The Diagnosis and Low Vision Management of Two Patients with Presumed Complete Achromatopsia

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Abstract:
A comparative analysis of two patients with a diagnosis of achromatopsia, presented for low vision evaluations with variations in their clinical findings. Several diagnostic tests are useful to determine final diagnosis and treatment options.

I. Case history

Patient A

- 28 year old Caucasian female presents for a low vision evaluation
- CC: Photophobia OU; reduced vision OU
- Patient medical history: Unremarkable
- Patient ocular history: Previous diagnosis of complete achromatopsia in 1990; denies prior ERG testing
- Family history: denies low vision/blindness/color vision deficits

Patient B

- 17 year old African-American male presents for a low vision evaluation
- CC: Photophobia OU; reduced vision OU
- Patient medical history: unremarkable
- Patient ocular history: Previous diagnosis of complete achromatopsia; denies prior ERG testing
- Family history: denies low vision/blindness/color vision deficits

II. Pertinent findings

Patient A

- VA: OD 20/125, OS 20/100 (in dim lighting)
- Refraction:
  - OD: -0.50 sph 20/125
  - OS: -0.50 sph 20/100
- Confrontation visual field: Full to finger count
- EOMs: Full and smooth, no restrictions; (-) Nystagmus OU; however, patient stated prior jerky eye movements as a child
- Contrast sensitivity: Normal
• Color vision:
  o Ishihara: 5/14, OD; 5/14, OS
  o D-15 Farnsworth
    ▪ OD: no discernable pattern
    ▪ OS: no discernable pattern
• SLE: Unremarkable OU
• IOP: 16 mmHg OD, 16 mmHg OS (Goldmann Applanation Tonometry)
• Ocular fundus examination: Foveal atrophy with parafoveal and perifoveal retinal pigment epithelial changes, (-) Foveal reflex. Small optic nerves and .2/.2 cupping. Nasal elevation of optic nerve head with distinct margins and no vessel obscuration.

Patient B
• VA: OD 20/100, OS 20/125 (in dim lighting)
• Refraction:
  o OD: +1.00 -1.50 x 015  20/100
  o OS: +1.00 -1.75 x 008  20/125
• Confrontation visual field: Full to finger count
• EOMs: Full, Jerky movements with no restrictions; (+) Rotary nystagmus OU with worsening on up gaze and dampening on convergence
• Color vision:
  o D-15 Farnsworth
    ▪ OD: no discernable pattern
    ▪ OS: no discernable pattern
• SLE: Unremarkable OU
• IOP: 18 mmHg OD, 18 mmHg OS (Non-Contact Tonometry)
• Ocular fundus examination: Flat and intact macula with retinal sheen and a foveal reflex OU. ONH perfused with distinct margins, .2/.2 cupping.

Patient A/B:
• Electroretinographic testing, 10-2 Humphrey Visual Field, Macular Cube OCT, and Fundus Photography
  o A side-by-side comparison of the similarities and differences

III. Differential diagnosis
• Leading:
  o Complete achromatopsia
  o Incomplete achromatopsia
• Others:
o **Blue cone monochromatism** is less likely due to the lack of residual color vision discrimination and X-Linked inheritance pattern
o **Ocular Albinism** is less likely due to no evidence of a blonde fundus and/or iris transillumination defects

IV. **Diagnosis/Discussion**

- Complete and incomplete achromatopsia is a stationary cone dysfunction syndrome of autosomal recessive inheritance. Achromatopsia typically presents with decreased visual acuity, abnormal color vision, photophobia, nystagmus that can wane with time, hyperopia, and absent or reduced photopic electroretinographic recordings with preservation of scotopic recordings. Incomplete achromatopsia is reserved for variants of the phenotype and have milder effects.
- Additional findings: shallow and/or broadening of the foveal depression, foveal atrophy with parafoveal retinal pigmentary changes, and central scotomas.
- There are six genes (CNGB3, CNGA3, GNAT2, PDE6C, ATF6, PDE6H) that have been associated with achromatopsia and three (CNGA3, CNGB3, and GNAT2) that account for the majority of achromatopsia.

V. **Treatment/Management**

- Low vision management:
  - Correct refractive error: although spectacle prescription did not significantly improve visual acuity, patient A/B educated on the importance of wearing protective/polycarbonate lenses.
  - Magnification devices:
    - Patient A: 4x Ocutech VES Sport improved acuity to 20/20 at distance, better acuity than expected can be attributed to decreased light/photophobia with device
    - Patient B: not interested in devices at this time; psychosocial component – patient does not want classmates to know he is visually impaired
  - Absorptive lenses to reduce photophobia:
    - Patient A: Fit with amber/rusty-red centered contact lenses with subjective improvement in photophobia and increased acuity to 20/80 OD, OS.
    - Patient B: Currently wearing over-the-counter grey sun lenses with subjective improvement in
photophobia; discussed tinted contact lenses; however, he is not interested at this time

- Genetic testing and/or detailed family history:
  - Patient A/B: Denies family history of decreased acuity, photophobia, and/or color vision deficiency further suggesting autosomal recessive inheritance

- Ocular health management:
  - Annual dilated fundus examinations with macular OCT testing and fundus photography to monitor foveal atrophy and central foveal thickness

- In the future:
  - Gene replacement therapy trials:
    - Replacement for both CNGA3 and CNGB3 have been studied in animal models and shown recovery of cone ERG amplitudes to nearly normal levels.
    - Studies have not shown age-dependent cone loss; therefore, implying candidates for gene therapy may be considered irrespective of age
    - Evidence of visual cortex activity in achromatic canine models following gene therapy.

- Literature review:

VI. Conclusion

- Management of achromatopsia is multifaceted, including making the appropriate diagnosis, correcting refractive error, reducing photophobia, and utilizing low vision devices.
- There is a variety of phenotypes and genotypes that correspond with this syndrome and varying clinical presentations and findings.