Abstract:

71 year old Asian female presents with complaints of double vision persisting for a few months. Characteristics of the diplopia lead to suspicion, and further investigation, of Myasthenia Gravis.

I. Case History
   i. 71 year old Asian female
      1. Chief complaint: Bilateral double vision with both horizontal and vertical components. Double vision was longstanding, previously corrected by progressive lenses with ground-in prism. Symptoms returned a few months ago and severity was increasing at the end of the day.
   
   ii. History
       1. Ocular history: diplopia secondary to decompensated phoria first observed, and corrected, in 2011
       2. Medical history: Hypothyroidism
   
   iii. Medications: Synthroid

II. Pertinent Exam Findings

   *Note to reader: Findings with an associated picture or video are starred and in bold

   i. Clinical (1st exam)
      1. Visual acuity: distance VA sc 20/20-2 OD, 20/40+1 OS; distance VA cc 20/30+1 OD, 20/25-1 OS
      2. Pupils: equal, round, reactive to light, No APD OU
      3. EOMs: Full range of motion OU
      4. Maddox Rod: in free space Maddox rod testing revealed 9 prism diopeters base down OS, >10 pd base out OS. Maddox rod testing behind the phoropter revealed 6 pd BD OS, 11 pd BO OS and 11 pd BO OD (6 pd left hyper and 22 pd esophoria).
      5. Cover Test: 12 pd esophoria, left hyper. CT performed in all positions of gaze. Subjectively, the patient reported that she was more symptomatic (eso) in downgaze because she reported that the targets were farther apart, and reported a smaller vertical component when looking in downgaze. Objectively, the patient was more eso in downgaze and there was less of a vertical component when looking in downgaze.
      6. Parks 3 Step: suspected right inferior oblique palsy/paresis. Left hyper in primary gaze, symptoms worsened when looking in left gaze, symptoms worsened when head tilted towards the left.
7. Habitual Spec Rx: +0.50-1.00x135, 2 pd BU and 2.50 pd BO OD; +1.00-2.75x165, 2 pd BD and 2.50 pd BO OS; 2.50 ADD OU
8. Refraction: plano OD, 20/20-2; +1.00-2.00x165 OS, 20/20-2
9. Trial frame: Rx was trial framed with new prism. Trial framed Rx with 6 pd BO OD and 6 pd BO OS, patient reported single clear vision. Current glasses had 5 pd BO total, so 7 pd BO Fresnel prism was applied to current left lens.

ii. Laboratory Results
1. Acetylcholine Receptor Antibody Complete Profile. AChR Binding Abs, serum was <0.3; AChR Blocking Abs, serum was 24; AChR Modulating Ab was <12. All results were negative, indicating an absence of Myasthenia gravis.

iii. Clinical (2nd exam)
1. VA: distance VA cc 20/25-2 OD, 20/40-2 OS. Near VA cc 20/30 OD, 20/40 OS.
2. *CT: 12 pd esophoria, 4 pd left hyper
3. IOP: 18/18 mmHg OD/OS
4. Confrontation Visual Fields: Full to finger count OD/OS
5. Final Spec Rx: plano, 2.0 pd BU and 6 pd BO OD 20/20-2; +1.00-2.00x165, 2.0 pd BD and 6 pd BO OS 20/20; 2.50 ADD OU
6. Anterior segment: unremarkable OU
7. *Posterior segment: clear and centered PCIOL OU, tilted optic disc with surrounding ring staphyloma OU, C/D ratio 0.30/0.30 OD and 0.35/0.35 OS

III. Differential Diagnoses
i. Primary: Myasthenia Gravis, Decompensation of an existing phoria
ii. Others: Isolated cranial nerve palsy, Thyroid eye disease

IV. Diagnosis and Discussion
i. Diagnosis: decompensated phoria
ii. Discussion: Double vision can be caused by something as simple as misaligned glasses or as fatal as a brain tumor. A detailed history is crucial when developing a list of differential diagnoses, and there are several pertinent questions that must be asked when investigating the patient’s symptoms. Perhaps the most important question to ask is whether the diplopia is monocular or binocular. Monocular causes of diplopia can include media opacities, refractive problems, dry eye, irregular cornea, dislocated lens or lens implant, macular disease or a retinal detachment. Binocular diplopia can be caused by Myasthenia gravis, a decompensating phoria, isolated cranial nerve palsies, thyroid eye disease, trauma, stroke, or a lesion of the central nervous system.

Myasthenia gravis is an autoimmune disease in which antibodies damage and destroy acetylcholine receptors in striated muscle. The impairment of neuromuscular conduction causes weakness and fatigability of skeletal muscles, but not of cardiac and involuntary muscles. The disease affects females twice as often as males. Myasthenia may be ocular, bulbar, or generalized. Systemic myasthenia typically presents in the 3rd decade of life, and is most frequently noted clinically with ptosis or
diplopia. Patients may develop painless fatigue which may be worse towards the end of the day. Ocular myasthenia occurs in 90% of systemic myasthenia cases and it is the presenting feature of 60% of patients. Two-thirds of patients will have both ptosis and diplopia. Diplopia is typically vertical, although any or all of the extraocular muscles may be affected. Bulbar myasthenia is suspected when the patient presents with difficulties swallowing, speaking and chewing. Investigations for the disease include an edrophonium test, raised serum acetylcholine receptor antibody levels, and a thoracic CT or MRI to detect thymoma.

Heterophoria describes the fusion-free position of the eyes, and therefore the magnitude of the deviation which must be overcome by the vergence system. In order for the vergence system to control the heterophoria, it requires the fusional vergence reserves to be at least twice the size of the heterophoria present. If the vergence system is unable to adapt to the patient’s phoria then it may often be the cause of the binocular vision dysfunction.

V. Treatment, Management

i. Treatment for decompensated phoria: ground in prism, Fresnel prism, eye muscle surgery, occlusion, or a combination of these treatments. The patient had previously responded very well to ground-in prism in her progressive lenses and this was her preferred method of treatment after discussing other options. Fresnel prism was used after the patient’s first exam to verify that the change in prism would alleviate her symptoms. After a trial with Fresnel prism, the patient reported resolution of the diplopia and a new spectacle prescription was released with an updated amount of ground-in prism.

ii. There is a general lack in consensus when it comes to which visual system is to blame for resultant binocular dysfunction. Clinicians rely on careful measurements of the patient’s dissociated phoria, associated phoria, fixation disparity, and fusional vergences when prescribing prism to treat the symptoms. Each of these measurements assess one specific aspect of binocular function and it is important to consider all of them, and possibly a combination of measurements, when deciding the most appropriate clinical intervention.

VI. Conclusion

i. This case emphasizes the importance of investigating the history, quality, severity and relieving factors of diplopia. We are reminded that binocular vision is a complex, sensitive system that requires thorough examination to maintain single clear vision.

VII. References

Case Report

A 31 year old African American male with Stargardt’s maculopathy was referred to our office for a low vision evaluation. He was diagnosed with this pathology three years previously and differentials were ruled out by the referring ophthalmologist.

Patient complaints included difficulty reading road signs, difficulty reading small print, and glare. The patient works as a designer of electrical systems and was especially concerned about losing his driver’s license and subsequently transportation to his job. He has a four-year-old son who he needs to drive to day care. The patient has a brother who also suffers from this visual condition. He lives in a house with his supportive wife and son. Review of Systems was positive for Asthma; however he was not currently taking any medications.

Visual Analysis:

- **Current Glasses:**
  - OD -3.25 + 0.50 X 094
  - OS -4.50 + 0.75 X 137
  - Note: glasses are 1 year old, removes for reading

- **Contrast:**
  - No reduction – Pelli Robinson 1.95 (range 0-1.95)

- **Macular Perimetry with SLO:** (Appendix A)
  - Both eyes show a moderately sized dense ring shaped central scotoma and an inferiorly eccentric preferred retinal locus (PRL).

- **Goldmann Perimetry:** (Appendix B)
  - Both eyes show full fields (125 degrees horizontal)

- **Manifest Refraction:**
  - OD -3.75 + 1.00 X 095, VA 20/70
  - OS -3.50 + 1.00 X 135, VA 20/80

- **Near Evaluation is not included in this case report in order to comply with the maximum page requirement.

- **Glare Control:**
  - Yellow clip-on filters reduced glare and enhanced visual comfort indoors.

- **Distance Evaluation:**

  **Preferred Eye:** OD due to better acuity and dominance

  **Estimated Magnification:**

  Divide denominator of distance acuity by denominator of goal acuity
  1. To achieve 20/40 => 70/40 = 1.75X
  2. To achieve 20/20 => 70/20 = 3.5X

  **3.0X Galilean adjustable focus bioptic telescope:**

  The patient achieved a visual acuity of 20/30+ using this device.
Recommendations:

1. Driving:
   a. Return to the office for a pre-driving evaluation to determine probable success/safety of driving with a bioptic telescope.
   b. Training to learn to spot/scan using a bioptic telescope.
   c. Once he passes the pre-driving evaluation and completes in-office training to use the device, the patient will be referred to a driving rehabilitation specialist for on-the-road training.

2. Light yellow clip-on to reduce glare in dim environments.

3. Scotoma/PRL awareness training to increase reading and spotting efficiency.

4. Recommendations for near tasks were provided, however are not included in this report in order to comply with the grand rounds time and maximum page requirement.

Follow-up 1:

This patient worked with an occupational therapist to implement the above mentioned recommendations. A pre-driving evaluation to assess cognition, visual perception, motor skills, balance, sign recognition, and reaction time was performed and the patient was successful in all areas. The therapist also demonstrated various tints to reduce glare and enhance contrast while driving. Screening tests will be discussed in further detail during the live grand rounds presentation. The patient was referred for on-road training with a certified driving rehabilitation specialist.

Follow-up 2:

A report was received from the driving rehabilitation specialist 3 months after the date of the initial low vision evaluation. This report indicated that the patient was seen at the training center for 10 hours of on-road training and then practiced on his own with a licensed driver for 20 hours prior to returning for a final on-road evaluation. The report indicated that the driver demonstrated improved use of his BTS with each training session and was accurate in his identification of signs, traffic signals, hazards including bikes and pedestrians within the recommended 1-2 second time frame. The final evaluation indicated that the driver was able to follow instructions, was not distracted via conversation, and physical intervention was not required. He also demonstrated ability to safely merge on and off a variety of expressways. Other driving maneuvers performed successfully were left and right turns, acceleration, braking, speed control, lane placement, left and right lane changes, use of direction signal, and scanning and awareness.

This report, in addition to in-office evaluation supported the conclusion that the patient was a good candidate for driving privileges. A Vision Specialists Statement of Examination including visual acuity, visual field, and bioptic training was completed on his behalf. The patient performed another road-test with the State’s Department of Motor Vehicles and was successful in obtaining driving privileges.
Discussion:

At present, visual acuity is the most common screening criterion for granting driver licenses\(^1\). Although it is obvious that some amount of vision is essential for safe driving, there is no conclusive research as to the exact level of visual acuity needed\(^2\). Many studies conclude that level of visual acuity is weakly related to crash rates\(^2,3\) and it is not an accurate determinant of safe driving potential\(^3\). In fact, a study of 24 participants who drove around a closed road circuit found that recognition performance was more strongly predicted by contrast sensitivity than visual acuity measured under standard photopic conditions\(^4\). Another study comparing 10 age-related macular degeneration patients with average visual acuity of 20/70 to a control group of 11 age-matched counterparts with normal vision found the control group to have a higher incidence of accidents in a 5 year period\(^5\). The study results indicate that the ARMD group may have had lower incidence of accidents due to compensatory attitudes, such as driving at slow speeds, limitation of driving to good conditions, and driving in familiar areas\(^2,5\).

According to Michigan law, an individual with progressive eye disease must have minimum visual acuity of 20/60 or better for driving privileges. Our patient missed the visual acuity requirement for driving by one line on a standard eye chart. Assuming good visual processing, cognitive skills and motor skills, he was possibly safe to drive in familiar areas and good conditions. However, the law is the law and training with a BTS was necessary to allow him driving privileges and continued independence.

There is much argument regarding the safety and benefits of using a BTS while driving. Some argue that the use of a BTS may be distracting and therefore increase the risk of crash involvement\(^3\). Studies performed in California, Texas, New York, and Maine show increased crash rates among bioptic drivers, while a study performed in Massachusetts reported lower crash rates among bioptic drivers\(^3\). It can be concluded that careful evaluation by the prescribing clinician must be taken to determine which patients will be good candidates for successful and safe driving using a BTS. The American Medical Association determined the skills necessary for driving to include vision, cognition, and motor function\(^6\). Verification of these skills, along with proper training and restrictions, may help reduce crash rates among the bioptic driving population.

Conclusion:

With training to use a BTS for driving, our patient is able to continue his employment and provide transportation for his child with less frustration. In addition to empowering him to continue driving, we were able to address near vision complaints and work-related difficulties. For an individual who is responsible for the care of a child, low vision rehabilitation proved to be of significance in improving his overall quality of life and wellbeing.

References:


Appendix A
DS= Dense Scotoma       VS= Variable Scotoma
Appendix B
Low Vision Evaluation and Management
of a Patient Who Requires a Bioptic Telescope for Driving
Ramanpal Deol, OD, FAAO

Case Report

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Patient complaints included difficulty reading road signs, difficulty reading small print, and glare. The patient works as a designer of electrical systems and was especially concerned about losing his driver’s license and subsequently transportation to his job. He has a four-year-old son who he needs to drive to day care. The patient has a brother who also suffers from this visual condition. He lives in a house with his supportive wife and son. Review of Systems was positive for Asthma; however he was not currently taking any medications.

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  3.0X Galilean adjustable focus bioptic telescope:  
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this device.
(various BTS models will be briefly discussed during the live presentation)

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Appendix A

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Appendix B
What holds the retina together?

- **Retinoschisin**
  - Secreted protein
  - Photoreceptor (and bipolar) cells.
  - Distributed all over the retina
  - Reaches the surface of retinal cells and mediates interactions/adhesion between photoreceptor, bipolar, and Muller cells
  - Contributes to the maintenance of the cytoarchitectural integrity of the retina

Can a female get X-Linked Retinoschisis

- In theory: Yes
- Lyonisation: All X chromosomes of the cells in excess of one are inactivated on a random basis
  - Heterozygous females do not phenotypically express their X-linked recessive genotype or do so only randomly.
- Female carriers of an RS1 gene mutation on one allele i.e. heterozygote, are in general asymptomatic with normal visual acuity and normal full-field electroretinogram (ERG) responses.
  - Subtle abnormalities in mERG (Kim, Seiple et al. 2007).
  - A reduced amount of retinoschisin synthesized in the retina of a female carrier appears to fulfil its function

Px One: 16yo Caucasian Male

- Referred for imaging due to:
  - Reduced BCVA
  - ‘Star’ pattern at the maculae
- Aware of reduced vision from the age of 5 but has not been given a reason
  - Denied any problems at school but has large handwriting and holds print very close to read
- Medical History: Unremarkable
- FOcHx: mother myopia otherwise unremarkable
  - Older brother and maternal uncle reportedly have good vision

Patient Two: 47yo Caucasian Male

- Routine check-up for X-Linked Retinoschisis
  - Diagnosed at aged 7
  - Has not been examined for approximately 5 years
  - Cousin, brother and maternal uncle all affected
- Reported unchanged vision since childhood apart from recent presbyopia
- Patching amblyopia therapy at age 8
- Smoker, hypercholesterolaemia (Crestor)
Entering Tests

<table>
<thead>
<tr>
<th>Early</th>
<th>Late</th>
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<tr>
<td>6/19+2</td>
<td>6/12-1</td>
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Amstler grid unremarkable

Standard D-15 passed

Desaturated D-15 failed:
  - 2 crossings / 3 crossings, axis non-specific

MARS Test:
  - 1.60 units OD and OS

Macular Appearance

Undefined OD
Patches of less distinct squares OS

9 Tritan crossings OD
4 Tritan crossings OS

MARS Test:
  - 1.20 units OD and OS

Macular appearance - OCT

Typical Retinoschisis

Outer Plexiform Layer
Reticular / Bullous Schisis

Nerve Fibre Layer

XLRS

Inner Nuclear Layer
Outer Nuclear Layer / Outer Plexiform
RNFL

Vitreous / Peripheral Retina

- XLRS as early as 1898
  - Vitreous veils, congenital vascular veils, congenital cystic retinal detachment

Optic nerve

- Difficult to assess with imaging

Visual Fields

Electrophysiology

Single Cone Flash
Electrophysiology

Rod ERG

Differentials

- Myopic foveoschisis
- Cystoid Macular Oedema / Dystrophies
- Optic Disc Pit
- Vitreo-macular traction / epiretinal membranes
- Stickler Syndrome / Wagners VR
- Goldmann-Favre Syndrome
- Enhanced S-Cone Syndrome

Management

- Vitrectomy
  - Surgical
  - Ocriplasmin
- Low Vision
  - Colour vision
  - Contrast Sensitivity
- Genetic Counselling

Summary

- X-linked retinoschisis is a rare, degenerative condition
- Differential diagnosis can be challenging
  - Multimodal imaging useful
- Genetic testing is available
- Management is limited
- Low Vision Management is critical