

# Ischemic optic neuropathy

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Ischemic optic neuropathy can potentially be a visually devastating condition among middle-aged and older individuals. It can be divided into anterior ischemic optic neuropathy (AION) and posterior ischemic optic neuropathy (PION) based on the anatomical vascular supply of the optic nerve head that is afflicted. AION is then further classified as either arteritic (A-AION), commonly caused either by giant cell arteritis (GCA), or non arteritic (NA-AION) with multiple causes other than giant cell. Likewise, PION has two subclasses in addition to a surgical classification (Figure 1). The most common of these conditions is NA-AION with PION being the rarest. This discussion will review the clinical presentation, pathogenesis, work up, prognosis and treatment of these neuropathies.

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## A-AION

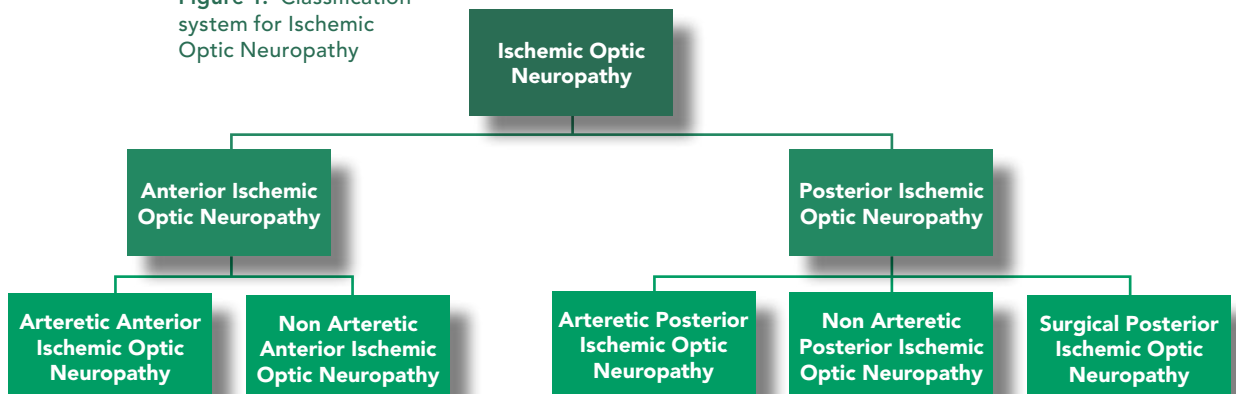
The primary cause of A-AION is GCA although other conditions such as polyarteritis nodosa, polymyalgia rheumatica, lupus and herpes zoster have also been known to cause A-AION. GCA is a type of vasculitis and has a predilection for medium and large size arteries, specifically the posterior ciliary arteries (PCA), which supply the anterior portion of the optic nerve. Consequently, this leads to the formation of a thrombotic occlusion of the PCA, thus causing an infarction of the anterior portion of the optic nerve.<sup>1</sup>

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Patients affected by A-AION present with acute unilateral vision loss with mean visual acuity of 20/400, to no light perception.<sup>2</sup> The average age of patients is 76 years old with women (70 percent) being affected more often than men (30 percent). The condition is also common in Caucasian patients, although other races are affected.<sup>3</sup> In addition, approximately thirty percent of patients may report episodes of transient vision loss, or amaurosis fugax, in the weeks preceding the acute event.<sup>4</sup> The patient will present with a corresponding afferent pupillary defect and dyschromatopsia secondary to optic nerve involvement. Extraocular motility disorders may also be present and are likely due to involvement of arteries supplying the extraocular muscles. Patients also present with assorted visual field loss, which may manifest as a central, nasal sectoral or altitudinal loss.<sup>5,6</sup>

Examination of the optic nerve is essential in diagnosing A-AION. Fundus examination may reveal a chalk white colored edematous nerve with/or without peri-papillary hemorrhaging. Less common findings include: cotton wool spots, central retinal artery occlusion and cilioretinal artery occlusion.<sup>7,8</sup> Once the edema has resolved, optic nerve pallor will develop. An important point to note is that fundus examination of the fellow eye may show a normal sized disc with a normal cup-to-disc ratio if unaffected. This is in contrast to NA-AION, in which the fellow eye has a smaller disc.

Figure 1: Classification system for Ischemic Optic Neuropathy



GCA is a systemic disease and, therefore, patients can also have concurrent symptoms of weight loss, jaw claudication, headache, scalp tenderness, neck pain, myalgia and malaise. Physicians should be careful to recognize that occult GCA may occur in which there is acuity loss, but systemic symptoms are absent.<sup>4,9</sup>



## A-AION is a true ocular emergency and immediate testing and treatment are indicated.

A-AION is a true ocular emergency and immediate testing and treatment are indicated. When A-AION is suspected, immediate testing includes erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP). Multiple studies have shown that a combination of these tests provides an excellent specificity of 97%, in confirming GCA.<sup>3,10,11</sup> Ancillary tests include: a complete blood count (CBC), fasting blood glucose, venereal disease research laboratory test (VDRL), fluorescent treponemal antibody absorption test (FTA-ABS), antinuclear antibody test (ANA), fibrinogen and platelet counts.

A definitive diagnosis of A-AION due to GCA is made with a temporal artery biopsy, with a positive result consisting of lymphocytic infiltration with accompanying macrophages and multinucleated giant cells in the arterial wall. It is an important point to note that the biopsy should be performed within one week of starting steroid therapy as treatment reduces the amount of inflammatory markers in the specimen. Additionally, the inflammatory components are sporadic or may skip a significant section of the artery which might be lost in a shorter biopsied section. If results are ambiguous or equivocal, a contralateral biopsy may be obtained for confirmation.<sup>12</sup>

Traditionally, the diagnosis of GCA depends upon a criteria outlined by the American College of Rheumatologists: fifty years of age or older, new onset of localized headache, temporal artery tenderness, elevated ESR, and positive temporal artery biopsy. The criteria states that three out of the five items are needed to confirm the diagnosis of GCA. However, this criterion is controversial and not standardized. Clinicians should take a guarded approach to using these guidelines as studies have shown that many patients would have never been diagnosed with GCA had this criteria been used.<sup>13,14</sup>

Treatment of GCA requires immediate use of high dose corticosteroids. Clinicians should initiate therapy as delay in treatment can result in the fellow eye becoming involved. Treatment may begin with intravenous methylprednisolone (1000 mg/day) or

oral prednisone (60 mg/day). The purpose of treatment is to prevent involvement of the fellow eye and other systemic vascular problems such as stroke or myocardial infarction.

Once vision loss ensues, recovery is rare. Hayreh et al., found that in spite of steroid treatment, only 4 percent of patients with visual loss showed improvement.<sup>6</sup> Further decline is possible as Danesh et al found that 27 percent of patients continue to suffer visual decline despite the use of high dose intravenous methylprednisolone.<sup>2</sup> Unfortunately, there are no strict guidelines for the duration of treatment and patients may be kept on steroids for a minimum of one year<sup>15</sup> with a slow taper. Others advocate for lifelong treatment with a low maintenance dose.<sup>3</sup>

### NA-AION

AION is caused by infarction of the short posterior ciliary arteries that supply the anterior aspect of the optic nerve. In the non-arteritic form, these vessels are compromised by vascular diseases such as hypertension, diabetes mellitus, hyperlipidemia, atherosclerosis and sleep apnea. Consequently, these conditions then lead to a transient non-perfusion or hypo-perfusion of blood to the eye.<sup>6</sup> This mechanism is supported by the finding that a majority of NA-AION cases (75 percent) are discovered upon waking. The normal physiological phenomenon of decreased blood pressure at night is furthered by hypotensive drugs and other pre-existing cardiovascular disorders. Other less common causes of hypo-perfusion include transient reductions in blood pressure secondary to shock or to embolic causes.<sup>6</sup> Interestingly, one report mentioned seven cases in which men between 50 and 69 years of age showed symptoms of NA-AION within 36 hours of taking sildenafil citrate (Viagra); however, authors noted that all subjects also had pre-existing conditions such as hypertension, diabetes, elevated cholesterol or hyperlipidemia.<sup>16</sup>

It is thought that vasodilation of blood vessels by the drug (Viagra), in combination with other systemic vascular factors, leads to alterations in perfusion to the optic nerve, which may ultimately result in ischemia.

Signs and symptoms of patients afflicted with NA-AION are similar to those persons affected by A-AION with minor, but important differences. Patients affected by NA-AION will present with acute and painless unilateral vision loss with acuity ranging from 20/20 to NLP. In general, these patients will have better entering and end acuity than those with A-AION, with a majority of these patients retaining better vision. Older individuals are affected, with the average age of patients being

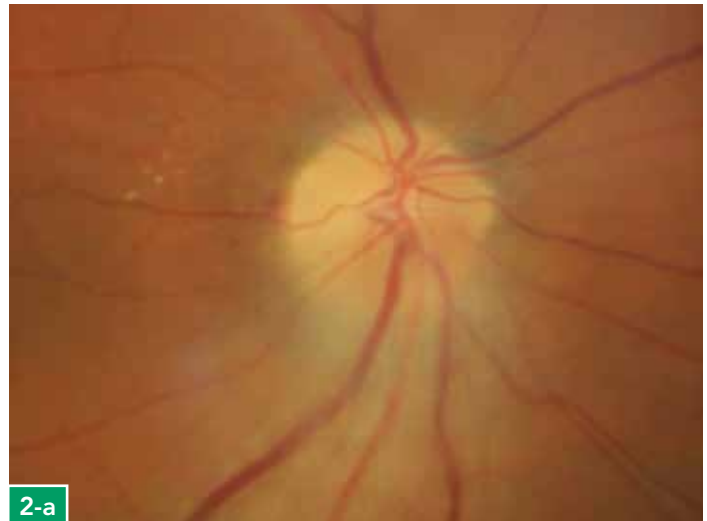
61 years old with no gender predilection.<sup>17</sup> Additional findings may include dyschromatopsia, an afferent pupillary defect, and visual field loss which correlates with the degree of acuity loss. Automated visual field tests may show arcuate or altitudinal defects but any part of the field may be compromised.<sup>18</sup>

Fundus examination of the optic nerve may reveal disc edema with possible peripapillary hemorrhaging. The end stage finding is palor of the nerve head which can be diffuse or sectoral depending on the amount of initial edema (Figure 2).<sup>7</sup> Examination of the fellow eye may show a "disc at risk." This term is used to describe the appearance of the fellow nerve, which is small and crowded with blood vessels, with minimal to no cup-to-disc ratio. This anatomical presentation is thought to compromise the blood supply to the optic nerve, leaving it at risk for possible future involvement.

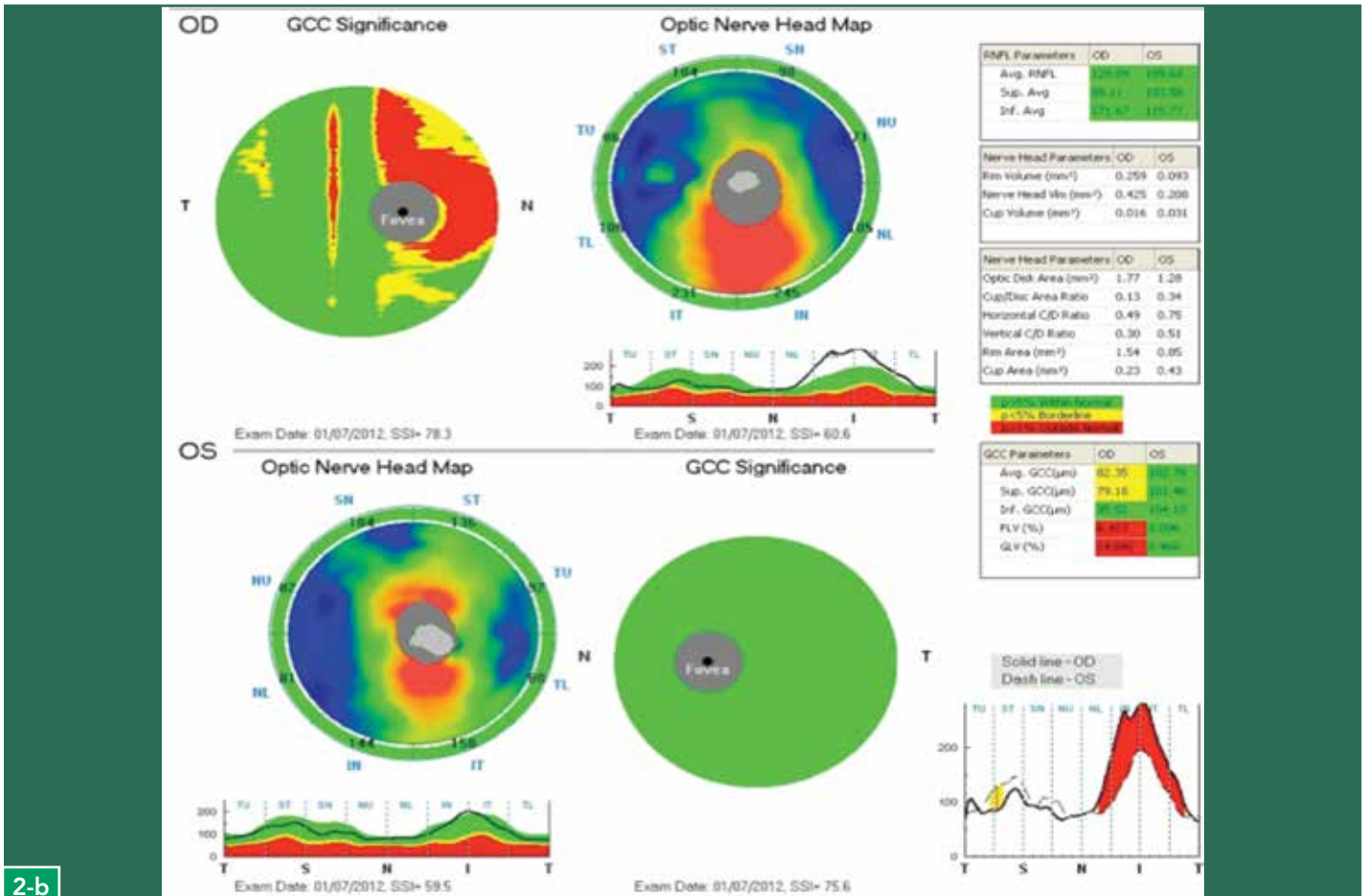
NAION is a diagnosis of exclusion and A-AION should be ruled out. Test results show a normal ESR and CRP as the condition is

not inflammatory but vascular in nature. Also, patients will rarely have episodes of amaurosis fugax, or systemic symptoms suggesting GCA. If a temporal artery biopsy is performed, it will also be negative. Additionally, since NA-AION may be associated with underlying systemic conditions, clinicians should be vigilant and perform or refer for appropriate testing to rule these conditions out. Table 1 summarizes important findings that are used to distinguish A-AION from NA-AION.

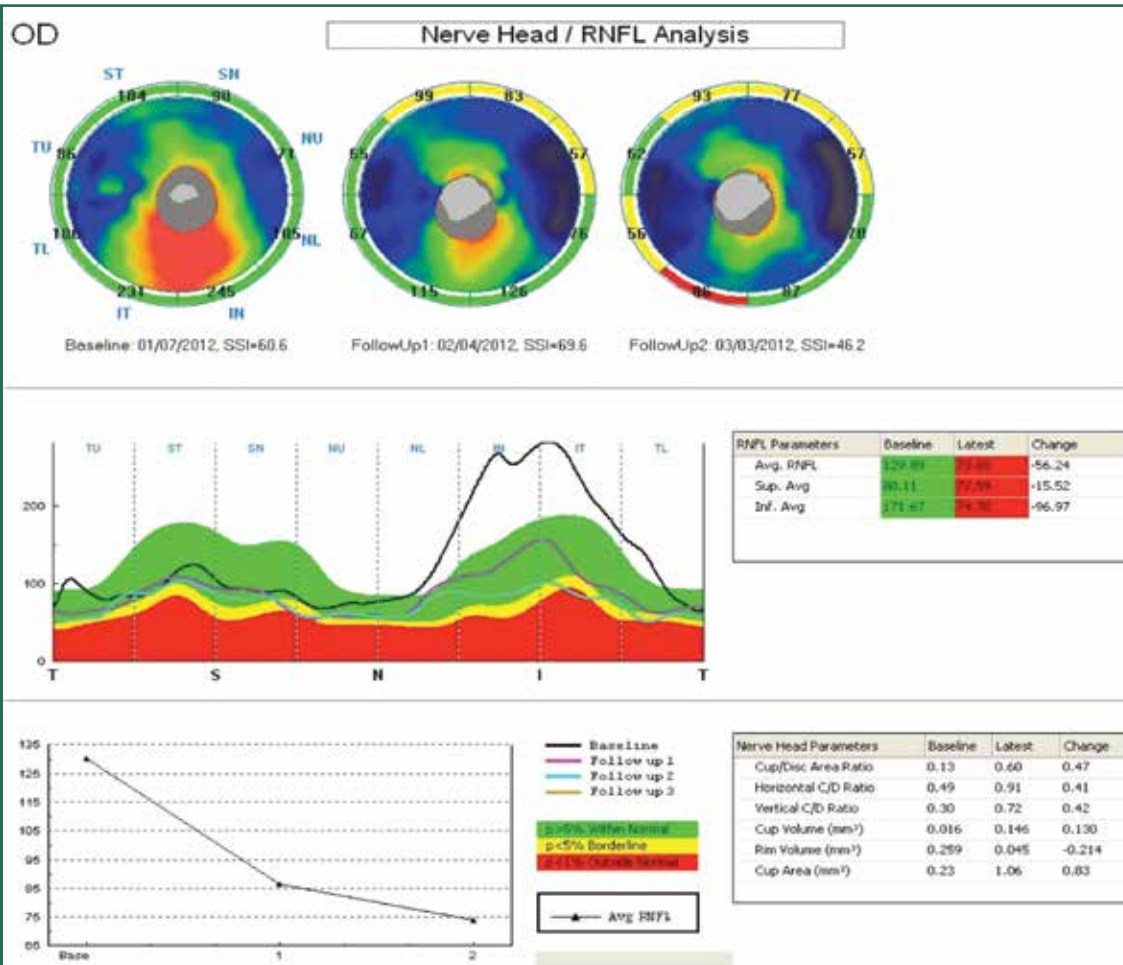
Figure 2: a) Fundus photograph of the right eye showing sectoral disc edema inferiorly during the acute phase of NA-AION. b) Spectral domain optical coherence tomography (SD-OCT) of the same eye showing marked nerve fiber layer (NFL) thickness inferiorly corresponding with inferior disc edema. c) Resolution of the inferior edema as seen with serial SD-OCT scans.



2-a



2-b



2-c

Table 1: Differentiating factors used in the diagnosis of A-AION and NA-AION

	A-AION	NA-AION
<b>Etiology</b>	Inflammatory	Vascular
<b>VA Loss</b>	Severe, > 20/400	Not as severe, 20/50-20/200 on average
<b>Amaurosis Fugax</b>	30% chance	Extremely rare
<b>ESR and CRP Testing</b>	Positive	Negative
<b>Temporal Artery Biopsy</b>	Positive	Negative
<b>Disc appearance</b>	Chalk white, diffuse edema	Diffuse or segmental edema
<b>Fellow disc</b>	Normal cupping	"Disc at risk"
<b>Systemic Disease</b>	Giant cell arteritis	Hypertension, diabetes, hypercholesterolemia
<b>Pain</b>	Pain associated with systemic symptoms such as scalp pain, headache, and jaw claudication	No pain

VA: Visual Acuity, ESR: Erythrocyte Sedimentation Rate, CRP: C - reactive protein.



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Clinically, the patient's vision worsens for two to three weeks and then stabilizes. Improvement has been reported in some studies, but acuity levels never return to levels prior to the ischemic event. Final visual acuity is variable with most patients falling in the 20/50 to 20/200 range with reoccurrences in less than 5 percent of patients.<sup>19</sup> Similar to A-AION, the fellow eye can be also involved with NA-AION. The fellow eye is involved in 15 percent of patients, with higher risk of involvement related to poor acuity in the initial eye along with a history of diabetes. Age, sex, smoking and aspirin use were not associated with fellow eye involvement.<sup>20</sup>

There are no accepted treatment guidelines although numerous surgical and medical therapies have been proposed including: optic nerve decompression, aspirin, anti-coagulants, thrombolytics, vasodilating agents, systemic steroids, intravitreal triamcinolone, anti-vegf agents, levodopa, diphenylhydantoin and hyperbaric oxygen. Literature on these treatments, however, is mostly of retrospective or prospective case series,<sup>19</sup> with the largest study on NA-AION treatment, the Ischemic Optic Neuropathy Decompression Trial, showed that

treatment actually exacerbated the condition.<sup>21,22</sup> The general consensus among clinicians is that the systemic vascular diseases that precipitate the condition should be well managed in hopes of averting or delaying bilateral ocular involvement and further systemic involvement.<sup>19</sup>

#### PION

While the anterior portion of the optic nerve is supplied by the PCAs, the posterior portion is supplied by the pial plexus. Since the ischemic event occurs behind the nerve head, the condition is termed posterior ischemic optic neuropathy (PION). PION is further classified based on the actual cause of the ischemic event: arteritic, non-arteritic, or surgical.<sup>23</sup> The pathogenesis of arteritic-PION and non-arteritic-PION are similar to A-AION and NA-AION with surgical PION having multiple causes including arterial hypotension (from general anesthesia, surgical trauma, and substantial blood loss), administration of intravenous fluids to compensate for blood loss, and orbital and peri-orbital edema secondary to surgical procedures.<sup>6,23</sup>

Patient presentation is also similar to the other ischemic optic neuropathies; however, in the case of surgical PION, patients

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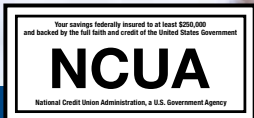
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discover their acuity loss when they regain their attentiveness post-surgery. Older individuals are more likely to be affected by all three types of PION. Vision loss is severe with more than 50 percent having count fingers vision or worse.<sup>23</sup>

Initial fundus examination shows a normal appearing optic nerve due to the ischemic event being located behind the nerve head. However after six to eight weeks, optic nerve palor does begin. Clinicians should be careful not to confuse this appearance with that of retro-bulbar optic neuritis. Although both conditions can present with acuity loss and a normal appearing nerve, PION can be differentiated by its occurrence in an older age group and absence of pain on eye movement.<sup>24</sup>

PION is also considered a diagnosis of exclusion, and appropriate testing including neuro-imaging is indicated to rule out compressive and inflammatory disease in addition to the standard testing for AION. Treatment is aimed at controlling the underlying cause.

Confirming the diagnosis of AION or PION can be challenging and frustrating, therefore, clinicians should use all necessary tests for confirmation. An ideal clinical outcome is dependent upon a prompt diagnosis and appropriate treatment.

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