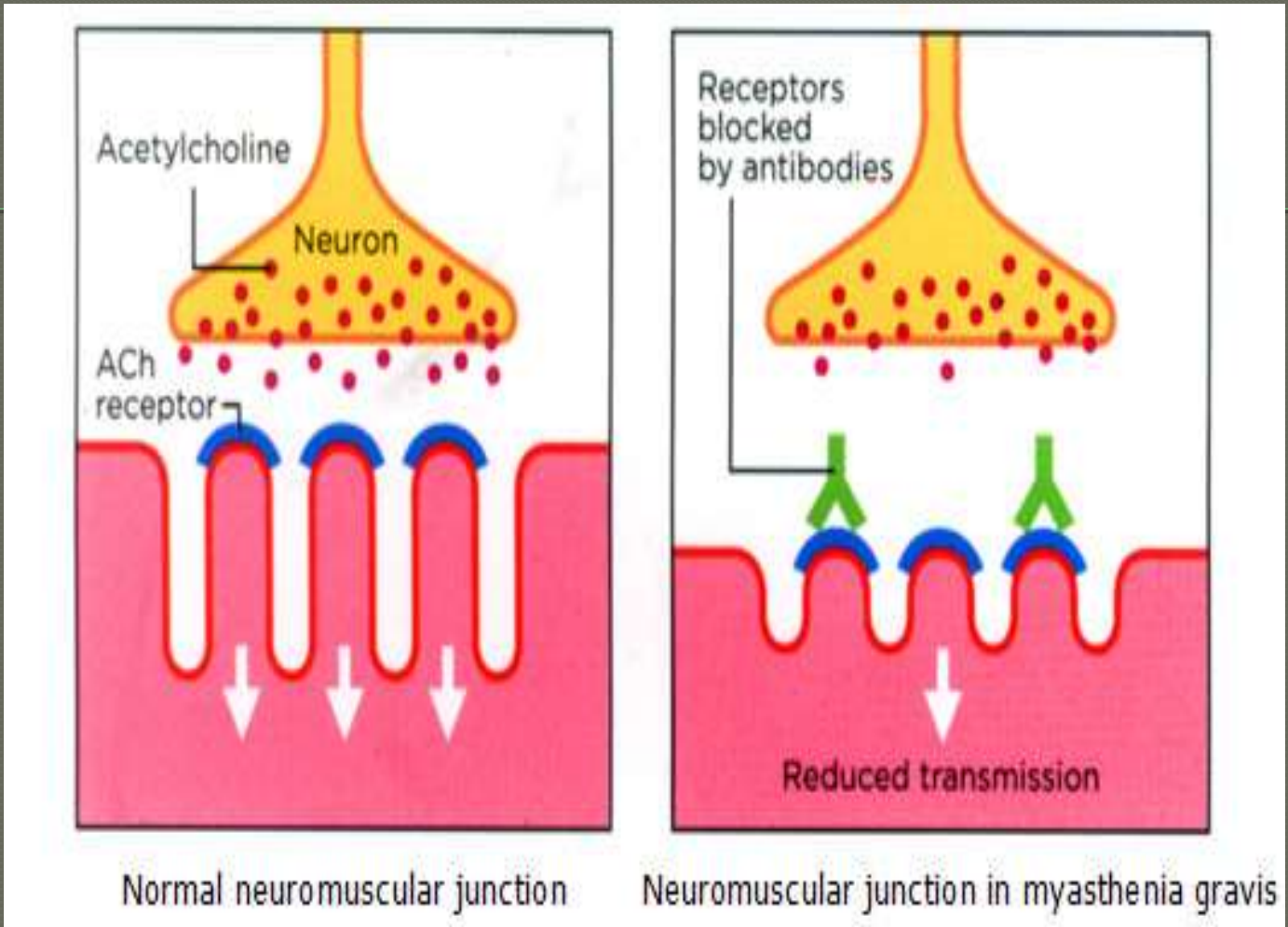
Myasthenia Gravis

- 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



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

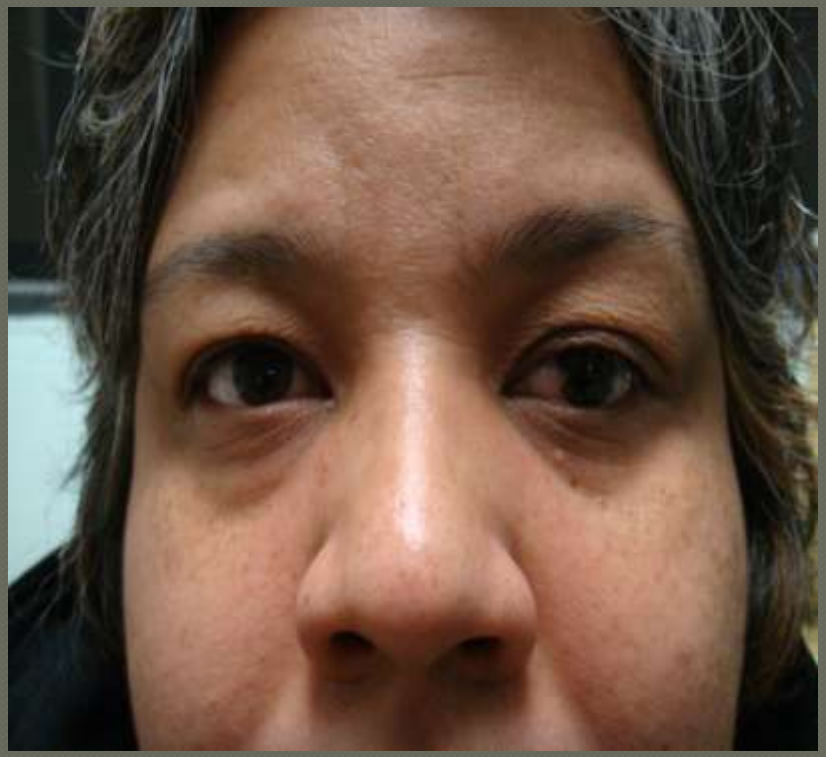
Medication Induced Myasthenia…

- 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