Optic Nerve: Itis, Opathy, and Edema

Instructor:

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Section:

Neuro-Optometry

COPE Course ID:

35927 NO

Expiration Date:

September 28, 2015

Qualified Credits:

2.00 credits - $49.00

COURSE DESCRIPTION:

This course will teach diagnosis and treatment of optic disc drusen, idiopathic intracranial hypertension, papilledema, optic neuritis, stroke of the optic nerve, meningiomas and gliomas, Leber hereditary optic neuropathy, and trauma, and related conditions.

LEARNING OBJECTIVES:

- Trauma causing optic nerve damage
- Leber hereditary optic neuropathy
- Meningiomas and gliomas of the nerve
- AION and NAION
- Optic neuritis
- Papilledema
- Intracranial hypertension
- Optic disc drusen
Eye care professionals are frequently required to evaluate patients with anomalous optic nerves. It is imperative that we understand the features, associated findings, pathology, and ancillary testing that will allow correct diagnosis and treatment.

Our first clinical case involves a 10 year old male presenting for a routine eye examination. Visual acuities without correction were 20/20 in the right eye, and 20/20 in the left eye. Color vision, performed monocularly, was normal. Pupils were equal in size, briskly reactive to light, with no afferent pupillary defect. Visual field testing with frequency doubling technique showed no defect in either eye. The anterior segment was unremarkable. Intra-ocular pressures with non-contact tonometry were 20 mm of mercury in the right eye, and 19 mm of mercury in the left. Results of a dilated fundus examination are shown in Figure 1. The optic nerve head was raised with indistinct margins in both eyes. Retinal blood vessels were not obscured, but displayed a trifurcation branching pattern with slight tortuosity. One optic nerve head drusen was visible superiorly in the left eye. The patient’s mother was examined on the same day. Fundus images of the mother are shown in Figure 2.
The patient and the mom were further questioned and reported no visual or systemic complaints, including no transient visual obscuration (TVO), headaches, tinnitus, numbness or tingling in the extremities, dizziness or diplopia. A B-scan (Fig 3) demonstrated an area of hyper-reflectivity at the optic nerve head, confirming the diagnosis of buried drusen.

The patient was diagnosed with pseudopapilledema due to buried optic disc drusen. The patient’s mom was told to watch for symptoms related to true papilledema and told to return for further serial fundus photos in one month.

The patient returned after three months. At this follow-up examination, the patient reported no visual or systemic symptoms. Objective testing was within normal limits. The appearance of the discs was identical to the images taken previously.

Drusen of the optic nerve are made up of calcified axonal debris on the surface of the disc. Optic disc drusen can cause the optic nerve to be elevated or to have blurred margins simulating papilledema. Pseudopapilledema due to disc drusen is common, occurring in 0.5% to 2% of the population. Optic disc drusen occurs most commonly in Caucasians and has a slight predilection for women. It is bilateral in 67 to 86% of cases. The drusen can be sporadic or inherited in an autosomal dominant fashion.

Examination of family members is crucial if the distinction between pseudopapilledema and true papilledema is in question. Often, extensive testing, including neuroimaging, lumbar puncture, and laboratory testing can be avoided based on clinical examination findings.

Despite progression of optic nerve drusen, most patients remain asymptomatic and usually have normal visual acuity. Some patients report blurriness or dimming of vision. Optic disc drusen does not cause other signs or symptoms related to increased intracranial pressure (ICP) such as headaches, tinnitus or diplopia.

Visual field defects (Fig 4) are found in 5-39% of patients with buried drusen, and 71-86% of those with visible optic disc drusen. These patients are typically asymptomatic. Visual field defects include arcuate defects that are usually located inferiorly or inferior-nasally, concentric constriction, or an enlarged blind spot. Rarely, central vision is affected, and should only be considered to be due to optic disc drusen when no other cause can be established. A relative afferent pupillary defect (APD) may be present if the condition is unilateral or asymmetric.
The optic nerve appearance changes throughout life in patients with optic nerve drusen. Nerve elevation of the disc due to disc drusen is usually apparent in childhood as a full optic nerve. (Fig 5a) With increased age, the optic nerve develops a scalloped appearance at the nasal disc margin. (Fig 5b) Finally, subtle excrescences appear at the surface of the disc. (Fig 5c) The drusen begin to enlarge, calcify, and become more visible. In later adulthood, the disc elevation decreases, the nerve becomes pale, and nerve fiber layer defects appear.

Surface drusen (Fig 5c) are round or slightly irregular, white or yellow, excrescences within or around the disc. They may be scattered or form conglomerates around the disc. Those affecting a portion of the disc are usually found nasally and are most easily seen at the rim margin. The drusen vary in size from pinpoint to 2-3 times the diameter of retinal blood vessels.

Buried drusen (Fig 5a) produce elevation of the disc and blurring of the disc margins. This is differentiated from true papilledema by the lack of hyperemia, dilated capillaries, or vessel obscuration.

Table 1 shows features to aid in differentiating pseudo-papilledema with true papilledema. With pseudo-papilledema due to disc drusen, the physiologic cup is absent and the center of the disc is most elevated.

Patients often have anomalous vascular patterns, including arterial or venous trifurcation, creating the appearance of increased number of vessels on the disc. Abnormal or premature branching, tortuosity, vascular loops, and cilioretinal vessels are also seen.
Additional testing may be necessary to differentiate between disc edema and pseudopapilledema due to disc drusen. CT (Fig 6b) and ultrasound (Fig 6a) can aid in visualizing the drusen when the diagnosis is in question. However, calcification may not be as great in children, making these tests less useful.

Buried and superficial drusen may be seen as translucent, glowing objects when a narrowed slit beam is positioned at the rim of the optic disc. (Fig 7a) Photography using red-free light can also help to highlight the drusen. (Fig 7b) Autofluorescence occurs when taking images of the disc drusen with the filter used for fluorescein angiography. This Autofluorescence helps to emphasize the disc drusen. Fluorescein angiography can help differentiate between true papilledema and pseudopapilledema. Drusen will hyper-fluoresce but there will be no leakage of the major blood vessels that is seen with disc edema.

Optical Coherence Tomography (OCT) shows a slow thinning of the nerve fiber layer associated with increased visible optic nerve head drusen. (Fig 8a) OCT can also aid in differentiating optic disc drusen from optic disc edema. Patients with edema of the optic disc have smooth internal disc contour, compared with the lumpy appearance found in optic disc drusen. (Fig 8b) In addition, optic disc edema demonstrates a V-shaped hypo-reflective space between the sensory retina and the Retinal Pigment Epithelium (RPE) that is minimal or absent with optic disc drusen. (Fig 8c) OCT is also useful to follow NFL layer changes over time.
Central acuity is preserved in most patients with disc drusen unless other pathology is present. Because most patients do show average progression of 1.6% per year, visual field testing is helpful in monitoring the condition.

**Case 2**

The next clinical case involves a 17 year old white female who presented with a one-week history of difficulty focusing and throbbing frontal headaches. She also reported transient visual obscurations that last less than one minute. Medical health was unremarkable except for acne, for which she was taking 200 mg minocycline daily for about four weeks. She had no other neurologic symptoms and reported no recent weight gain.

Visual acuities were 20/20 in both eyes. Color vision was normal. Extra-ocular muscle testing was unremarkable. Pupils were equal, reactive to light, with no afferent pupillary defect. The anterior segment examination was unremarkable, and intra-ocular pressures were 12mmHg in both eyes.

Dilated fundus examination revealed moderate disc edema in both eyes. (Fig 9) Visual field testing demonstrated an enlarged blind spot in both eyes. (Fig 10)

The patient was told to discontinue the minocycline and begin taking two 250mg tablets of Diamox two times per day. She was referred for an MRI and an MRV, which were remarkable for an empty sella and a flat globe. (Fig 11) A spinal tap revealed an opening pressure of 460 mmH2O in the fetal position.

After 1 month, the papilledema had decreased significantly, and the patient had no visual complaints or headaches. The visual acuities were 20/20 in both eyes. After two months, the disc edema had resolved completely. Visual field testing was unremarkable in both eyes, and no pallor was evident on examination of the optic nerves.
The term papilledema should be reserved for disc edema that is caused by raised intracranial pressure (ICP). Other types of disc edema should be denoted by a general term such as “optic nerve head edema” or by etiology such as optic neuritis or anterior ischemic optic neuropathy.

Idiopathic intracranial hypertension (IIH) is characterized by three findings: increased ICP, normal cerebrospinal fluid (CSF) composition, and no abnormality with neuroimaging that would cause the increased ICP, including hydrocephalus, intracranial mass, or cerebro-venous sinus thrombosis.

Many factors affect the ICP, including medications, toxins, venous pressure, meningeal irritation, and brain volume. Either blockage of the CSF outflow, reduction of the CSF reabsorption, or increased CSF production can cause papilledema.

Idiopathic Intracranial Hypertension is most commonly seen in obese women of childbearing age. The only known risk factors are weight gain and obesity. Women are 9 times more likely to develop IIH compared to men, and the peak incidence is in the 3rd decade of life. The pathogenesis of IIH is not
known, however it has been postulated that hormone changes may increase CSF secretion. Venous hypertension commonly found in obese patients may also play a role by decreasing CSF drainage.

About 10% of patients with IIH, especially men and non-obese women, have a cause of the increased ICP. When a secondary cause is found, the syndrome is termed Pseudotumor Cerebri. These causes, listed in Table 2, include some metabolic or systemic conditions such as pregnancy, hypo or hyperthyroidism, anemia, sleep apnea and systemic hypertension. Some drugs can produce Pseudotumor Cerebri. These include corticosteroids, tetracycline, minocycline, doxycycline, cyclosporine and retinoids. Withdrawal of corticosteroids can also cause Pseudotumor Cerebri.

Between 90 and 98% of patients with IIH present with headaches. The headache is thought to be caused by stretching of the meninges or damage to the sensory nerves. The headache is pulsatile, worse in the morning, not usually localized, and worsened with increased cerebro-venous pressure due to straining, such as in Valsalva maneuver, or coughing. The headache may also become worse with changes in posture. These headaches improve significantly after lumbar puncture.

Other manifestations of IIH include nausea and vomiting (40%), pulsatile tinnitus (16-60%), dizziness, and photophobia. Pulsatile tinnitus is described as a whooshing sound that may be unilateral or bilateral. Visual symptoms of IIH include transient visual obscurations (32-80%) and horizontal diplopia (30-32%). During transient visual obscurations (TVO), the patient will experience mild blur to total blindness in one or both eyes. Some patients describe a graying out of vision. Others experience positive visual phenomenon that obscures vision, including photopsias or phosphenes. The episodes are often brought on by postural changes from supine to a standing position. Vision usually recovers within seconds. Diplopia occurs due to stretching of the 6th cranial nerve either unilaterally or bilaterally. These patients will have esotropia that is worse at distance than at near.

It is rare for patients with IIH to have loss of central vision, color vision dysfunction, RAPD, or visual field defects other than an enlarged blind spot. Normal visual acuity helps to distinguish papilledema from other
causes of disc edema, where visual acuity is often affected earlier.

Other features that help differentiate papilledema from other causes of disc edema are listed in Table 3.

The appearance of the optic nerve and retina can help determine the presence of papilledema. Papilledema is usually bilateral and symmetric. The optic nerve head will appear hyperemic. Paton’s lines, or circumferential retinal folds surrounding the disc, are often present. (Fig 12) Linear or curved linear folds in the choroid may develop, which is often accompanied with the progression of hyperopia.

Flame-shaped hemorrhages, cotton wool spots (CWS), and tortuous retinal vessels on or surrounding the disc may be observed. (Fig 13) Flame-shaped hemorrhages indicate acute or sub-acute edema. A thin, radial hemorrhage on or around the disc margin can indicate distended capillaries of the optic nerve, an early sign of papilledema. Hard exudates and hemorrhages may be present in the macula. These will have a star-shaped appearance that is worse on the side towards the disc.

Lack of spontaneous venous pulsation (SVP) can indicate an increase in ICP. SVP is absent in cases of papilledema, however only 80% of normal people have a SVP, so the absence of the pulse does not necessarily mean papilledema is present.

If swelling lasts for several months, the optic nerve takes on a grey appearance and superficial exudates may develop on the disc. (Fig 14) These have a similar appearance to optic nerve head drusen. Patients will often have slit defects or diffuse loss of the NFL. Optociliary shunt veins may develop secondary to compression of the central retinal vein. These will typically go away with treatment of the ICP.

Over time, an untreated papilledemetic disc will become atrophic. Retinal blood vessels will become narrowed, and some patients will have persistent choroidal folds. If the raised ICP is severe and constant, this can occur within days or weeks. Other cases may take months or years for atrophy to develop.

Patients with IIH should undergo neuroimaging, followed by lumbar puncture. An MRI with contrast will rule out abnormalities of the brain which may cause true papilledema. An empty sella (Fig 15a) is present in most cases. In addition, orbital imaging may show dilation of the subarachnoid space...
surrounding the optic nerves (Fig 15b), protrusion of the optic nerve into the posterior globe, and flattening of the posterior sclera.

MRV should be performed on patients suspected of IIH, especially atypical patients such as men, children, and non-obese women, as well as patients who are post-partum, taking oral contraceptives, or have known coagulopathy.

The opening pressure should be obtained during lumbar puncture with the patient lying on his or her side. (Fig 16) Using of fluoroscopy during the procedure is helpful for obese patients. An opening pressure over 250 mmH2O is required to diagnose IIH in adults. The CSF should be assessed for evidence of cellular content, protein, and glucose concentration. This evaluation should be normal in patients with IIH.

Lumbar puncture is relatively safe, however there are risks associated with this procedure. Removal of CSF in patients with a tumor can cause compression of intracranial structures, causing the brain to shift downwards, causing death. For this reason, neuroimaging should always be obtained prior to performing a lumbar puncture. Other complications include headache following the lumbar puncture, visual obscurations, and 6th nerve palsy.

Treatment of IIH involves alleviating symptoms and preventing vision loss. Medical treatment should always occur first, followed by surgical procedures if necessary. In some cases, IIH is self-limiting. If the patient is asymptomatic, and an underlying etiology is excluded, close observation is sufficient. If a secondary cause is found, it should be addressed appropriately. Because ICP can remain high for two to five weeks after discontinuation of tetracyclines, medication to lower ICP is recommended.

Weight loss is necessary for long-term remission of IIH. Loss of 6% of body weight has correlated to decreased papilledema. Bariatric surgery may be considered if other efforts to lose weight are inadequate.

Medication without surgical intervention is adequate if symptoms are limited to headaches, and no visual deficit is present. Carbonic anhydrase inhibitors (CAIs) work by decreasing the production of CSF. They also have a mild diarrhetic effect. The most common, acetazolamide, is used 1-4g per day. Side effects include paresthesias of the extremities, lethargy, and altered taste sensation, especially with carbonated beverages. More severe side effects include allergy, aplastic anemia, and kidney stones.
Weekly follow-up visits are necessary until vision stabilizes or improves. Once stabilized, patients should be followed every few months looking for changes in vision and changes in visual fields.

Headaches can be treated with medications such as topiramate or nonsteroidal anti-inflammatory agents (NSAIDs). Topiramate has the added benefit in that it often produces weight loss. Co-management with neurology is helpful in the management of the headaches.

Surgical treatment of IIH is performed when vision loss progresses despite the use of medical treatment. Optic nerve sheath decompression is recommended if vision loss is severe but headaches are mild. If vision loss is accompanied by severe headaches, a shunting procedure is often the preferred treatment. Optic nerve sheath decompression should be performed in the eye with the worst vision first.

In Figure 17, we can see the multiple slits made in the dural sheath surrounding the optic nerve. Risks associated with optic nerve sheath decompression include retinal vascular occlusion, or ischemia of the optic nerve resulting in permanent vision loss. Diplopia and infection may also occur.

A ventriculoperitoneal or lumboperitoneal shunt is effective at lowering ICP, but the shunts tend to become obstructed over time. In addition to obstruction, complications include excessively low pressure, infection, radiculopathy, and abdominal pain.

Papilledema will generally resolve within days or weeks of treatment. New hemorrhages may appear during healing due to changes in hemodynamics. The last sign to resolve is the blurring of disc margins.

More severe papilledema results in a worse visual prognosis. Narrowing of blood vessels, loss of NFL, and optic nerve head pallor that is present at the time of the papilledema also result in a worse prognosis. Patients with loss of visual acuity have a very poor prognosis for recovery. Recurrence is common, making follow-up for many years necessary. Depression and tension headaches are also common in patients with IIH.

Papilledema occurs in 60-80% of those with brain tumors. An intracranial mass can increase ICP by acting as a space-occupying lesion. It may also produce cerebral edema, which blocks CSF drainage, causes direct infiltration of the arachnoid villi or venous sinuses, or cause production of toxins that block the arachnoid villi.
When a cerebral venous sinus is occluded, as in the case of cerebral venous thrombosis or in compression, venous sinus pressure increases. This causes a reduced absorption of the CSF into the venous sinuses, resulting in increased ICP. The superior sagittal and transverse sinuses are most commonly affected.

This can be caused by systemic conditions associated with coagulopathy, hematologic disorders, infection, trauma, tumor, or a dural arteriovenous fistula. (See Table 4 for complete list)

Other causes of increased ICP include Arnold-Chiari malformation, Craniosynostoses, congenital or acquired aqueduct stenosis, subarachnoid hemorrhage, infectious or inflammatory meningitis or encephalitis.

Symptoms of true papilledema are similar to those found with IIH. Patients may also complain of symptoms related to intracranial mass, including double vision, mental decline, coordination problems, seizures and focal numbness or weakness. Risk factors for thrombosis must be excluded.

It’s rare for papilledema to cause the loss of central vision, color vision dysfunction, relative afferent pupillary defect (RAPD), or visual field defects other than an enlarged blind spot. If these signs are present, suspect that the lesion causing the increased ICP is also causing damage to the visual pathway. An MRI with contrast should be performed to look for identifiable causes of the papilledema. An MRV should also be obtained to rule-out cerebral venous sinus thrombosis. Laboratory testing, including CBC with platelet count, ANA, Lupus anticoagulant, and other coagulation testing may be necessary if patients are at risk for thrombosis. Fluorescein angiography can be used to distinguish early papilledema with the presence of capillary dilation and dye leakage. As discussed earlier, OCT can also be useful in the diagnosis and follow-up of disc edema.

Management of papilledema involves treatment of the underlying medical condition. Acetazolamide is useful in decreasing the ICP. Cerebral venous thrombosis requires systemic anticoagulant therapy such as
as heparin. Scanning laser tomography and OCT should be used to assess the degree and resolution of papilledema. Obtaining proper imaging is critical, as failure to recognize and treat a brain tumor or cerebral venous sinus thrombosis can result in stroke or death.

**Case 3**

Our next clinical case involves a 35 YO white female who presented reporting strain and dimming of peripheral vision in the left eye over a period of three weeks. The symptoms were worsened with exercise. She reported that they eye pain had gradually resolved, but then she began experiencing cloudiness of the central vision in her left eye that worsened over a period of 1 week. Vision then stabilized two days prior to the visit. In addition, the patient noticed persistent tingling in the left hand, and vertigo that lasted 2-4 weeks about four months previous. Medical history was positive for acne rosacea, for which she was taking doxycycline and an unknown topical dermatological product. She did not have a family history of any neurologic disease.

**Visual acuity at the time of examination was 20/20 in the right eye, and 20/70 in the left eye. Color vision was normal in the right eye, but she only correctly identified one out of 10 Ishihara plates with the left eye. She also reported subjective red desaturation in the left eye. Ductions, versions, saccades and pursuits were unremarkable. The patient had no nystagmus or intranuclear ophthalmoplegia (INO). Pupils were equal and reactive with a moderate RAPD in the left eye.**

The anterior segment exam was unremarkable. Intraocular pressures were 16mmHg in both eyes. On dilated fundus exam, the optic nerve, vessels, and macula were unremarkable in both eyes. (Fig 20) Visual field testing was normal in the right eye, but revealed an overall diffuse depression in all quadrants of the left eye. (Fig 21)

The patient was diagnosed with presumed retrobulbar optic neuritis of the left eye of 2-3 weeks duration. Additionally, she had other neurologic symptoms over the
past 6 months. She was scheduled for a brain MRI in three days. We coordinated with home health care to do IV steroid injections of 3g per day for 3 days. The patient was asked to return to the clinic to check healing and to repeat the visual field in 4-6 weeks.

Diagnostic imaging (Fig 22) showed enhancement of the left optic nerve. In addition, the MRI revealed a lesion in the right cerebral peduncle, and a periventricular lesion anterior to the horn of the left lateral ventricle.

At the 6-week follow up examination, she reported that vision was significantly improved. She was now 20/20 in both eyes, and was seeing a neurologist to determine if treatment for Multiple Sclerosis was warranted.

By far, the most common cause of optic neuritis is demyelination. Optic neuritis occurs in up to 50% of those with Multiple Sclerosis (MS). It is the presenting sign in up to 20% of those with MS. The prevalence of acute optic neuritis is approximately 115 per 100,000 people. Optic neuritis occurs most frequently in young adults between the ages of 20 and 50 years, and the mean age is 30-35 years. Females are affected more than males, and 85% of optic neuritis patients are Caucasian.

Symptoms of optic neuritis include acute vision loss, usually in one eye. Vision often worsens over hours to days, then stabilizes, and is followed by improvement over several weeks. Vision loss varies from minimal reduction to no light perception. Most patients describe a diffuse loss, although occasionally they recognize that the loss is mainly confined to the central region.

In addition to vision loss, 87-92% of patients experience pain behind the eye that is worsened with eye movement. The pain is often mild but can be extreme. This feature helps to differentiate from other causes of optic neuropathy associated with painless vision loss, such as anterior ischemic optic neuropathy (AION). The pain generally resolves over a few days, usually about the time that the vision loss begins.

Patients may also experience photopsias. These take the form of flashing lights, or showers of sparks. In addition, other symptoms of MS, including areas of numbness, vertigo or loss of balance that lasts days or weeks may be reported.

Most cases of optic neuritis present with reduced visual acuities that range from 20/20 to no light perception. Color vision and contrast sensitivity are also additionally impaired. In fact, reduced color vision is often much greater than that expected by the degree of acuity loss. An RAPD will be present.
unless there is previous damage to the contralateral optic nerve. These patients will also report decreased brightness sensation in the affected eye.

Almost any type of visual field defect can occur with optic neuritis. Diffuse visual field defects are seen in 48% of patients with field loss, and focal defects are present in the other 52%. Focal defects can include altitudinal, arcuate, nasal step, central or cecocentral, and hemianopic patterns.

Optic neuritis in adults is almost always unilateral. However, the Optic Neuritis Treatment Trial showed that although asymptomatic, the fellow eye commonly had visual deficits. Decreased VA in the fellow eye was found in 14% of patients. 22% had color vision deficiency in the fellow eye. 48% demonstrated visual field loss in the contralateral eye. These deficits usually resolved over several months. Only 1/3 of optic neuritis patients have visible swelling of the optic nerve head. Optic disc swelling may be mild or severe, and does not correlate with loss of visual acuity or visual field. It is rare to find peripapillary hemorrhages, exudates, or cotton wool spots. Occasionally cells may be present in the vitreous, especially over the optic nerve. If this is extensive, another diagnosis, such as Sarcoidosis, Syphilis, Cat-scratch disease or Lyme disease should be suspected.

Over 4-6 weeks the optic nerve develops pallor. (Fig 23) This occurs even with improvement of visual function. The pallor is typically temporal, but can be sectorial in other areas of the disc or diffuse.

Atypical features such as lack of pain, severe optic disc edema, peripapillary hemorrhages, macular exudates or no light perception vision are at low risk for developing MS, and are unlikely to require immunomodulation therapy. These features are more likely to have an infection origin, so appropriate testing should be ordered to determine the etiology.

Brain MRI with contrast (Fig 24) is useful in predicting the development of MS in patients with optic neuritis. The MRI should be elevated for evidence of white matter lesions that are consistent with demyelination. These are typically located in the periventricular area. Dedicated orbital neuroimaging is only necessary if another cause of inflammation is suspected, or to aid in predicting the visual and systemic prognosis. Scanning the nerve fiber layer with OCT shows significant reduced thickness after optic neuritis as well as MS. This is true even if the fellow eye has not had clinically evident optic neuritis. In addition, reduced NFL thickness correlates with an increased Expanded Disability Status Scale (EDSS) score even when the patient did not have a history of optic neuritis. This is thought to occur due to a relationship between axonal loss and neuronal degeneration in the brain.
Patients treated with IV steroids recover vision faster. However, compared to placebo and oral steroids, those taking IV steroids, have similar recovery of visual acuity, contrast sensitivity, color vision, and visual fields at 6 months and 1 year. Although there is no difference in long term visual outcome, if severe pain or vision loss is present, it is recommended that patients be treated with IV methylprednisolone, 1 g in a single daily dose for 3 days. Also, consider the use of steroids in monocular patients, and those with occupational requirements that necessitate quick recovery. The treatment is typically performed using home health nursing units, but these patients should be monitored closely for side effects. Follow the patient in 2-4 weeks to assure that vision is improving appropriately. Patients should also be referred to neurology to discuss the risk of MS and possible treatment options.

Vision loss should not progress two weeks after onset, and rapid improvement should be evident at four weeks. Most recovery begins prior to five weeks, but continued improvement can occur up to 1 year. Whether or not steroids are used for treatment, up to 93% of patients have recovery of vision to at least 20/40, and 74% will have 20/20 or better acuities. Color vision defects and RAPD often persist. Patients will often report that vision is “not quite right.” They may experience patchy scotomas, decreased contrast sensitivity, decreased sensation of brightness, photopsias, and transient vision loss with overheating or exercise (Uhthoff’s phenomenon).

Optic neuritis has a recurrence rate of 28% within five years, and 35% within 10 years. This rate does not differ significantly between those receiving either placebo or IV steroids, but the rate is higher in those with MS and those receiving oral steroids.

The risk of developing MS after isolated optic neuritis is 25-50%. The majority will develop MS within 3-5 years. The risk is dependent upon the number of MRI lesions at the time of the optic neuritis episode. Of those with no brain lesions upon initial MRI, 16% developed MS after 5 years, and 25% developed MS after 15 years. Of those with 3 or more lesions on the initial MRI, 51% developed MS after 5 years, and 78% developed MS after 15 years. (Table 5) Even one white matter lesion more than doubles the risk of developing MS from 22% to 56% over a 10 year period.

Other less influential risk factors for developing MS include Caucasian race, family history of MS, neurologic symptoms, and a previous episode of optic neuritis. Among those with no MRI lesions at baseline, patients with no pain, either mild or severe acuity loss, optic nerve swelling, peripapillary hemorrhages, retinal exudates, or male gender were less likely to develop MS.
Case 4

Our next clinical case involves a 49 YO Caucasian male who presented complaining of decreased vision in the right eye suddenly that morning. He reported no prior episode of transient visual obscuration (TVO), no jaw claudication, and has had constant tinnitus for years. He did report a right-sided headache for the last two weeks. The patient had a history of traumatic brain injury 22 years prior, in which he fell off of a ladder. He lost consciousness at the time, and the left side of his body was paralyzed for six months. He does have some residual neurologic and cognitive deficit. He reports taking 300 mg per day of Carbatrol for the last 20 years to control seizures, and Synthroid for hypothyroidism. His current occupation is a farm worker and he reports no history of alcohol or tobacco use.

Visual acuities were 20/200 in the right eye and 20/20 in the left eye. Fixation, pursuits and saccades were normal. Color vision with Ishihara Pseudoisochromatic Plates was 7/8 in the right eye and 8/8 in the left eye. Comparing a red cap between the two eyes, he reported that the cap was black with the right eye, and a bright red with the left eye. Pupils were equal and briskly reactive to light with a slight RAPD in the right eye.

Anterior segment evaluation was unremarkable.

Intraocular pressures were 12mmHg in both eyes. A dilated fundus exam revealed severe hyperemic disc edema in both eyes. (Fig 25) The disc edema was more severe superiorly than inferiorly in the left eye. Ischemia and flame-shaped hemorrhages were seen on the disc in both eyes, and no cup was present in either eye.

Due to the bilateral nature, and MRI and MRV were performed immediately to rule out causes of papilledema. A CBC, ESR, and CRP were also obtained to rule out Giant Cell Arteritis. Both the CRP and the ESR were high. On MRI, a cystic lesion was found in the left frontal lobe, as well as degeneration in the temporal lobes. (Fig 26) This was thought to be related to the prior brain injury. There was mild enhancement of the left optic nerve sheath, but no flattening of the globe or empty sella was present. Due to the high CRP and ESR, the patient was scheduled for a temporal artery biopsy. He was discharged on oral prednisone 80 mg per day.
At the one-week follow up, the patient reported that vision did not seem as dark. Visual acuity was 20/60 in the right eye, and 20/20 in the left eye. Color vision was normal in both eyes. Pupils were briskly reactive with no RAPD. A relative superior altitudinal defect was present in both eyes with visual field testing. No improvement of the optic nerve appearance was evident.

The temporal artery biopsy found no indication of arteritis. Additional blood testing revealed a negative Lupus anticoagulant, but other tests (Anticardiolipin antibody IgM and Anti-B2 glycoprotein IgG and IgM) revealed an increased risk of thrombosis. At this time, the prednisolone was discontinued, and it was recommended that the patient take a baby aspirin once per day.

At the one-month follow up visit, visual acuities had improved to 20/30 in the right eye. Visual field testing revealed an enlarged blind spot in the right eye, and a superior nasal altitudinal defect in the left eye. Visual acuity further improved in 20/20 in both eyes at the 1 year follow up visit. Four years after the original event, the patient sees 20/20 in both eyes, the optic nerve heads are shown in Fig 27, and he has had no new ocular or systemic issues.

**AAION**

Giant Cell Arteritis (GCA), also known as Temporal Arteritis, is the most common cause of arteritic anterior ischemic optic neuropathy (AAION), but it accounts for only 6% of ischemic optic neuropathy cases. GCA is a chronic vasculitis that commonly affects branches of cranial blood vessels. Visual manifestations of GCA occur in approximately 14-22% of patients. The prevalence of GCA is dramatically higher with increased age. The mean age of AAION is 75-76 years, and it is rare under the age of 50. Women and Caucasian patients are more frequently affected.

Patients with AAION typically have systemic symptoms of the condition. These include headache, pain on chewing, pain and tenderness of the temporal artery or scalp, malaise, anorexia, weight loss, fever, and joint and muscle pain. However, 20% do not have any systemic symptoms despite vision loss.

Loss of vision usually occurs over hours to days. This is most often unilateral, but bilateral simultaneous vision loss occurs much more frequently that that seen with non-arteritic anterior ischemic optic neuropathy (NAION). Transient visual obscurations prior to complete vision loss are common. Diplopia can also be reported with GCA.

Vision loss is typically severe with AAION. Mean acuity is 20/400, and acuity worse than 20/200 accounts for 70-83% of patients. Color vision is diminished and an RAPD will be present. Visual field is severely reduced, but early on the most common visual field defect is altitudinal. Intraocular pressure has been shown to be significantly lower in patients with AAION compared to those with NAION and
Disc edema is more likely to be pallid with AAION than with NAION. (Fig 28) Flame hemorrhages and CWS are associated with AAION, and the optic disc of the fellow eye is usually of normal diameter with an average-sized cup.

Within 6-8 weeks, the optic disc will develop atrophy, with cupping similar to that of glaucoma. Unlike that seen with glaucoma, however, AAION patients will have pallor of the remaining neuroretinal rim.

Immediate laboratory blood work should be obtained for patients suspected of GCA. ESR can be markedly increased in patients with AAION. Rates above 70-100 mm/hr are not uncommon in this condition. However, ESR can be normal in biopsy-proven GCA, and can be elevated in other conditions including anemia, inflammatory disease, malignancy, or infection. Measurement of CRP can aid in the diagnostic accuracy. Values greater than 2.45mg per deciliter and ESR greater than 47 mm/hr can detect GCA with 97% specificity.

Thrombocytosis is commonly seen in GCA and is a risk factor for permanent vision loss. A positive temporal artery biopsy is more likely if the platelet count is elevated (above 400x10^3 uL).

A temporal artery biopsy can confirm the diagnosis of GCA. These patients often need corticosteroid treatment for up to one year. Because long-term steroid treatment can have severe systemic complications, the diagnosis of GCA should always be confirmed with a temporal artery biopsy to avoid unnecessary treatment. However, a negative biopsy does not rule out GCA – a false negative result can occur.

Fluorescein angiography with AAION will likely show peripapillary choroidal nonperfusion and prolonged choroidal and central retinal artery filling times.

GCA is an ophthalmic emergency! Patients with GCA are at risk for developing vision loss in the other eye, as well as systemic complications such as stroke or myocardial infarction. Therefore treatment should be started immediately for those suspected of GCA without waiting for the temporal artery biopsy.

The aim of treatment is to prevent progression of vision loss or the involvement of the contralateral eye. IV methylprednisolone 1g/day for 3-5 days is recommended. This should be done under the supervision of an internist after admission to a hospital. After initial therapy, oral prednisone of at least 1mg/kg/day should be instituted followed by a very slow taper. The treatment is usually maintained for at least 9-12
months while monitoring the patient’s symptoms, ESR and CRP. Due to the side effects of steroid use, calcium supplements, vitamin D supplements, and peptic ulcer prophylaxis should be recommended. Co-management with an internist is important. If thrombocytosis is present, anti-platelet therapy should be considered along with corticosteroid therapy. Low dose aspirin has been shown to decrease the rate of visual loss and stroke in patients with GCA.

Recovery of vision is unlikely, despite treatment of AAION. Even with IV steroid treatment, vision in 16-27% of eyes will deteriorate within the first week, and then stabilize. Without therapy, 54-95% will develop AAION of the fellow eye within hours or days. Disc edema resolves and atrophy ensues within 4-8 weeks. Attenuation of retinal vessels and excavation of the optic disc frequently occur with AAION. Recurrences occur in up to 10% of patients. Systemic symptoms usually resolve within 1 week of corticosteroid treatment. If this does not occur, an alternative diagnosis should be considered.

**NAION**

The most common cause of disc edema in patients over the age of 50 is NAION. The mean age of onset is approximately 61-66 years. 23% are younger than 50 years. Caucasians are affected more than African Americans or Hispanics. Males are affected as commonly as females.

NAION is most frequently an idiopathic hypoperfusion, or non-perfusion, of the optic nerve head. (Fig 29) These patients usually have vasculopathic risk factors such as hypertension, atherosclerosis, or diabetes. Most people with NAION also have a ‘Disc at Risk’: a small, crowded optic nerve head with a small or non-existent physiological cup. NAION can also occur with papilledema, optic nerve head drusen, elevated IOP, radiation, acute systemic hypotension, and sleep apnea. Some drugs have been found to be associated with NAION, including Amiodarone and erectile dysfunction medications.

With NAION, vision loss occurs over hours to days, and often occurs within two hours of awakening. These patients usually do not have headache, jaw claudication or scalp tenderness that is associated with AAION. Rarely do they have pain with eye movements that we associate with optic neuritis. In addition, patients with NAION rarely experience transient visual loss, which is common with AAION.

Visual acuity loss with NAION is usually not as severe compared with that in AAION. About 67-75% of patients have acuity better than 20/200, and about half have acuity better than 20/30. Color vision is decreased proportionally to vision loss. Altitudinal visual field loss, usually inferior or inferior-nasal, is the most common visual field defect, but any other pattern can occur.
Diffuse or segmental disc edema is present with NAION. (Fig 30) Edema can be more severe either superiorly or inferiorly, and this localized edema may or may not correlate with altitudinal visual field defect. Swelling can be hyperemic or pale, but pallor is less likely than that seen with AAION. Disc edema may precede vision loss, producing an early sign of NAION. Peripapillary hemorrhages and focal retinal attenuation around the disc is common. The contralateral optic nerve head is often undersized with a small or absent cup, and associated mild disc elevation and blurred margins. Increased perfusion surrounding the ischemic area, in the form of hyperemic telangiectatic vessels, may be seen on the surface of the optic nerve and corresponds to sparing of the visual fields.

Erythrocyte Sedimentation Rate (ESR) and C-Reactive Protein (CRP) are normal with NAION, but they should be obtained to rule out GCA. No additional testing is necessary if the presentation is typical for NAION and the ESR and CRP are normal. If the patient presents with pain or the neuropathy does not follow a typical course, neuroimaging is necessary. Progression of vision loss, prolonged disc edema, and patients under the age of 50 years require neuroimaging as well as additional blood testing. Evaluation for thrombotic risk factors or vasculitides may be necessary if clinical evidence is suggestive of these conditions. OCT is helpful in monitoring the NFL following NAION.

Unfortunately there is no proven therapy or prophylactic measures that have been shown effective for NAION. Some experts recommend aspirin. Although the role in NAION has not been proven, it is effective in reducing the risk of stroke and myocardial infarction in at-risk patients. Patients with NAION should be referred to a primary care physician for evaluation of risk factors such as hypertension, diabetes, and hyperlipidemia.

Vision with NAION generally remains stable, although 40% of patients do recover at least three lines of Snellen acuity and ¼ of patients have visual field improvement. Disc edema resolves and diffuse or sectorial disc pallor develops within 4-6 weeks. No cupping typically occurs, which helps to distinguish this from pallor resulting from AAION. Involvement of the contralateral eye within 5 years is seen in approximately 15-19% of patients with NAION. This is more common in patients with diabetes and those with acuity worse than 20/200.

Diabetic Papillopathy is considered an atypical form of NAION. It is more likely to be bilateral than seen in non-diabetics, and it may occur with or without diabetic retinopathy. These patients often have no symptoms. An enlarged blind spot or arcuate visual field defect may be present. The visual field defect is more likely to be mild than seen with non-diabetic NAION. Unilateral or bilateral disc swelling is present with Diabetic Papillopathy. Also, dilated telangiectatic vessels on the optic nerve head are commonly seen. These tend to resolve as the disc swelling decreases, and can be mistaken for proliferative diabetic retinopathy, and treated with pan-retinal photocoagulation (PRP), producing
unnecessary retinal damage. Similar to NAION, the contralateral eye will have a ‘Disc at Risk.’ It is more common that the disc edema precede vision loss in diabetic patients.

**Part 2 continues on the next document**