The Patient with Visual Loss: Localization of Neuropathologic Disease and Select Diseases of Neuropathologic Interest

Steven A. Kane, M.D., Ph.D.
The Edward S. Harkness Eye Institute

Shared embryology

- Eye and brain develop from neuro-ectoderm
- Their functions and responses to disease are related
- Blood ocular/brain barriers
- The eye is a window into the brain and systemic disease
Ocular anatomy

- Unique example of structure supporting function
- Optics
- Neuro-transduction
- Neuro-transmission

Normal left ocular fundus

- Optic disc
- Retinal vessels
- Transparent retina
- Macula
- Retinal pigment epithelium
- Choroid
Retinal nerve fiber layer anatomy

- Papillomacular bundle begins the macular-cortical projection
- Ganglion cells and axons respect the horizontal raphe

Retro-bulbar visual anatomy

- Optic nerves carry information from each eye
- Axons from the nasal retinas cross at the optic chiasm
- Optic tracts carry right and left sided visual information
- Thalamus
- Optic radiations
Localization and characterization of impaired vision

- Pattern of visual loss may identify the lesion site
- Disease course and accompanying symptoms may clarify its nature

Patterns of visual loss

- Scotomas
- Central vision
- Peripheral vision
- Symmetry/congruity change as information nears cortex
Ocular causes of impaired vision

- Refractive error
- Media opacity
- Retinal disease
- Optic nerve disease
Retinoblastoma

- Most common intraocular malignancy in childhood
- Leukocoria and strabismus
- 13 q14 mutation
- Spreads along the optic nerve into the brain

Retinoblastoma

A rapidly growing primitive neuroectodermal tumor that may show retinal differentiation in the form of Flexner-Wintersteiner rosettes
Retinal causes of impaired vision

- Symptoms
- Age-related macular degeneration is the most common cause of visual loss > 65 years
- Diabetic retinopathy is the most common cause of visual loss < 65 years

Symptoms and signs of optic nerve disease

- Blurred vision
- Dimming of vision with decreased color perception
- Decreased pupillary response to light
- Centrocecal, and arcuate scotomata
Centrocecal scotomas
Bilateral optic atrophy with centrocecal scotoma

- Hereditary (dominant, Leber’s)
- Toxic (medications, methanol, heavy metals)
- Nutritional (folate, B12)
- Demyelinating (optic neuritis, multiple sclerosis)
Unilateral optic nerve disorders

• Ischemic (anterior ischemic optic neuropathy, retinal occlusive disease)
• Compressive (orbital, anterior fossa)
• Inflammatory (demyelinating, infectious, rheumatologic)

AION

• Patients usually > 50
• Sudden, usually stable visual loss
• Altitudinal scotoma
• Optic atrophy in 4-6 wk

Causes
• Idiopathic (anatomic)
• Giant cell arteritis
Giant cell arteritis

- Senior citizens
- Subacute, granulomatous, stenosing arterial disease
- Headache, amaurosis fugax, arthralgia, myalgia, weight loss
- Brain, cardiac, eye, skin, muscle end artery damage

Compressive optic neuropathy

- Progressive scotoma
- Initially normal disc
- Signs of atrophy
  - Decrease in color
  - Decrease in vessels
  - Decrease in NFL
Inflammatory optic neuropathy

- Children and younger adults
- Centrocecal, arcuate, and hemianopic scotomas
- Subacute, often painful
- Retrobulbar neuritis or papillitis

Papillitis and retrobulbar neuritis

Childhood  Adult
Other causes of optic atrophy

- Glaucoma
- Secondary to retinal degeneration
- Central retinal artery obstruction
- Post-papilledema
- Congenital anomalies: hypoplasia, coloboma

Glaucoma

- Common, usually bilateral, often asymmetric optic neuropathy
- Initial selective damage to branching axons
Retinal degeneration

- Photoreceptor and/or retinal pigment epithelium disturbance
- Vascular narrowing is earliest sign
- Pigment released from damaged RPE cells clumps or migrates into the retina
- Many causes

Central retinal artery obstruction
Papilledema

- versus other disc swelling
- Intracranial mass
- Pseudotumor cerebri
- Hydrocephalus
- Intracranial hemorrhage
- Venous thrombosis
- Meningitis
Papilledema in a 12 year old with idiopathic intracranial hypertension

Other causes of disc swelling
- Optic neuritis
- Anterior ischemic optic neuropathy
- Central retinal vein occlusion
- Diabetic papillopathy
- Infiltrative disorders
- Hypertension
- Pseudopapilledema
Lesions of the chiasm

- Usually compressive
- Pediatric
  - Hypothalamic glioma
  - Craniopharyngioma
- Adult
  - Pituitary adenoma
  - Meningioma
  - Craniopharyngioma
  - Aneurysm
Retrochiasmal lesions

- Hemianopic scotoma
- Grossly incongruous field defects
- Small afferent defect
- Children: neoplasm > vascular > trauma
- Adults: vascular > neoplasm > trauma

Retrogeniculate lesions

- Normal pupils, nerves unless perinatal
- Superior hemianopia: temporal lobe
- Inferior hemianopia: parietal lobe
- More posterior, more congruity
Select Neuro-ophthalmic manifestations of systemic diseases

- Tay Sachs & Sandoff's
- Niemann Pick type A
- Metachromatic leukodystrophy
- Sialidosis
- Farber disease

Cherry red spots
Retinal pigmentary degeneration

- Mucopolysaccharidoses, Gaucher’s, Refsum
- Neuronal ceroid lipofuscinosis, cystinuria
- Abetalipoproteinemia, Kearns-Sayre
- Hallervorden Spatz, Spinocerebellar ataxias
- Usher, Cockayne
Optic atrophy

- Krabbe, Metachromatic leukodystrophy
- Adrenoleukodystrophy, Alexander
- Spinocerebellar ataxia type I
- Friedreich’s ataxia, Canavan’s
- Pelizaeus-Merzbacher, Alper’s

Ocular manifestations of diabetes

- Clinical background and pre-proliferative disease
- Proliferative disease
- Diabetic papillitis
- Neovascular glaucoma
- Cataract
Ocular manifestations of hypertension

- Narrowed arterioles
- Hypertensive retinopathy
- Hypertensive choroidopathy
- Hypertensive optic neuropathy

Neurofibromatosis

- Dominant with complete penetrance and variable expressivity
- Skin, brain, eye, bone, visceral
- Ocular signs: Lisch nodules, optic nerve glioma, choroidal hamartoma
**Tuberous sclerosis**

- Hamartomas: skin, kidney, eye, brain, heart
- Dominant and new mutations
- Symptoms: seizures, MR, facial angiofibromas, hydrocephalus
- Cortical hamartoma = tuber
- Retinal astrocytic hamartoma

**Sturge-Weber syndrome**

- Port wine stain
- Glaucoma
- Leptomeningeal angioma and seizures
Summary

• Visual loss can be understood when knowledge of neuropathophysiology is combined with knowledge of ocular embryology and anatomy.

• The pattern of visual loss can localize and identify neuropathologic disease.

• The number of systemic diseases having neuro-ophthalmic manifestation is legion.