Optic Atrophy

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Introduction

Optic atrophy is the ultimate end result of diseases that cause degeneration of axons of the ganglion cells, and manifests as changes in the color and the structure of the optic disc. It is associated with variable degrees of visual dysfunction.

The optic nerve contains approximately 1.2 million axons of the ganglion cells (1st order neurons) of the retina. The axons possess a myelin sheath provided by oligodendrocytes. Once damaged, the axons do not regenerate.

Light incident from the ophthalmoscope undergoes total internal reflection through the axonal fibers, and subsequent reflection from the capillaries on the disc surface gives rise to the characteristic yellow-pink color of a healthy optic disc. Degenerated axons lose this optical property which explains the pallor in optic atrophy.

Alternatively, the loss of pial capillaries which supply the optic disc may be the cause of disc pallor. The Kestenbaum index is the number of capillaries counted on the optic disc, which normally is around 10. Less than 6 capillaries indicates optic atrophy; more than 12 suggests disc hyperaemia.
Histopathologic changes in optic atrophy

- Deepening of the disc cup with baring of the lamina cribrosa
- Loss of both myelin and axons
- Glial cell proliferation
- Widening of the subarachnoid space with redundant dura
- In nerve transaction, the severed end produces bulbous axonal swellings (Cajal end bulbs).

Classification of Optic Atrophy

Ophthalmoscopic classification

- **Primary optic atrophy**: (e.g., pituitary tumor, optic nerve tumor, traumatic optic neuropathy).
  - Nerve fibers degenerate in an orderly manner and are replaced by columns of glial cells.
  - No alteration in the architecture of the optic nerve head.
  - Disc is chalky white and sharply demarcated.
  - Retinal vessels are normal.
- **Secondary optic atrophy**: (e.g., papilledema, papillitis)
  - Atrophy is secondary to prior disc swelling.
  - Excessive proliferation of glial tissue which causes the disc to appear dirty grey, and obscures the lamina cribrosa.
  - Poorly defined margins.
- **Consecutive optic atrophy**: (e.g., retinitis pigmentosa, myopia, central retinal artery occlusion)
  - Waxy pallor of the disc.
  - Marked attenuation of arteries.

- Normal physiologic cup and disc margin.
- **Glaucomatous ('cavernous') optic atrophy**:
  - Marked cupping along with vertical enlargement of cup.
  - Lamina cribrosa pores seen (laminar dot sign).
  - Bayoneting and nasal shifting of the retinal vessels.
  - Peripapillary halo and atrophy.
- **Temporal pallor**: may be observed in traumatic or nutritional optic neuropathy, but is common in patients with a history of optic neuritis.

Etiological classification

- **Hereditary**
  - Leber optic atrophy
  - Congenital or infantile optic atrophy (recessive or dominant form)
  - Behr hereditary optic atrophy (autosomal recessive)
- **Consecutive atrophy**: due to diseases of the retina and/or choroid
  - Chorioretinitis
  - Pigmentary retinopathies
  - Extensive retinal laser photocoagulation/long standing retinal detachments
- **Vascular**: ischemic optic neuropathy (arteritic or non-arteritic).
- **Toxic or drug-induced**: tobacco, methyl alcohol, ethambutol, sulphonamides, etc.
- **Metabolic atrophy**: nutritional amblyopia, juvenile diabetes mellitus and thyroid opthalmopathy.
- **Demyelination**: multiple sclerosis and Devic’s disease.
- **Pressure atrophy**: diseases such as glaucoma and papilledema.
- **Post-inflammatory**: optic neuritis, perineuritis secondary to meningitis.
- **Traumatic optic neuropathy**: optic nerve avulsion and transection, optic nerve sheath hematoma, and optic nerve impingement from a penetrating foreign body or bony fragment can contribute.

**Pathologic classification**

- **Anterograde degeneration** (Wallerian degeneration): Degeneration begins in the retina and proceeds toward the lateral geniculate body (e.g., toxic retinopathy, chronic simple glaucoma). Larger axons disintegrate more rapidly than smaller axons.
- **Retrograde degeneration**: Degeneration starts from the proximal portion of the axon and proceeds toward the optic disc (e.g. optic nerve compression by intracranial tumor).

**Epidemiology**

Optic atrophy can be seen in any age group. There is no sex predisposition noted.

**Differential diagnosis**

Non-pathologic disc pallor is seen in axial myopia, myelinated nerve fibres, optic disc pit, tilted disc, and disc drusen. Viewing the disc in a pseudophakic eye, or using a brighter ophthalmoscope than usual can cause the disc to look paler.

**Clinical Work-up**

**Visual acuity**

It is measured using Snellen’s optotypes or using a LogMAR chart. Visual acuity is reduced, occasionally to no light perception.

**Color vision**

Color vision is more decreased in patients with optic nerve disorders than in those with retinal disorders especially in patients with ischemic and compressive optic neuropathy.

Color vision may be assessed with pseudoisochromatic tests (e.g., Ishihara color blindness test, Hardy-Rand-Rittler polychromatic plates, Dvorine plates) or the Farnsworth-Munsell 100 Hues test or the Farnsworth panel D-15 test.

**Pupillary evaluation**

Pupil size should be noted, as well as the magnitude and the latency of the direct and consensual responses to light and near stimulation.

A relative afferent pupillary defect (RAPD) is a hallmark of unilateral or asymmetric afferent sensory abnormality. Occasionally it is the only objective sign elicited. RAPD can be quantitatively graded by balancing the defect using neutral density filters.

Clinically, it is graded as follows:

- Initial constriction, but greater escape to a larger intermediate size than when the light is swung back to normal eye (trace).
- No changes in initial pupillary size, followed by dilation of the pupils (1-2+)
- Immediate dilation of the pupil, instead of normal initial constriction (3-4+)

**Contrast sensitivity test**

This test measures the ability to perceive slight changes in luminance between regions that are not separated by definite borders, and is a sensitive test for optic nerve function.

It can be tested using Pelli-Robson contrast.
sensitivity chart, Cambridge low-contrast grating test or Arden gratings.

**Pulfrich phenomenon**

In optic nerve damage, the transmission of impulses to the occipital cortex is delayed. In patients with unilateral or markedly asymmetric optic neuropathy, when an oscillating small target in a frontal plane is viewed binocularly, the target appears to move in an elliptic path rather than in a to-and-fro path.

**Extraocular movements**

Restriction can be obtained in cases of compressive optic neuropathy due to either the mass effect or the involvement of the nerve supplying the muscle.

**Cranial nerve examination**

All cranial nerves are examined to rule out associated nerve involvement to help determine the site of the lesion.

**Ophthalmoscopic features**

**Optic disc**

Optic disc changes can present with temporal pallor, focal pallor or bow-tie pallor (as seen in compression of the optic chiasma), or cupping (glaucomatous damage).

In the early stages of the atrophic process the optic disc loses its reddish hue. The substance of the disc slowly decreases, leaving a pale, shallow exposed lamina cribrosa. In the end stages of the atrophic process the retinal vessels of the normal caliber still emerge centrally through the otherwise avascular disc.

Focal notching or diffuse obliteration of the neuroretinal rim with preservation of color of any remaining rim tissue is characteristic of glaucoma.

Optic disc cupping also develops in patients in non-glaucomatous eyes due to ischemia, compression, inflammation, hereditary disorders or trauma.

**Peripapillary retinal nerve fiber layer**

Early focal loss of axons produces dark wedge-shaped defects (best seen with a red-free filter on slit-lamp bio-microscopy) in the peripapillary retinal nerve fiber layer.

**Retinal vessels**

In most cases of optic atrophy, the retinal arteries are narrowed or attenuated. In cases of non-arteritic anterior ischemic optic neuropathy, the vessels may be focally narrowed or completely obliterated.

**Investigations**

**Visual field testing**

In optic neuropathy, visual field changes can include enlargement of the blind spot, caeco-central scotoma, altitudinal defects (e.g. anterior ischemic optic neuropathy, optic neuritis), and bitemporal defects (e.g. compressive lesions, similar to optic chiasma tumors).

**Neuro-imaging**

Neuro-imaging is indicated to find the cause of atrophy.

- Ultrasonography is recommended when orbital tumour is suspected.
- For post-traumatic optic neuropathy a non-contrast CT scan is preferred.
- In optic neuritis or multiple sclerosis, a gadolinium-enhanced MRI/fluid-attenuated inversion recovery (FLAIR) sequence is useful to detect hyperintense areas of demyelination.

**Electroretinogram (ERG)**

Abnormal electroretinogram (ERG) results that
can be seen are as follows:

- Subnormal: Potential less than 0.08 microvolts; seen in toxic neuropathy
- Negative: a preserved a-wave but absent b-wave. May be seen in arteritic AION or central retinal artery occlusion.
- Extinguished ERG: seen in complete optic atrophy.
- N95:P50 ratio in pattern ERG is low in optic neuropathy and normal in maculopathy.

**Visually evoked potential (VEP)**

In optic neuritis the VEP has an increased latency period as compared to the normal eye which persists even after visual recovery. Compressive optic lesions tend to reduce the amplitude and cause waveform changes of the VEP.

**Unexplained optic atrophy**

As optic atrophy is a sign of end-stage optic nerve damage and not a diagnosis in itself, further investigation is required if the above tests do not reveal its cause. These include:

- Blood glucose level
- Blood pressure, cardiovascular examination
- Carotid Doppler ultrasound study
- Venereal Disease Research Laboratory (VDRL)/Treponema pallidum hemagglutination (TPHA) tests
- Serum vitamin B-12 levels
- Anti-nuclear antibody levels
- Sarcoid work-up
- Homocysteine levels
- Antiphospholipid antibodies
- ELISA for toxoplasmosis, rubella, cytomegalovirus, herpes simplex virus (TORCH panel)

**Treatment**

No proven treatment exists to reverse optic atrophy. At present, the best defense is early diagnosis.

If specific treatment of the cause is initiated before the development of optic atrophy, useful vision may be salvaged. For example, early diagnosis and prompt treatment can help in compressive and toxic neuropathies.

Neuro-protective agents like gingko biloba have been tried with anecdotal success.

Research in stem cell therapy may provide answers in the not-too-distant future.

Low-vision aids should be considered for occupational rehabilitation.

**Suggested further reading**


Figure 1     Healthy Optic Discs

Figure 2    Primary Optic atrophy

Figure 3   Secondary (post-papilloedema) atrophy

Figure 4   Glaucomatus atrophy

Figure 5   Consecutive optic atrophy (post pan-retinal photo coagulation)