The clinical spectrum of non-arteritic anterior ischemic optic neuropathy as seen in a bilateral sequential case
Yangdi Chen, OD

Abstract
Typical unilateral non-arteritic anterior ischemic optic neuropathy (NAION) does not create a tremendous diagnostic challenge. Relatively unusual presentations, including bilateral sequential involvement, warrant a more thorough investigation.

Case History
- Patient demographic: 71-year-old Caucasian male
- Initial purpose of visit: follow-up for non-arteritic anterior ischemic optic neuropathy (NAION) OS with onset seven months prior
  - Chief complaint: the patient reports no change in vision since previous follow-up visit.
- Ocular history
  - NAION OS, onset seven months prior, stable
  - Cataracts OU, mild visual significance
  - Refractive error and presbyopia
- Medical history
  - Coronary artery disease status-post three vessel bypass in 1996, with three stents placed in 2005, two more stents placed in 2008 and two more placed in 2014
  - Peripheral neuropathy
  - Tremors
  - Depression
  - Benign prostate hypertrophy
  - Barrett’s esophagitis
  - Hyperlipidemia
  - Hypertension
- Medications
  - Acetylsalicylic acid 81mg per day for anticoagulation
  - Atenolol 50 mg per day for hypertension
  - Clopidogrel bisulfate 75mg per day for anticoagulation
  - Diltiazem 120mg per day for hypertension
  - Gabapentin 400mg 3x/day for peripheral neuropathy
  - Hydrochlorothiazide 25mg half tablet per day for hypertension
  - Lisinopril 40mg per day for hypertension
  - Pantoprazole 40mg 2x/day for esophagitis
  - Propranolol 60mg per day for hypertension
  - Sertraline 50mg 3x/day for depression
  - Simvastatin 40mg per day for hyperlipidemia
  - Tamsulosin 0.4mg per day for benign prostate hypertrophy
- Other salient information
  - No known allergies

Pertinent Findings
- Pertinent exam findings (initial visit)
  - Visual acuity (VA): OD 20/25- pinhole no improvement
    OS 20/40+2 pinhole no improvement
  - Optic nerve assessment: OD 0.2H/V, crowded disc with fuller inferior rim
    OS 0.15H/V, distinct margins with subtle optic disc pallor
  - Spectral domain optical coherence tomography (OCT) of nerve fiber layer:
    - OD global thickness 141 microns (um), within normal limits all sectors but thicker inferiorly compared to five months earlier
- OS global thickness 69um, outside norms nasal and superior sectors; reduced thickness compared to five months earlier
  - Humphrey visual field 24-2:
    - OD essentially clear
    - OS repeatable dense inferior arcuate defect with absolute defects inferior nasal, defects appear stable compared to previous field from five months earlier
  - Given relative retinal nerve fiber layer swelling OD on spectral domain OCT without definitive clinical corroboration, fluorescein angiography was performed.
  - Fluorescein angiography (FA):
    - OD mildly slow venous filling with late phase staining of inferior-temporal disc margin (3:32 time mark), confirms optic disc edema OD
  - Given confirmation of optic disc edema OD by FA, lab tests were ordered with consideration for possible etiologies for bilateral optic disc edema:
    - Erythrocyte sedimentation rate (ESR): 6mm/hr (normal)
    - Platelet count: 172 K/cmm (normal)
    - C-reactive protein (CRP): 2.2mg/L (normal)
    - Rapid plasma regain: nonreactive
    - Purified protein derivative skin test: negative
    - Lyme disease antibody test: negative
    - Bartonella antibody test: negative
  - Radiology report for magnetic resonance imaging (MRI) of the brain:
    - No MRI findings to suggest etiology of ophthalmologic exam – specifically no intracranial findings to suggest intracranial hypertension.
  - Assessment/plan: Given prior NAION OS and all negative lab and imaging results, the optic disc edema OD was indicative of bilateral sequential NAION OD. As the patient is asymptomatic, plan to follow up in 2 months.

- Pertinent exam findings (second visit, four weeks later)
  - Patient returns with a chief complaint that he notices peripheral vision changes all around. He feels that this peripheral vision change is occurring in both eyes and onset a couple weeks prior.
  - VA: OD 20/25-1 (stable)
    OS 20/30+2 (stable)
  - Optic nerve assessment: OD 0.2H/V, blurred margins with inferior rim hemorrhage
    OS 0.15H/V, distinct margins with subtle optic disc pallor
  - Humphrey visual field 24-2:
    - OD mild new superior defects correlating with greatest inferior disc edema
    - OS repeatable dense inferior arcuate defect densest at inferior-nasal edge, similar to initial visit
  - Spectral domain OCT of nerve fiber layer:
    - OD global 195um, thicker all sectors compared to initial visit
    - OS global 69um, stable compared to initial visit
  - Lab testing updates
    - ESR: 9mm/hr (normal)
    - Platelet count: 167 K/cmm (normal)
    - CRP: 6.62mg/L (higher end of reference range)
  - Assessment/plan: Bilateral sequential NAION OD, now symptomatic and manifesting visual field defects. Advised tight blood pressure control. Plan to follow up in 4 weeks.

Differential Diagnosis
- Primary/leading
  - NAION OD (bilateral sequential presentation)
- Differentials for bilateral disc edema
  - Bilateral sequential presentation of NAION
  - Papilledema (elevated intracranial pressure)
  - Malignant hypertension
Optic disc drusen
- Anomalous appearance of crowded discs
- Nutritional and toxic etiologies
- Infectious and inflammatory etiologies: syphilis, Lyme, cat-scratch disease, sarcoidosis, tuberculosis
- Infiltrative causes: lymphoma, leukemia, multiple myeloma

Diagnosis and Discussion
- Elaborate on the condition
  - NAION is the most common acute optic nerve disease of adults older than 50 years old. It affects Caucasians more. Often, patients present with sudden painless loss of vision in one eye associated with optic disc swelling. Almost 50% can have normal visual acuity. Estimated annual incidence in the United States is up to 10.2 per 100000 individuals.¹
  - Pathophysiology
    - Acute ischemia of optic nerve head²
      - Blood flow to optic nerve influenced by blood pressure, vasoactive agents, autoregulation
    - Largely hypotensive, not embolic or thrombotic disorder
    - Optic nerve head supplied by arterial circle from short posterior ciliary arteries (SPCA), which have distinct halves. As a result, altitudinal defects are often seen as a result of NAION.
  - Risk factors
    - Systemic factors: hypertension, hypotension, diabetes, atherosclerosis, migraine, vasospastic disorders, sleep apnea, hematologic disorders²
    - Local factors: elevated intraocular pressures, location of SPCA watershed zone, disc at risk
    - Drugs: phosphodiesterase inhibitors can cause hypotension and vasoconstriction³
  - Diagnosis
    - FA can show disc edema and circulatory insufficiency in peripapillary choroidal areas of the SPCA. Often times, no permanent occlusion is seen so this argues for NAION not being a thromboembolic occlusive disorder.⁴
    - Visual acuities, visual fields, pupils, color vision, OCT, B-scan ultrasonography in ophthalmological exam are helpful diagnostic measurements.
    - Lab testing and MRI can assist in ruling out infectious, inflammatory, infiltrative etiologies and intracranial mass(es).
- Expound on unique features
  - Visual field defects explained by pattern of location of watershed zone between posterior ciliary arteries in relation to optic nerve head⁶
    - The part of the optic nerve head located in watershed zone is most vulnerable to ischemia (often times, this is the temporal part of optic disc that is more vulnerable than nasal disc which results in more nasal visual loss).
    - Most common visual field defects: absolute inferior-nasal defect⁵
  - Fellow eye risks (based on Ischemic Optic Neuropathy Decompression Trial)⁷
    - 21.1% of patients with NAION showed history previous NAION or other optic neuropathy in fellow eye.
    - New NAION in fellow eye in 14.7% of patients at risk during median follow-up of 5.1 years, with greatest risk in the first year.
    - Cumulative prevalence of fellow eye involvement is 30.6%.
    - Significant risks for fellow eye becoming affected: diabetes and baseline visual acuity of 20/200 or worse.
  - Clinical spectrum from asymptomatic to classic presentation of NAION
    - Incipient/incipient NAION
      - In Hayreh’s study, 25% of incipient NAION patients progressed to classic NAION (median 5.8 weeks).⁸
      - In Almog’s study, conversion rate to AION in asymptomatic optic disc edema population was 40% if they had AION in fellow eye.⁹
A recent article published by Subramanian et al describes 4 patients with optic disc swelling without visual acuity or visual field loss who developed symptoms typical for NAION over several weeks of clinical surveillance.\textsuperscript{10}

Given there is no effective treatment option once vision loss occurs, it would be interesting to see if there are treatments that can target this population group who experience a period of asymptomatic optic disc swelling.

**Treatment and Management**

- No real treatment exists.\textsuperscript{11}
  - optic nerve decompression (in which slits are placed in ON sheath to release CSF and reduce pressure) was shown to not be effective. Patients did not fare better versus those who were followed carefully without treatment.\textsuperscript{12}
- Action should be taken to control systemic factors if a patient is diagnosed with asymptomatic optic disc edema that aligns with clinical diagnosis of NAION.
- Active areas of clinical research include levodopa\textsuperscript{13} and QRK207 NAION clinical study (to be published in September 2016 in Journal of Neuro-Ophthalmology)
- Prognosis
  - In one study, Hayreh shows that median time resolution of optic disc edema from the onset of visual loss was 7.9 weeks.\textsuperscript{14}
  - Spontaneous improvement of visual acuity in 42.7% at 6 months in those who were simply monitored.\textsuperscript{12}
  - Visual acuity doesn’t seem to worsen after optic disc edema resolves.
  - Recurrence in affected eye is <5% (thought that atrophy relieves crowding).\textsuperscript{11}

**Conclusion**

- Normal visual acuity and visual field does not rule out NAION as some patients can present initially with asymptomatic disc edema.
  - These patients can either remain asymptomatic and clinically silent or develop classic features later.
  - As optic disc edema can be difficult to clinically detect, there is value in diagnostic imaging such as OCT and FA to confirm disc edema.
  - There is also importance in lab testing and imaging to rule out differentials before concluding the diagnosis of NAION.
- About 43% spontaneous improvement in visual acuity at six months, so despite there being very little treatment options, there is cautious optimism that a patient’s vision may improve slightly.
- Bilateral sequential NAION is not uncommon: about 15% risk of fellow eye developing NAION over five years.
Bibliography

12. The Ischemic Optic Neuropathy Decompression Trial Research Group. Optic nerve decompression surgery for nonarteritic ischemic optic neuropathy is not effective and may be harmful. JAMA 1995;273:625–632.