Optic Nerve Hypoplasia

- Abnormally small optic nerve head
- Congenital decrease optic nerve fibers

Septo Optic Dysplasia - any combination of optic nerve hypoplasia, pituitary gland hypoplasia and midline brain abnormalities

Epidemology

- One of leading causes of childhood blindness
- Incidence
  - Olmstead County, MN- 2.4 per 100,000 children (0-19 years) or 1 in 2287 live births
  - Alaska, 1 per 1000 live births
  - Manitoba Canada- 1 in 1,875 live births or 53.3/100,000 children < 19 years old Paediatr Child Health 2017 Nov;22(8):445
  - Stockholm, Sweden- 17.3/100,000 children < 18 years old Acta Ophthalmol 2014 Sep;92(6):563

Risk Factors

- Young maternal age
- First parity
- Maternal smoking
- Preterm birth

Diagnosis

Clinical Features

- Peripapillary ring- “Double ring sign”
- Small optic nerve
- Thinning of the nerve fiber layer
- Possible tortuosity of retinal vasculature
- Possible persistent grey appearance of the nerve

Optic Nerve Measurements

- Fundus Photography
  - Ratio of Mean Disc Diameter (DD) to Macula-Disc distance (DM)
    - (Horizontal + Vertical Disc Diameter /2) : Distance from center of disc to the center of the macula

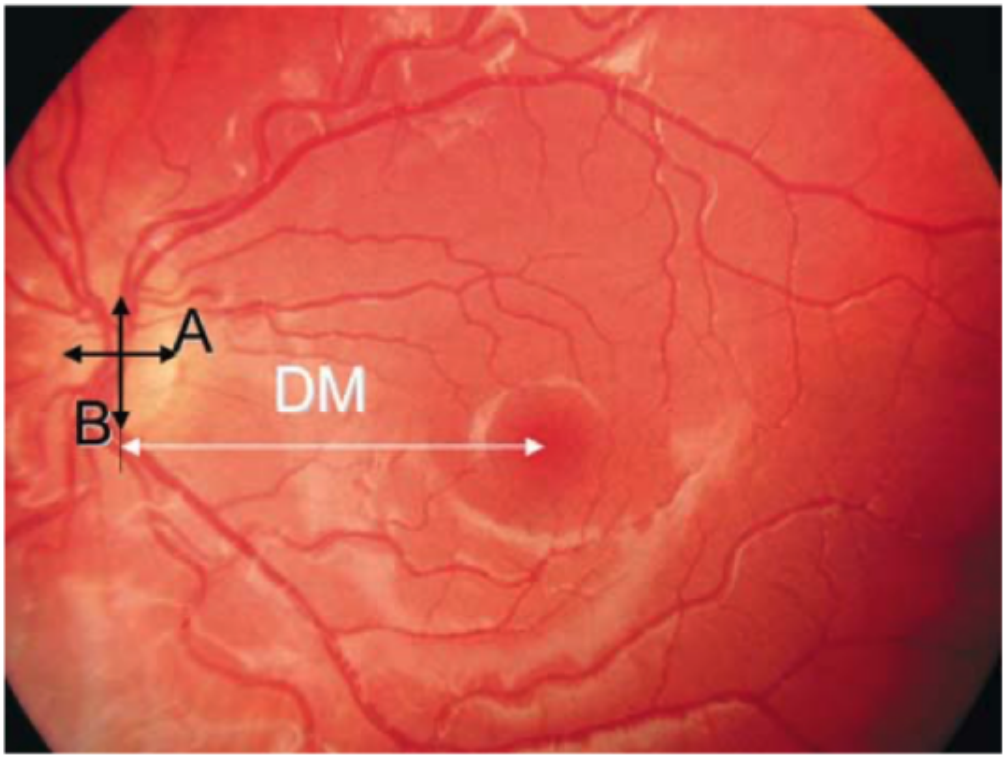

Figure 4 ONH. The mean disc diameter (DD) is (A + B)−2. The perpendicular distance between the centre of the disc and the macula is shown as DM (the distance between the centre of the disc and the centre of the macula). When the ratio of DM to DD is greater than 3, ONH is suspected, and when it is greater than 4, ONH is very likely.

    - from Dutton GN. Congenital Disorders of the optic nerve: excavations and hypoplasia. Eye.2004;18:1038-1048
  - OPTOS photographs of 188 adults and children with OHN (108) compared to normals (88)
    - Normal optic nerve horizontal diameter: 1.70 mm (95% CI 1.49, 2.14)
    - Hypoplasia horizontal optic nerve diameter: 1.23 mm (95% CI 0.38, 1.45)
    - Arnold AW et al. Direct OPTOS Nerve Size Determination of Prevalent Optic Nerve Hypoplasia in Alaska. Clinical Ophthalmology 2020;14:491-499
  - Optical Coherence Tomography
    - Hypoplasia may be present the disc area is **<1.3 mm²**
    - Many commercial devices will attempt to plot the disc diameter and area
    - Optic Disc Area Calculator
    - Normal values for optic discs measured by OCT
- MRI

Genetics

- 11 rare single nucleotide variants were identified in 10 persons (34%) in one 2020 study, including:
  - 2 variants in COL4A1
  - 2 variants in COL4A2
  - 2 variants in CYP26C1
  - 1 variant in each of OPA1 (in a patient who also had a COL4A1 variant), KIF7, SPG7, CYP26A1, and UBE3B
  - 1 copy number variant was identified in SOX5 in 1 patient

See PLoS One 2020;15(2):e0228622

Associated Findings

- Brain Anomalies
  - More common
    - Microcephly, absent septum pellucid, posterior pituitary ectopia, migrational anomalies (hypoplasia of corpus callous)
  - Less common
    - porencephaly, schizencephaly, arachnoid cyst, epidermoid cyst
- Pituitary Dysfunction
  - neonatal hypoglycemia
    - associated with neonatal cholestatic jaundice, convulsions and or coma after anesthesia
  - growth hormone deficency
  - diabetes insipidus
- olfactory hypoplasia

In Olmstead County, MD population

- Premature birth- 32%
- Maternal diabetes- 16%
- Bilateral- 84%
- Developmental Delay- 63%
- Neurologic defects- 53%
  - Microcephaly (16%)
  - Cerebral palsy (16%)
  - Corpus callous hypoplasia (11%)
  - Septum Pellucidum aplasia (11%)
  - White matter hypoplasia (11%)
  - Hydrocephalus (11%)
  - Decreased visual acuity- 47%

    - Strabismus- 42%
        - Esotropia 21%
        - Exotropia 21%
    - Endocrine dysfunction- 26%
        - Growth hormone deficiency (16%)
        - Hypothyroid (16%)
        - Diabetes insipidus (11%)
        - Adrenal insufficiency (5%)
        - Hypopituitarism (5%)
        - Precocious puberty (5%)
    - Nystagmus- 26%
    - Refractive error can be myopia, hyperopia and or astigmatism
    - Amblyopia- 11%

Associated Disorders

- Aicardi Syndrome
- CHARGE Syndrome
- Dominant inheritance
- Prenatal Drug exposure
    - Anticonvulsants
        - Phenytoin (dilantin)
        - Phenobarbital
    - Ethanol
    - Isotretinoin
    - Valproic Acid
- Chromosome abnormalities
    - Distal 5q deletion syndrome
    - Chromsome 1 anomaly- Muscle eye brain disease
    - Partial deletion chromosome 6p
    - Chromosome 7(q22→q34) and 7q32-34 interstitial duplication
    - Chromosome 17 interstitial deletion
- Frontonasal dysplasia
- Goldenhar syndrome
- Idiopathic growth hormone deficiency (ONH seen in 9%)
- Nevus sebaceous of Jadassohn (cutaneous, possibly malignant, phacomatosis)
- Maternal Diabetes
- Orbital hemangioma
- Periventricular leukomalacia
- Suprasellar teratoma

Resources

- Mohoney BG et al. Incidence and Associated Endocrine and Neurologic Abnormalities of Optic Nerve Hypoplasia. JAMA Ophthalmol. 2013:131(7)898-902.
- Dutton GN. Disorders of the optic nerve: excavations and hypoplasia.Eye 2004;18:1038-1048
- Arnold AW et al. Direct OPTOS Nerve Size Determination of Prevalent Optic Nerve Hypoplasia in Alaska. Clinical Ophthalmology 2020;14:491-499
- Pang Y. et al. Comparison of Heidelberg Retina Tomograph with disc macula distance to disc diameter ratio in diagnosing optic nerve hypoplasia
- Hellström A. et al. The Clinical and Morphologic Spectrum of Optic Nerve Hypoplasia. JAAPOS 1999;3(4):212-20

optic disc