Abstract:
Optic nerve pallor is a sign of insult or damage to the nerve fiber layer commonly from trauma, ischemia, infection, inflammation, or a space occupying lesion. This exam finding warrants a proper investigation and potentially a work-up to determine the underlying cause.

Learning Objectives
1. Review management of optic nerve pallor through case presentations.
2. Review important case history questions, proper ancillary testing, and ocular findings that may reveal underlying cause of optic nerve pallor
3. Review role of labs and imaging in diagnosing and when it is appropriate to order them

I. Optic Nerve Characteristics
A. Normal color
   - Result from small vessels on disk and nerve fiber layer
B. Pallor
   - Sign of irreversible damage to normal optic nerve
   - Diffuse or sectoral atrophy
   - Unilateral or bilateral
   - Visual acuity, visual field, color vision level correlated with degree of atrophy
C. Ancillary Testing
   - Best corrected visual acuity
     - Decreased vision = Papillomacular bundle involvement in ON pallor
     - Glaucoma typically no have decreased vision until late stages
   - Pupils
   - Visual Fields
     - Altitudinal defects in ischemic optic neuropathy
     - Central or cecocentral in toxic/nutritional, hereditary neuropathies
     - Hemianopic defect respecting vertical midline → chiasm or posterior chiasm
     - Junctional scotoma → compressive at junction of ON and chiasm
   - Color Testing
     - Often have red color desaturation
     - Red cap test: “faded, pink, washed out”
     - Asymmetry rare
   - Nerve fiber layer analysis
     - Pattern of NFL loss more diffuse with ON pallor
- More horizontal thinning temporal >> nasal quadrants vs Glaucoma
- Average macular thickness significantly lower in non-GLC analysis
- SD OCT intraretinal, round hyporeflective structures at macula, pseudocysts associated with severe ON fiber loss of any cause, imply poor functional outcome (Wolff et al. 2013; Abegg et al. 2014)

- Imaging:
  - Routine diagnostic neuroimaging unnecessary
  - Only order selectively in atypical cases
  - 91 patients with unexplained optic atrophy, 18 (20%) had compressive lesion and 73 (80%) had no etiology on neuroimaging (Lee et al. Ophthalmology 2005)

D. Personal/Medical History Questions
- Age
- Medications, Diet, Social History (Alcohol, Smoking)
- Diabetes, Hypertension, High Cholesterol
- Vision loss gradual or acute? Progressive?
- Painful or painless loss of vision?
- Eye pain with movement
- Trauma, Blood loss
- Temporal pain, jaw claudication, TMVL, diplopia, fatigue → A-AION
- Diplopia? Facial pain? → inflammatory or neoplastic lesions

E. Differential Diagnosis
- Pseudophakia Pallor
- Trauma Related
  - Purtscher’s retinopathy, Traumatic Optic Neuropathy
- Toxic Optic Neuropathy (Nutritional, Medication)
  - Ethambutol, Amiodarone, Alcohol, Methotrexate, Cyclosporine
- Vascular
  - Non-Arteritic Ischemic Optic Neuropathy, Arteritic AION, Artery Occlusion
- Infectious/Inflammatory
  - Optic Neuritis
- Optic nerve compression
  - Pituitary Adenoma, ON glioma/meningioma, dolichoectatic carotid artery)
- Glaucoma
  - Less neuroretinal rim pallor, larger C/D ratio, notching, vertical elongation, PPA, backward bowing or excavation of lamina cribrosa, positional change of BV 2/2 loss of supportive structure, asymmetric of these characteristics between eyes
  - In absence of disk edema, disk hemorrhage 100% specific for glaucoma
  - Greenfield et al Study on NTG: Age < 50 years, VF defects obeying vertical midline, vision loss, pallor > cupping specific for nonglaucomatous cupping associated with compressive lesions
- Congenital defect
  - Optic Nerve Hypoplasia, can be sectoral
II. Anterior Ischemic Optic Neuropathy
   A. Characteristics
      - Acute unilateral vision loss, typically noticed in the morning ~80%
      - Temporary hypoperfusion or nonperfusion of anterior optic nerve circulation
      - Predisposing risk factors: systemic HTN, nocturnal hypotension, diabetes, hyperlipidemia, atherosclerosis
      - Optic Nerve Head: absent or small cup, location of watershed zones
      - Precipitating risk factors, "last straw": Nocturnal Hypotension, ED medication
   B. Management
      - Disk at risk? Risk in contralateral eye
      - Sectoral pallor common
      - Baseline visual field, may improve up to 6 months
         - Altitudinal defect
      - OCT, commonly sectoral thinning
      - Management of systemic disease
      - Discontinue erectile dysfunction medication and/or patient education regarding link
      - Consider switching BP medications from PM to AM if no contraindication
      - ESR, CRP, Platelets?

III. Retinal Arterial Occlusion
   A. Characteristics
      - Diffuse pallor for CRAO, sectoral for BRAO
      - Central Retinal Artery Occlusion
         - 63% pale disks within 1 month, 79% pale disks within 2 months, 91% pale disks within 4 months
      - Cilioretinal collaterals (CRAO)
         - 4% within 1 month, 18% within 3 months with permanent CRAO
         - 32% within 3 months for CRAO with cilioretinal artery sparing
      - Sclerosed or sheathed vessels
      - Artery >> Venous attenuation
      - Macular RPE changes in CRAO
   B. Management
      - Carotid Ultrasound, EKG/ECG
      - Manage systemic disease
      - Education regarding stroke risk as applicable

IV. Nutritional Optic Neuropathy
   A. Characteristics
      - Painless, symmetrical bilateral vision loss
      - Central or cecocentral scotoma (papillomacular bundle)
      - Bilateral nerve pallor/atrophy, temporal
Phosphenes proceed or accompany decreased visual acuity
- Associated with alcohol, heavy tobacco use, methanol, tuberculosis medications, epilepsy medications (Vigabatrin), Disulfiram
- Poor Nutrition (Cuba food shortage)
- Prisoners of War
- Residents of Nigeria/Jamaica (Cassava staple food contains cyanide)

B. Management
- MRI to rule out tumor
- Visual Field, Color Vision, OCT
- B1, B2, B6, B9, B12, Folate, Cysteine, Zinc deficiency
- Vitamin B supplement
- Discontinue source of toxicity, improve nourishment/eating habits if possible

V. Optic Neuritis
A. Characteristics
- Multiple Sclerosis most common cause
- Autoimmune disease (Sarcoidosis, Lupus), infection causes (Syphilis, TB), inflammatory and post vaccination (sinusitis, vaccinations against measles and rubella)
- Young adult women 15 - 50 years
- Unilateral, subacute, PAIN (90%) with vision loss, dyschromatopsia
- Vision loss ranges 20/20 to NLP
- Initial presentation 20% MS patients, occurs 50% of patients during course of disease

B. Management
- Co-manage with Neurology, disease modifying drugs (DMDs)
- MRI
  - Initial # lesions on first scan strongly related to risk of developing MS
  - First episode but normal brain scan = 25% risk of MS at 15 years vs. 72% risk if lesion detected on 1st scan
- DMDs
  - Interferon Beta-1a (Avonex), 1b (Betaseron), Glatirimer Acetate (Copaxone)
    Given to patients at high risk of developing MS as prophylaxis
- Visual Acuity
  - Slightly worse in MS related incidents vs. Non-MS
  - Recovery observed within 2-3 weeks > 80% without treatment
  - Vision stabilizes and continues to improve up until 1 year
- Pupils, Contrast Sensitivity, Color Vision
- Visual Field
  - Any type: Diffuse depression, central or cecocentral scotoma
  - Rarely altitudinal or quadrantic
- OCT
  - MS patients may have RNFL thinning even without prior episode of optic neuritis – diffuse neurodegenerative process
-Highest degree of RNFL thinning in temporal quadrant
-RNFL thickness may predict visual recovery following optic neuritis
-Future outcome measure for neuroprotective therapies in clinical trials

VI. Segmental Optic Nerve Hypoplasia: Topless Optic Disk Syndrome
A. Characteristics
-Congenital
-Association with poor maternal diabetic control (Type 1 and gestational), shorter gestation time, low birth weight
-Segmental optic nerve hypoplasia: Superior disk pallor, sectoral scleral halo, relative superior entry of central retinal artery, superior NFL loss with inferior field defect
-Women > Men
-Bilateral > Unilateral
B. Management
-Young healthy patients, asymptomatic for inferior blind spot oriented VF loss
-Normal vision, color, pupil response
-Recommend siblings have eye exam with screening visual field
-Avoid misdiagnosis and unnecessary medical testing

VII. Chiasmal Syndrome
A. Characteristics
-Association with trauma: young males, motor vehicle accidents, motorbike, falls, cycling, horse riding, assault 2/3 suffered skull fractures
-Direct tearing, contusion hemorrhage, contusion necrosis of optic chiasm
-Bow Tie Optic Atrophy
-50% brain tumors have VF defects
-25% brain tumors arise from chiasmal area
-More congruous defects -> more posterior lesion
B. Management
-Visual acuity may be spared with only VF defect
-Visual field most important
-Common to have bitemporal defect
-Non pituitary adenoma more likely 6.25 times w/ complete VF defect vs. incomplete VF defect
-Anterior lesion: total field loss one eye and temporal hemianopia in fellow eye
-MRI
-37% go on to develop Diabetes due to endocrine damage
-Co manage with Neurology and Endocrinology/Primary Care
Bibliography


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