SUNY Downstate Department of Ophthalmology

Grand Rounds
February 26, 2009
Allison Rand, M.D.
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
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.
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

practice based learning and improvement
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
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 strabismus)
- 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)
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
1. Loss and Simplification of AchR in the post synaptic folds
2. Widened synaptic cleft
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 degradation 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
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
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
- Diplopiea is difficult to treat with AchEI
Immunosuppressive Therapy

- Corticosteroids and Cytotoxic agents, ie Prednisone, Azathioprine, Cyclophosphamide, Cyclosporin
- Combination
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

patient care
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
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.
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.
References

- The ice test versus the rest test in myasthenia gravis
  Kenneth C Kubis, Helen V Danesh-Meyer, Peter J Savino, Robert C Sergott
  Ophthalmology

- M J Kupersmith and G Ying
  Ocular motor dysfunction and ptosis in ocular myasthenia gravis: effects of treatment

- A prospective study assessing the utility of Cogan's lid twitch sign in patients with
  isolated unilateral or bilateral ptosis
  Gregory P. Van Stavern, Aash Bhatt, James Haviland, Evan H. Black
  Journal of the Neurological Sciences

- Therapeutic options in ocular myasthenia gravis
  A. Evoli, A.P. Batocchi, C. Minisci, C. Di Schino, P. Tonali
  Neuromuscular Disorders
  March 2001 (Vol. 11, Issue 2, Pages 208-216)

- SFEMG in ocular myasthenia gravis diagnosis
  Luca Padua, Erik Stalberg, Mauro LoMonaco, Amelia Evoli, Annapaola Batocchi, Pietro Tonali
  Clinical Neurophysiology
  1 July 2000 (Vol. 111, Issue 7, Pages 1203-1207)
Thank you

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