Optic Nerve Anomalies
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Goals for today
• Review some of the optic nerve anomalies that can be seen in practice
• Review signs and symptoms of varied conditions
• Understand management and treatment options
• Review clinical tips and cases

Optic Disc Pits

Optic Disc Pits: Background
• Spectrum of congenital cavitary anomalies of the optic disc, which also includes optic disc coloboma, morning glory syndrome
• Due to incomplete closure of the superior edge of the embryonic fissure
• Optic disc pits are usually unilateral and sporadic in occurrence
• Rare and occur equally in men and women with an estimated incidence of 1 in 11,000 people

Signs and Symptoms

• Signs
  • Single, oval-shaped depressions at the optic disc
  • Commonly found at the infero-temporal aspect
  • Can be found elsewhere, including centrally
  • Occasionally, an optic disc can have more than one pit
  • ODPs are usually grayish, but may also be yellow or black
  • Maculopathy

• Symptoms:
  • Asymptomatic
  • Decreased VA
  • VF: enlarged blind spot, paracentral scotoma
Optic Disc Maculopathy

- Optic disc pit maculopathy: macular changes that occur which include intraretinal and subretinal fluid accumulation, and RPE changes
- Maculopathy occurs in 25–75% of patients with an ODP
- Fluid source: vitreous, CSF, blood vessels, choroid
  - ODPs are congenital, but the development of maculopathy has no known triggers

Optic Disc Maculopathy

- Can occur at any age, from early childhood to the ninth decade of age
  - Usually occurs in the third and fourth decades of life
  - PVD process?

Optic Nerve Pits

- No established guidelines for the treatment of ODP-M, and no consensus on the mechanism of pathogenesis or the optimal surgical technique
- Argon laser photocoagulation
  - Laser scars at temporal disc margin will create a chorioretinal adhesion which will act as a barrier between the ODP and the subretinal space
- Vitrectomy with gas tamponade
  - Traction relief
  - Gas barrier that blocks passage of fluid through the pit

Idiopathic Intracranial Hypertension (Pseudo-tumor Cerebri)
Idiopathic Intracranial Hypertension

- Disease of increased intracranial pressure with no known cause
- Can lead to progressive visual loss (acuity and field)
- The annual incidence of IIH is 0.9/100,000, 3.5/100,000 in females 15 to 44 years of age.
- More than 90% of IIH patients are obese and over 90% are women of childbearing age.

Disease Background: Etiology/Pathogenesis

- Poorly understood
- Most popular: reduced CSF absorption due to dysfunction of arachnoid granulations
- Absorption dysfunction possibly through lymphatics
- Increased intra-abdominal pressure with cerebral venous hypertension
- A good hypothesis should account for why it occurs in obese women in childbearing years

Mechanism of VA Loss

1. Disruption of axonal transport
   - Elevated CSF disturbs normal pressure gradient resulting in axoplasmic stasis
2. Intraneuronal optic nerve ischemia
   - Hayreh: delays in arterial filling with FA
   - Visual field defects similar to other optic neuropathies

Symptoms

- VA loss
- Headache
  - Usual presenting sign
  - Severe, constant, pulsatile
- Transient Visual Obscurations
  - Usually less than 30 seconds
  - Possibly due to transient ischemia of the ONH
- Tinnitus
  - Thought to be due to transverse sinus collapse (venous stenosis) from high CSF pressure

Signs:

- Papilledema: cause of visual loss
  - Grading system from 0-5
- Ocular Motility Disturbance:
  - Sixth nerve palsy, horizontal diplopia
- Perimetry
  - Enlargement of blind spot
  - Visual field loss other than enlarged blind spot in 92% of patients
  - Inferior nasal step, peripheral nasal loss, arcuate
  - Good for following pt for improvement

Diagnostic Testing

- Intracranial imaging – CT adequate for mass lesions
- MRI & MRV are preferred due to superior ability to diagnose venous sinus thrombosis.
- Lumbar Puncture –
  - Measure opening pressure and send CSF for analysis (routine, infection, cytology, etc.)
Modified Dandy Criteria

- Signs and symptoms of increased intracranial pressure, such as papilledema and headache
- No localizing findings on neurological examination except for cranial nerve six palsy
- Normal MRI/CT scan
- High intracranial pressure of 250mmH2O or above on a spinal tap, with no abnormalities of cerebrospinal fluid
- Is awake and alert
- Has no other cause of increased intracranial pressure found

Treatment/Outcomes

- Most important factor is amount and progression of visual loss
- Severity of patient symptoms
- Eliminate presumed causal factors
  - Oral contraceptives
  - Tetracyclines
  - Nalidixic acid (anti-biotic)
  - Vitamin A
Treatment: Medical Therapy
- Weight Loss
  - Papilledema can resolve with modest weight loss (5-10% of total body mass)
- Lumbar Puncture
- Corticosteroids-side effects, rebound pressure increase
- Diamox
  - Reduces CSF production at the choroid plexus
- Topomax
  - CAI, weight loss common, comparable to diamox

Surgical Therapy
- Optic Nerve Sheath Fenestration
  - Preferred treatment for patients with progressive VA loss and mild headaches
  - CSF drains into orbital fat where it is absorbed into the venous circulation
- CSF Shunting Procedures
  - Indicated if failed medical therapy or intractable headache
  - Initial success but reoperations in almost 50% of patients

Idiopathic Intracranial Hypertension Treatment Trial
- Multicenter, double-blind, randomized, placebo-controlled study
  - All patients lifestyle modification program of weight reduction with a low-sodium diet.
  - Then randomized to receive either acetazolamide or matching placebo
- Outcomes:
  - better visual outcomes than those taking placebo along with the diet.
  - significantly improved papilledema
  - quality of life measures
  - lower cerebrospinal fluid pressure.

Optic Nerve Head Drusen
- consist of acellular, intracellular, and extracellular protein deposits (hyaline) that often become calcified over time
  - Due to disturbance in axonal metabolism with slowed axoplasmic flow
- Typically buried early in life and generally become superficial, and therefore visible, later in childhood
  - Average age of 12 years

Background
### Background

- 1% of general population affected
- Higher risk in **Caucasian** population
- Can be associated with other conditions (pseudoxanthoma elasticum, retinitis pigmentosa, angioid streaks)

### Signs and Symptoms

- **Signs:**
  - 75-85% bilateral
  - Yellowish deposits on and around optic nerve
  - Edges of optic disc or cup may be distorted
  - Scallop
  - Loss of optic cup and disc borders (may resemble papilledema)
  - Marked bifurcations and trifurcations
- **Symptoms:**
  - Usually asymptomatic
  - Up to 8.6% reported to have transient visual obscurations
  - Visual field defects
  - Central visual acuity loss may occur

### Complications:

- Visual field defects
- Hemorrhages
- Choroidal neovascular membrane
- Nonarteritic anterior ischemic optic neuropathy
- Retinal vascular occlusions

### Clinical Pearls

- **How can I confirm the ONH drusen?**
  - Gold standard…
  - OCT
  - FAF
  - Autofluorescence of drusen depends on its depth
  - Deep buried drusen may be difficult to assess using FAF.

- **It looks like IIH?**
  - Symptoms… (headaches, VA loss, tinnitus)
  - Presence of a spontaneous venous pulse (SVP)
  - Rules out true papilledema?
  - Absence of SVP occurs in 20% of the normal population
No definitive therapy available

Clinical pearl:
- Should I prescribe glaucoma drops for ONHD?
- Depends on the IOP.
  - VFL occurs more frequently in eyes with ONHD that also have OHT.
  - Patients with elevated IOP and ONHD should remain under close surveillance for disease progression and be treated appropriately to prevent additional visual field loss.
  - In the absence of elevated IOP, there is no evidence that IOP reduction will have any effect on preventing visual morbidity.
  - Problems with both thoughts of research...all retrospective.
    - no controlled clinical studies that show a benefit to lowering IOP in any eyes with ONHD.
Problems with long-term iop treatment??
- Anti-VEGF for CNVM
- Manage concurrent conditions

Nutritional and Toxic Optic Neuropathies

Toxic and nutritional optic neuropathies often both present in the same patient and have similar clinical presentation
- History of exposure to foreign substance
  - Would need to ask appropriate history questions...
- Onset usually after months of exposure
  - Acute in some cases...
  - May be asymmetric presentation, but usually equal

Pathogenesis remains unknown in most cases
- For vitamin B12 deficiency and at least some toxic agents, including methanol, ethambutol, and linezolid, the final common pathway probably involves damage to mitochondrial oxidative phosphorylation
  - Decreased ATP and generation of ROS
- Leads to damage to the papillomacular bundle

Clinical Picture
- Signs:
  - Optic nerve pallor (temporal) (papillomacular)
  - Visual field defects (ceco-central)
  - Color vision defects
  - OCT: RNFL thinning, especially in the papillomacular bundle

- Symptoms:
  - Painless, bilateral, gradual vision loss

Causes:
- Toxic:
  - Methanol, ethylene glycol (antifreeze), ethambutol, isoniazid, digitalis, cimetidine, vincristine, cyclosporine, toluene (feedstock, paint thinner), and amiodarone

- Nutritional:
  - Associated with malnutrition or poor dietary habits, incorrectly applied vegetarian diet, or chronic alcohol abuse
    - Folic acid
    - Vitamin B complex deficiency: B1, B2, B12
    - Patients after bariatric surgery
    - Copper
**Optic Nerve Head Hypoplasia**

- **Nutritional:**
  - Blood testing
  - Administer appropriate nutrient
  - Prognosis depends on length of exposure and individual factors

- **Toxic:**
  - Immediate withdrawal from toxic agent
  - Prognosis dependent on toxicity of agent, length of exposure, individual factors

**Background**

- Optic Nerve Hypoplasia is the under-development of the optic nerve combined with possible brain and endocrine abnormalities.

- Possible systemic associations:
  - Endocrine abnormalities
  - Developmental delay
  - Cerebral palsy
  - Seizures

- There is a greater incidence of clinical neurologic abnormalities in patients with bilateral ONH (65%) than patients with unilateral ONH.

**Pathophysiology**

- ONH occurs due to diminished number of axons in the involved nerve with normal development of supporting tissues and the retinal vascular system.

  - 16-17 weeks, there are approximately 3 million optic nerve axons which ultimately are reduced to approximately one million at the time of birth.

  - Hypoplasia may therefore be an overdone, but normal, process of involution.

- The timing of coexistent CNS injuries suggest that some cases of optic nerve hypoplasia may result from intrauterine destruction of a normally developed structure whereas others represent a primary failure of axons to develop.
Signs and Symptoms

Signs:
- Small optic disc with large vasculature
- Visual field defects
- May be associated with nystagmus
- (OCT) shows a mild degree of foveal hypoplasia with associated thinning of the retinal ganglion cell and nerve fiber layer

Symptoms:
- 20/20 to NLP
- Acuity worse??
- Does size play a factor?
- VA remains mostly unaffected and the finding of visual field defects later in life may result in a late diagnosis
- Localized visual field defects, often combined with a generalized constriction of the visual fields

Figure 1. Optic Disc Size Measurement

Measurement of optic disc size:

Biomicroscopy:
- Use a lens
- Measure length of slit beam

Correction factors:
- Volk 40 D x 1.0
- Volk 78 D x 1.1
- Volk 99 D x 1.3

Average vertical diameter: 1.6 mm
Average horizontal diameter: 1.7 mm

Vertical and horizontal disc diameters can be obtained during slit lamp examination with a funduscope, applying correction factors according to the lens magnification.

Source: Felipe A. Naderes, MD, PhD
Clinical Pearls:

- In more mild cases, disc to macula distance/disc diameter ratio will be increased. A ratio of ≥1.5 is seen in the normal population and greater than three indicates milder forms of ONH Hypoplasia.

- The "double ring sign" can be seen in some patients and is characterized by a pigmented ring surrounding the disc.

- Retinal vascular tortuosity is also an important but inconsistent sign.

- None of the above is considered pathognomonic

Treatment

- No treatment for optic nerve hypoplasia.
  - Monocular precautions
  - Low vision rehab

- Appropriate referrals:
  - Pituitary abnormalities: pediatric endocrinologist for hormonal supplementation is necessary.
  - Neuro
  - Occupational, physical and speech therapists