VISUAL MANIFESTATIONS OF EHLERS-DANLOS SYNDROME

Christy Alfano, OD
Pediatric and Vision Therapy Rehabilitation Resident
Northwest Eyecare Professionals | Clackamas, OR

DISCLOSURES

• No financial disclosures

OBJECTIVES

• Provide an overview of Ehlers-Danlos Syndrome
• Overview of common ocular findings associated with Ehlers-Danlos Syndrome
  • Structural ocular findings
  • Functional visual findings
• Review a case of a symptomatic Ehlers-Danlos patient

OVERVIEW OF EHLERS-DANLOS SYNDROME

EHLERS-DANLOS SYNDROME (EDS)

• Inheritance
  • Majority of cases are autosomal dominant
  • Rare forms are autosomal recessive
• Prognosis
  • Variable
  • Does not typically affect hypermobile or classic types of EDS
• Vascular EDS patients have a median lifespan of 48 years
TYPES OF EDS

- 13 different types of Ehlers-Danlos Syndrome
- Hypermobile EDS – most common type

<table>
<thead>
<tr>
<th>Classifications</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Type I and II</td>
<td>Classical</td>
</tr>
<tr>
<td>Type III</td>
<td>Hypermobile</td>
</tr>
<tr>
<td>Type IV</td>
<td>Vascular</td>
</tr>
<tr>
<td>Type VI</td>
<td>Kyphoscoliosis</td>
</tr>
<tr>
<td>Type VI A and VI B</td>
<td>Arthrochalasia</td>
</tr>
<tr>
<td>Type V and VI C</td>
<td>Dermatosparaxis</td>
</tr>
</tbody>
</table>

COMMON SYSTEMIC FINDINGS OF EDS

- Joint hypermobility
- Skin hyperextensibility
- Fragile tissues
- Chronic joint pain
- Muscle fatigue
- Bruises easily
- Heart valve problems

HOW EHLERS-DANLOS IS DIAGNOSED

- 2017 International Diagnostic Criteria
  - A list of major and minor criteria for each of the 13 types
  - Lists clinical signs and symptoms for each type
  - Most types will need a confirmation with genetic testing
  - Medical doctors (primary care physicians) are able to diagnose EDS
  - Many cases may need a referral to a geneticist

OCULAR FINDINGS WITH EHRLERS-DANLOS SYNDROME

- Dry Eye
- Blue Sclera
- Keratoconus
- Lens subluxation
- Pterygium
- Retinal Detachment
- Angioid streaks
- Glaucoma
- Strabismus

STRUCTURAL OCULAR FINDINGS WITH EHRLERS-DANLOS SYNDROME

- Dry Eye
- Blue Sclera
- Keratoconus
- Lens subluxation
- Pterygium
- Retinal Detachment
- Angioid streaks
- Glaucoma
- Strabismus
STRUCTURAL OCULAR FINDINGS WITH EHLERS-DANLOS SYNDROME

- Dry Eye
- Blue Sclera
- Keratoconus
- Lens subluxation
- Myopia
- Retinal Detachment
- Angular streaks
- Strabismus

DRY EYE

- Large percentage of EDS patients experience dry eyes
- Due to inadequate closure of eyelids
- Exposure keratitis
- Symptoms worse in the morning
- May experience fluctuating vision and light sensitivity

KERATOCONUS

- Due to loss of collagen integrity of the cornea
- Clinical Findings:
  - Paracentral corneal thinning
  - Scissor reflex with retinoscopy
  - Steepening on topography
  - Vogt striae

MYOPIA

- Due to loss of collagen integrity of the sclera
- Tends to progress quickly
- Able to correct with glasses or contact lenses
- Be cautious with refractive surgery
- One study 23% of EDS patients had complications post-refractive surgery
- Complications due to healing of the cornea

RETINAL DETACHMENTS

- Weakened Bruch’s Membrane
- Angular streaks
- Irregular radiations in the peripapillary region
- Elongation of the eye increases risk
STRABISMUS

- Small misalignments
  - Patient may report occasional diplopia and eye fatigue from keeping proper alignment
  - Exotropia
  - May be due to cranial nerve 3 palsy
  - Sudden onset diplopia
  - Monitor for ptosis and papillary involvement

- Esotropia
  - Potential cause of CN 6 palsy in EDS patients
  - Cavernous Sinus Fistula
    - Spontaneous craniofacial sinus fistula is a well-known complication in vascular-type EDS patients
    - Cranial nerve 6 travels through the cavernous sinus
    - Idiopathic Intracranial Hypertension
      - Not well researched in association to EDS
      - Increased pressure on nerve as it stretches over the petrous ridge of the temporal bone

FUNCTIONAL VISUAL FINDINGS WITH EHLERS-DANLOS SYNDROME

- Convergence Insufficiency
- Oculomotor Dysfunction
- Accommodative Insufficiency
- Basic esophoria or exophoria
- Dizziness

SMALL STUDY IN FRANCE

- Published September 2019
- Retrospective study of 21 patients
  - 17 women
  - 4 men
- Most frequent ophthalmological signs:
  - Ocular motility disorders (71.4%)
  - Convergence insufficiency (61.9%)
  - Blue sclera (38%)
  - Dry eye syndrome (33%)
  - High myopia (9.5%)

CASE REPORT
CASE REPORT

- 19 year old white female
- Referred to our clinic from her chiropractor for a binocular vision evaluation

Reported visual symptoms:
- Has experienced 2 years of constant headaches
- Dizziness
- Difficulty with balance and walking
- Difficulty with reading
- Eye fatigue
- Severe light sensitivity

Onset of symptoms was 2 years ago
- Symptoms happened after taking Tramadol for severe body pain
- Took Tramadol for 5 weeks, then started becoming very symptomatic
- Later was diagnosed with Ehlers-Danlos Syndrome
- Also diagnosed with endometriosis and postural orthostatic tachycardia syndrome (POTS)
- At the time of the exam, was undergoing testing for Chiari malformation

VAs sc: 20/20 OD, OS, OU
- PERRL, (-) APD OD, OS
- Quick pupillary rebound
- VOR: quickly became dizzy, horizontal VOR was more symptomatic than vertical

NPC: 5 cm with effort, reduced with repetition, became quickly fatigued
- Distance cover test orthophoria
- Near cover test & prism dippers esophoric
- VOR: quickly became dizzly, horizontal/VOR was more symptomatic than vertical

Subjective Refraction:
- OD: +0.25 DS OS: +0.25 DS
- Distance Von Graefe phoria: 2 exo
- Near Von Graefe phoria: 2 eso
- Intermittent OD suppression

Distance Vergence Ranges:
- BO: 8/20/2
- BI: 10/18/6
- Near Vergence Ranges:
- BO: 8/16/6
- BI: 10/18/12
CASE REPORT

- NRA: +2.00 net
- PRA: -2.75 net
- FCC: +1.25 net

Treatment and Management

- Glasses:
  - Trialed prism and low-plus – no improvement in symptoms
  - Trialed small amount of broad occlusion – improvements in gait, able to walk straighter and more comfortably
  - Added FL-41-2 tint to improve light sensitivity

- Recommended weekly vision therapy
  - Focus on accommodative skills, balance, central-peripheral integration, accommodation, and binocularity

TAKE AWAY PEARLS

- Ehlers-Danlos is becoming more prevalent
- Large variation of types and clinical findings
- Many ocular findings secondary to EDS
- Refer to PCP for further evaluation

Systemic | Ocular
--- | ---
Joint hypermobility | BV issues (CI, OMD, AI, tenderness)
Stretchy skin | High myopia
Chronic pain | Dry eyes
Easily bruised | Keratoconus
Muscle weakness | Retinal Detachment

THANK YOU

- Email if you have any further questions or comments
- drchristy@doctorbruce.net
KG

60 yo WF presents to clinic 8 months following an MVA
Visual concerns are as follows:
Vertigo – when she wakes up, worsens throughout the day
Dizziness and nausea
Intermittent blur vision at distance and near
Light sensitivity, sound sensitivity
New floater – arc shaped
Difficulty with spatial recognition
Difficulty in busy places, riding as passenger
Difficulty reading – limited to 10 minutes paper, 10-15 minutes on the computer
Difficulty with anything that requires cognition – filling out the TBI questionnaire

LEE 6 months ago
Habitually wears PAs, Rx is 6 months old

Exam Findings

- VA cc @ Distance
  - 20/25 OD
  - 20/25 OS
- VA cc @ Near
  - 20/30
- Pupils: PERRL (-) APD
- EOM: full/no restrictions OD, OS
- CVF: Full to finger counting OD, OS
- CT cc @ Distance
  - Superior: 1 m. c. 4 esophoria, reported nausea
  - Primary: 1 m. c. 4 esophoria
  - Inferiorly: 1 m. c. 4 esophoria
- CT cc @ Near 10 esophoria

Disclosures

The Presenter and Organizers for "The Dizzy Patient From a Visual Standpoint"
By Dr. Stephanie Hwang has no financial relationship with any company or products mentioned in this presentation

- Ocular Health: myopia, astigmatism and presbyopia, PVD OD
- Medical History: (+) concussion
- Medications/Vitamins: Vitamin D and B
- Family Ocular and Medical History: (+) Stroke - Mother, (+) DM - Mother
- Allergies: NKDA
- Other Rehabilitation – occupational and physical therapy once a week due to accident, waitlist for SLP
Subjective Findings:
- -1.00-1.00 x 107 20/20
- -0.50-0.25 x 070 20/20
- FCC +2.25
- NS +2.50
- NBA/RA +2.00-0.75
- Von Graefe with new manifest @ D: ortho, ortho
- Von Graefe with NS @ N: 6 exo, L suppression
- Vergence Ranges:
  - At distance: Convergence 5/4/0
  - At near: Convergence 5/4/0
- Divergence: x/7/5

Assessment and Plan
- Diagnosis:
  - Esophoria
  - Convergence insufficiency
  - Binocular vision disorder
  - Dizziness and giddiness
  - Unspecified subjective visual disturbances: Visual Motion Hypersensitivity (VMH) and Visual Midline Shift (VMS)
  - Light sensitivity
  - Post-concussional syndrome
- D/c PALs until dizziness resolved. Prescribed two pairs of glasses: distance and computer/reading bifocals for work. Schedule visual processing assessment and start vision therapy working on equalizing eye movements, visual spatial awareness, proprioceptive feedback. Refer to functional neurologist for further evaluation.
- RTC for progress evaluation after 10 VT sessions

Dizziness
- Balance system consists of 3 pillars:
  - Vestibular system
  - Visual system
  - Proprioceptive
- Causes:
  - Benign Paroxysmal Positioning Vertigo (BPPV)
  - Meniere’s Disease
  - Persistent Postural Perceptual Dizziness
  - Vestibular Migraines
  - Convergence Dizziness
  - Visual induced dizziness/visual vertigo

Assessment
- Case History
- Dizziness Handicap Inventory

Testing
- Standing pursuits and saccades
- Vestibular Motion Hypersensitivity
- Vertical Molline Shift
- Vertical heterophoria
- Von Graefe
- Maddox rod
- OKN
- Walking/gait assessment
Treatment

- **Uninasal or binasal occlusion**
  - Scotch tape
  - Bangerter filter

- **Base In prism**

- **Vertical prism**

- **Syntomics**

- **Vision therapy:** Seated → standing → moving → balance
  - Phase 1: equalizing skills of pursuit, saccade, and accommodation
  - Phase 2: MPRF, binocular, stereopsis
  - Phase 3: high powered yoked prism

Referral

- Audiologist – inner ear disorders such as BPPV
- ENT doctors – disorders and diseases of ears, nose, throat, head, and neck
- Functional neurologist – brain and brain stem linked conditions
- Chiropractor, cranialsacral, massage therapy
- TMJ specialist
- Vestibular PT

Back to KG

- 28 total sessions of vision therapy
  - Progress evaluation after 10 sessions of VT
    - Decreased body sway during sensorimotor examination and visual midline testing
    - Improved stationary and ambulation, no breaks were needed
    - Able to perform pursuits but still reported dizziness
    - Decreased prisms in distance and computer/reading bifocals to 0.5 BU yoked and 1.0 BI

- 2 months with functional neurology
  - No more dizziness
  - Progress evaluation after another 10 sessions of VT
    - Removed prisms from glasses, returned to PALs

- Currently working on convergence/divergence, saccades, central/peripheral integration in VT

Clinical Pearls and Take away

- During case history, ask about experience walking down the supermarket aisle, walking across patterned floor, going to the movies (moving movement over a large area), scrolling on phone, tablets or screens
  - The power of uninasal or uninasal occlusion during a dizzy spell
  - Making a peace sign and placing hand at bridge or nose

- Have patients stand while checking pursuits and saccades
  - Observe for any body sway or movement

- Observing for gait abnormalities, walking speed, and walking behavior
- Limit hand movements when talking or excessive movement

References

What is Amblyopia?

- Definition: decreased best corrected visual acuity in one, or less frequently both eyes, in the absence of any obvious structural anomalies or ocular disease
- Visual pathway fails to develop normally due to abnormal visual experience during a sensitive period
- Most common cause of monocular vision loss in children
- 2% prevalence in the US
- 1.2% increased risk of vision loss in the sound eye

Classification of Amblyopia

- Strabismic
- Refractive
- Anisometropic
- Isoametropic
- Deprivation
- Combined mechanism

Ocular Effects

- Common signs/symptoms:
  - Reduced visual acuity
  - Reduced stereopsis
  - Increased sensitivity to contour interaction (crowding effect)
  - Abnormal spatial distortions and uncertainty
  - Reduced contrast sensitivity
  - Unsteady and inaccurate monocular fixation
  - Inaccurate accommodative response
  - Suppression

Amblyogenic Factors

- Hyperopia >1.00D >5.00D
- Myopia >3.00D >8.00D
- Astigmatism >1.50D >2.50D

Characteristics of Strabismic Amblyopia:
- Laterality: unilateral
- Fixation Distance: far and near

Characteristics of Deprivation Amblyopia:
- Physical obstruction along the line of site
Management Strategy

- Optimal Refractive Correction
- Occlusion Therapy
- Active Vision Therapy

Case Discussion

- 7 y.o Caucasian female
- Chief complaint: Referred by school for difficulties with reading
- Secondary complaints: headaches, teasing, difficulty distinguishing left and right
- Struggling with fluency of sight words, sounds out words OK, frequent letter reversals
- First eye exam

Case History

- Date: unknown
- POH: unremarkable
- PNIH: unremarkable, no complications during birth and reached normal developmental milestones
- DD/HH: unremarkable, (-) learning disabilities
- Medications: Allergies pm
- Allergies: seasonal

Examination Findings

- Entering uncorrected acuities with Snellen
  - Distance VA: Near VA:
  - OD 20/30-1 20/40
  - OS 20/125-1 20/200
  - OU 20/40 20/63-2

- EOM: full and unrestricted OD/OS
- NPC: 7/11cm; 8/15cm
- CT: 4XP; 6XP
- Stereo: 100" lateral disparity
- Pupils: ERRL (-) APD OD/OS

Refraction and DFE

- Dilated with 1% cyclopentolate and 1% tropicamide
- Ocular Health Examination: anterior and posterior segment unremarkable

<table>
<thead>
<tr>
<th>Type of Refractor</th>
<th>Refraction Findings</th>
<th>Distance VA's</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dry Autorefractor</td>
<td>OD: +2.25 -0.25 x 126</td>
<td>20/30-2</td>
</tr>
<tr>
<td></td>
<td>OS: +6.50 -0.75 x 153</td>
<td>20/100+1</td>
</tr>
<tr>
<td>Wet Autorefractor</td>
<td>OD: +3.75DS</td>
<td>20/30-2</td>
</tr>
<tr>
<td></td>
<td>OS: +7.50 -0.50 x 167</td>
<td>20/100+1</td>
</tr>
<tr>
<td>Wet Retinoscopy</td>
<td>OD: +3.00 -0.25 x 180</td>
<td>20/30-2</td>
</tr>
<tr>
<td></td>
<td>OS: +7.00 -0.75 x 170</td>
<td>20/100+1</td>
</tr>
</tbody>
</table>

Assessment & Plan

- Anisometropic Refractive Amblyopia, OS
- Prescribed the following for full-time wear:
  - OD: +2.00 DS
  - OS: +6.00 -0.50 x 170
- RTC in 1 week for VT Evaluation.
- RTC in 6-8 weeks for follow-up on new prescription and amblyopia.
Vision Therapy Evaluation

**Visuoconstructive**
- *Rapport*
- *Genius*
- *Reading: 52nd percentile*
- *Orientation: 17th percentile*

**Execution**
- *GRAPH: RS 119 seconds, < 1%*
- *movement: unstable; 60 errors*

**Oculomotor**
- *TOWRE*
  - Sight word efficiency: 8th percentile
  - Phonemic decoding efficiency: 25th percentile
- *DDT*
  - Unable to perform

Laterality/Directionality
- *DEM*
  - Vertical – RS 119 seconds, < 1%
  - Horizontal – unreliable, 30+ errors

**Dyslexia/Language Processing**
- *Fazekas*
  - Right visual efficiency: 8th percentile
  - Left visual efficiency: 20th percentile
  - *6/27: unable to perform*

Referral to a reading specialist!

Amblyopia and Reading

- Children with strabismic and/or anisometropic amblyopia vs non-amblyopes
- Compared reading rates, # of forward and regressive saccades, and fixation duration

Conclusion:
Children with amblyopia read slower and have more forward and regressive saccades during reading.

**Management Strategy**

- **Optimal Refractive Correction**
- **Occlusion Therapy**
- **Active Vision Therapy**

**Prescribing Pearls**

- Based on cycloplegic refraction using cyclopentolate
- Prescribe full amount of anisometropia, astigmatism, and myopia
- Cut Rx symmetrically between eyes

Optimal Refractive Correction

<table>
<thead>
<tr>
<th>Type of Amblyopia</th>
<th>Average lines of VA improvement</th>
<th>Resolution</th>
<th>Plateau</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anisometropia</td>
<td>@ 18 weeks: 2.8</td>
<td>27%</td>
<td>&lt;15 weeks</td>
</tr>
<tr>
<td>Strabismus</td>
<td>@ 18 weeks: 3.2</td>
<td>32%</td>
<td>&lt;25 weeks</td>
</tr>
<tr>
<td>Combined Mechanism (Strab + Aniso)</td>
<td>@ 18 weeks: 2.3</td>
<td>28%</td>
<td></td>
</tr>
<tr>
<td>Isoametropia</td>
<td>@ 52 weeks: 20/25</td>
<td>75%</td>
<td>&lt;52 weeks</td>
</tr>
</tbody>
</table>

**Follow-Up #1**

- **Compliance**: ~75% with Rx
- **Visual Acuity**
  - OD: 20/20-2 OS: 20/60-1
- **Stereopsis**
  - RD: (+) LD: (-)
- **MM**
  - DD: +0.75 DS: +1.00
- **Over-Retinoscopy**
  - DD: +0.25 DS: -0.50 DS

**Plan**: Introduce daily patching OD x 2 hours/day

**Conclusion**: Refractive correction alone can resolve amblyopia
**Management Strategy**

- **Optimal Refractive Correction**
- **Occlusion Therapy**
- **Active Vision Therapy**

**Occlusion Therapy Approach**

- Direct vs Indirect
- Total vs Partial
  - Total occlusion
    - Adhesive patch
    - Protx patch
    - Extended contact time
    - LF Bangerter foil
  - Partial occlusion
    - Adhesive amuletation
    - Bangerter foil
- Full time vs Part-time

**How Long Do You Occlude?**

**PEDIG ATS STUDIES CONCLUSIONS:**

- **Moderate Amblyopia ages 10 and younger** –
  - 6 hours of daily patching as effective as daily atropine
  - 2 hours of daily patching is as effective as 6 hours of daily patching
  - Weekend atropine is as effective as daily atropine
  - Full time Bangerter foils are as effective as 2 hours of daily patching

- **Severe Amblyopia ages 7 and younger** –
  - 6 hours of daily patching as effective as full-time daily patching

**Summary of Follow-Ups**

- Poor compliance with direct, total patching OD x 2 hours daily
- Updated Rx in attempts to improve visual acuity and resolve amblyopia
  - Additional +0.75DS hyperopia on over-refraction improved acuity 20/20-1 OS in office with loose lens
  - No changes in visual acuities with Rx update
- VA's stabilized to 20/20-1 OD, and 20/50+1 OS with Rx alone
  - Stereo improved to 250' RDS and 40' LD
- Switched to full time Bangerter Foil, OD
- Educated on contact lenses to eliminate aniseikonia

**Where are we today?**

- FT Bangerter foil, OD
  - 100% compliance with occlusion therapy
  - Visual Acuity: OD: 20/20-1; OS: 20/69 single line; 20/40 single letter
  - Stereo: 250' RDS, 40' LD

Scheduled to initiate vision therapy to improve visual acuity and binocular function

**Management Strategy**

- **Optimal Refractive Correction**
- **Occlusion Therapy**
- **Active Vision Therapy**
When Should You Refer For Vision Therapy?

- Eliminate eccentric fixation
- Reached a plateau with passive treatment
- Decrease treatment time
- Treat underlying binocular dysfunction
- Anti-suppression therapy
- Newer technologies
  - Dichoptic binocular video-based games
  - Alternative Fisher-Glass

What About Regression?

- About 1/3 of patients regress after 1 year of cessation with occlusion therapy
- Risk of recurrence is greater when occlusion is stopped abruptly versus taper

TAKE HOME:
- Follow-up in 6 months to recheck vision
- Taper occlusion therapy

Clinical Pearls

- Compliance is KEY!
- Close follow-up
- Don't try to push everything at once
- Monitor binocular function, not only monocular function
- Know when to refer for vision therapy

References

- Evans E. Refraction in children using the R x 1 autorefractor. Br J Orthopt 1984; 41:46-52

THANK YOU!

Any further questions, please feel free to email me at: prashna.mistry@pacificu.edu