

# Giant Cell Arteritis

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## KEYWORDS:

Diplopia

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Ophthalmology

Temporal Arteritis

Temporal Artery Biopsy

Vision Loss

Giant cell arteritis, also known as temporal arteritis, is a condition that can present in patients with a headache, scalp tenderness, anemia, jaw claudication, diplopia or sudden severe vision loss. The main differential diagnosis is non-arteritic anterior ischemic optic neuropathy. Upon suspected diagnosis of giant cell arteritis, laboratory workup for erythrocyte sedimentation rate, C-reactive protein, and complete blood count are performed. A temporal artery biopsy serves as confirmatory evidence of the disease. The immediate treatment for suspected giant cell arteritis is systemic steroids. This article will review giant cell arteritis, its pathophysiology, patient symptomatology, differential diagnosis, and treatment. Included in this review will be a video of a temporal artery biopsy.

## INTRODUCTION

Giant cell arteritis (GCA), also known as temporal arteritis, is a chronic, granulomatous, inflammatory disorder with a predilection for the elastic tissue-rich, medium-to-large arteries in the head and neck.<sup>1</sup> Giant cell arteritis is a true ocular emergency.<sup>2</sup> Although GCA will likely present to an eye care practitioner when its most severe symptom of sudden vision loss occurs, it will often present initially to the primary care physician as a patient with a new onset headache, scalp tenderness or jaw claudication.<sup>2</sup> The goal of GCA management is to identify the disease before arteritic ischemic optic neuropathy, or permanent vision loss develops. Thus, it is important that every primary care physician be familiar with the symptoms, laboratory testing, and treatment of GCA.

## EPIDEMIOLOGY

The likelihood that a primary care physician will be involved in the care of someone with GCA is high since this disease is the most common systemic vasculitis in North America.<sup>3</sup> The disease mainly affects Caucasians, especially those of Scandinavian descent.<sup>2</sup> It is rare in African Americans, Native Americans or those of Asian descent.<sup>2</sup> Age is the greatest risk factor for the disease with an overall prevalence of about 1 in 750 of those over the age of 50.<sup>4</sup> This prevalence increases with age and peaks in the age group 70-79

years.<sup>5</sup> Specifically, the incidence rates per 100,000 in the population increases from two individuals in the 50-59 year age group to 52 individuals in the age group 80 years and older.<sup>5</sup> Women are more commonly affected than men, by two to three times.<sup>2</sup> Other risk factors include those who have had a recent stroke or myocardial infarction, congestive heart failure, aortic aneurysm, anemia, or polymyalgia rheumatica.<sup>1</sup>

## SYMPTOMS & SIGNS

A new onset headache, often in the temporal region and usually occurring on one side, is the most common symptom presenting to a primary care physician. Palpation along the temple will often denote a palpable, tender, nonpulsatile temporal artery. Other common symptoms include scalp tenderness, pain when brushing or styling one's hair and jaw claudication, particularly when chewing.<sup>1</sup> Recent weight loss or diplopia may also be reported.<sup>1</sup> Less common ailments may include general malaise or fatigue, changes in mental status, ear, throat or neck pain or facial swelling<sup>6</sup> (Table 1, page 18).

## Ocular Signs

Significant visual acuity loss, often resulting in counting fingers or worse vision, is a hallmark sign that the disease is progressing. Amaurosis fugax, which is a painless transient vision loss or blackening of vision, may occur in up to 40% of patients before permanent vision loss.<sup>7</sup> Pupil abnormalities, including tonic pupil, light-near dissociation (pupil does not constrict to light but does constrict to convergence at near), miotic Horner's syndrome pupil, or an afferent pupillary defect may also be noted.<sup>6</sup> Anterior segment examination may infrequently show ischemia including corneal

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edema or fine keratic precipitates.<sup>8</sup> A posterior segment examination may show a pale, swollen optic disc that may also have flame-shaped hemorrhages, known as arteritic ischemic optic neuropathy (AION)<sup>6</sup> (Figure 1 and Figure 2 show AION with flame-shaped hemorrhages at two different time points).

## DIFFERENTIAL DIAGNOSES

Non-arteritic ischemic optic neuropathy (NAION) is the most common ocular differential diagnosis from GCA, when it presents as AION. Patients with NAION are usually slightly younger than the typical AION patient, lack the subsequent complaints of those with GCA and usually present with less severe vision loss. NAION may have sectorial or segmental optic nerve edema (Figure 3) while patients with AION will have a pallid swollen disc.

Other ocular differentials include inflammatory optic neuritis which typically has pain on eye movements, compressive optic nerve tumor which presents with slowly progressive vision loss and retinal vascular occlusions such as vein occlusions that present with multiple diffuse retinal hemorrhages or artery occlusions, which present with retinal edema and a red macula (cherry red spot).<sup>6</sup>

**TABLE 1:**

Signs and Symptoms of Giant Cell Arteritis

	SYSTEMIC	OCULAR
Symptoms	<ul style="list-style-type: none"> <li>- New headache</li> <li>- Scalp tenderness</li> <li>- Pain with hair styling</li> <li>- Jaw claudication</li> <li>- Recent weight loss</li> <li>- General malaise</li> <li>- Ear, throat, neck pain</li> <li>- Facial swelling</li> </ul>	<ul style="list-style-type: none"> <li>- Vision loss</li> <li>- Diplopia</li> <li>- Amaurosis fugax</li> <li>- Eye pain</li> </ul>
Signs	<ul style="list-style-type: none"> <li>- Palpable, tender, nonpulsatile temporal artery</li> <li>- Anemia</li> <li>- Change in mental status</li> <li>- Recent myocardial infarction</li> <li>- Congestive heart failure</li> <li>- Aortic aneurysm</li> </ul>	<ul style="list-style-type: none"> <li>- Abnormal pupils</li> <li>- Afferent pupillary defect</li> <li>- Anterior segment ischemia</li> <li>- Pale, swollen optic disc</li> <li>- Visual field defect</li> <li>- Central retinal artery occlusion</li> <li>- Cranial nerve 3, 4 or 6 palsy</li> </ul>

A systemic differential is polymyalgia rheumatica (PMR). PMR is a disease of adults over age 50, with a prevalence that increases progressively with advancing age.<sup>9</sup> The lifetime risk of PMR is second only to rheumatoid arthritis as a systemic rheumatic disease in adults.<sup>10</sup> The primary presenting symptom of PMR is new-onset bilateral shoulder pain and stiffness.<sup>11</sup> Other symptoms include fatigue, depression, weight loss or a low-grade fever.<sup>11</sup> Many of these symptoms overlap with GCA. The overlap is considerable as 16-21% of patients with PMR have GCA on temporal artery biopsy, and symptoms of PMR are present in 40-60% of patients with GCA.<sup>12</sup>

Since a headache is a common finding in GCA, migraine and cluster headache should be considered in the differential. Both of these headache types have a much earlier age of onset, usually before the age of 40.<sup>13</sup> Also, the character of the headache types is different from a GCA headache that is usually painful to the touch in the temple region. A migraine is a unilateral, throbbing head pain or pulsing sensation, which may be preceded or accompanied by visual alterations, difficulty speaking, numbness of the face, nausea, vomiting and extreme sensitivity to light and sound.<sup>14</sup> Cluster headaches often wake the patient from sleep with a very rapid onset and peak intensity. They exhibit a boring or penetrating pain, and patients often have accompanying nasal congestion, lacrimation, rhinorrhea and conjunctival edema and injection.<sup>15</sup>

Jaw claudication as seen in GCA results from ischemia of the masseter muscle during chewing. Temporomandibular disorder (TMD) can mimic jaw claudication, but patients have the greatest risk of onset between the ages of 18 and 44.<sup>16</sup> Instead of ischemia, TMD symptoms are characterized by acute or chronic musculoskeletal pain triggered by jaw motion, dysfunction of the masticatory system, temporomandibular joint (TMJ) tenderness and cervical spinal dysfunction.<sup>17</sup> Clicking or popping noises with jaw function is a common finding with TMJ dysfunction.

## PATHOPHYSIOLOGY

Giant cell arteritis is a vasculitis with a preference for the extracranial branches of the carotid artery including the temporal arteries, the terminal branches of the ophthalmic artery and the posterior ciliary arteries.<sup>1</sup> An integral part of this disorder is the presence of small calcifications within the internal elastic membrane (Figures 4, 5, and 6). The body reacts to these small calcifications with a release of foreign-body giant cells that accumulate and break down the internal elastic membrane calcifications.<sup>18</sup> This accumulation causes lymphocytes to surround these calcifications resulting in a widespread inflammatory reaction cascade. Following this event, lymphocytes are joined by plasma cells, mononuclear cells, multinucleated giant cells, and eosinophils, all of which obstruct the laminae of the involved vessels.<sup>2,18</sup>

## WORK-UP

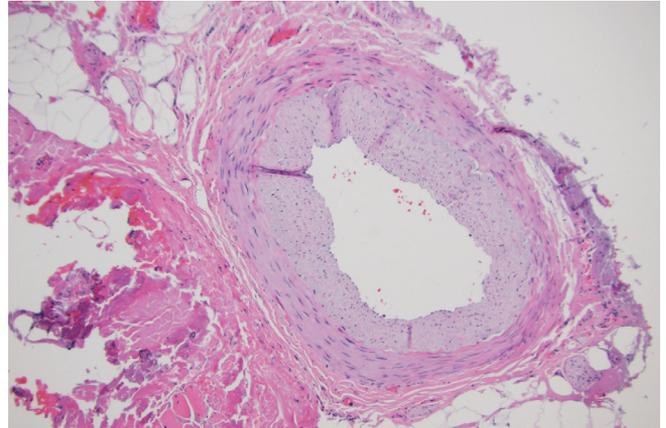
When a physician suspects the diagnosis of GCA, laboratory tests including C-reactive protein (CRP), complete blood count (CBC) and erythrocyte sedimentation rate (ESR) should be ordered immediately. Those with temporal arteritis will likely have a markedly elevated ESR (over 40mm/hr in 90% of confirmed cases).<sup>2</sup> However, ESR is dependent on age and sex and can be affected by anemia, which also affects many of those with temporal arteritis. Ten

**FIGURE 1:**

Arteritic ischemic optic neuropathy showing pallid swollen optic disc.  
Day 1, initial presentation

**FIGURE 4:**

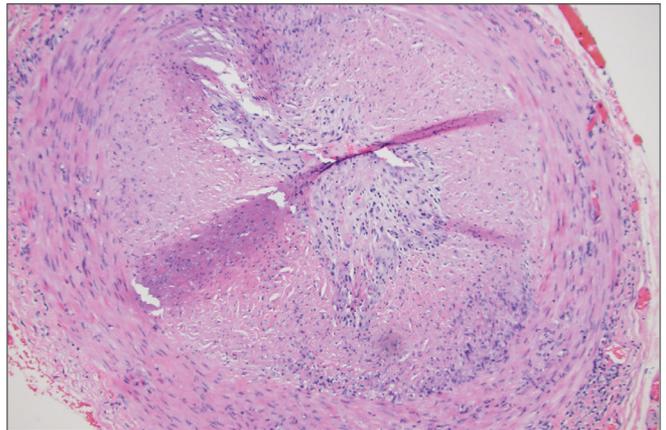
Histology slide of normal temporal artery

**FIGURE 2:**

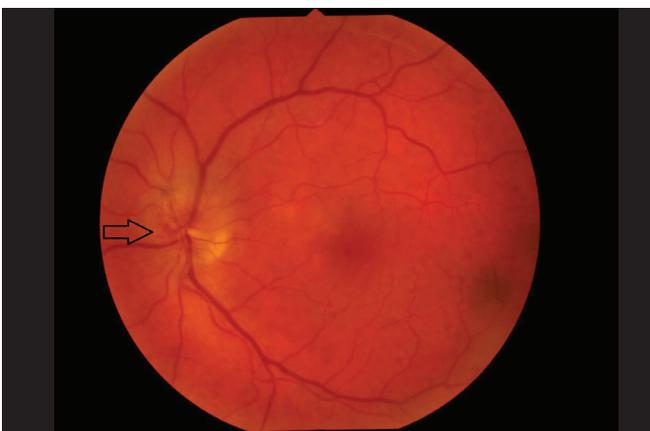
Resolving disc edema after initiating steroid treatment.  
Day 19 presentation

**FIGURE 5:**

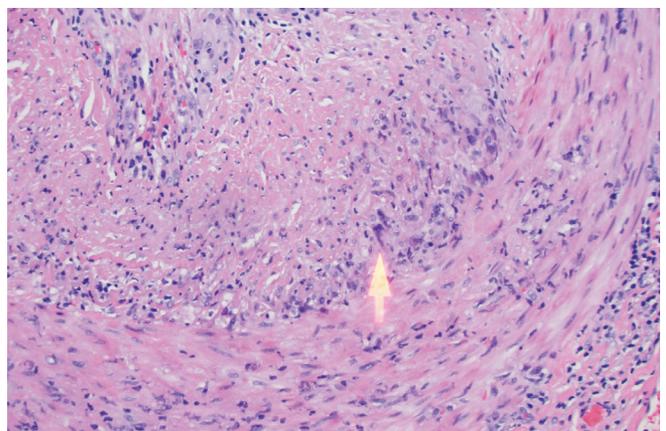
Histology slide of artery with temporal arteritis

**FIGURE 3:**

Non-arteritic ischemic optic neuropathy showing segmental  
optic disc edema (arrow)

**FIGURE 6:**

Histology showing changes of lumen and increased vessel wall thickness  
with multinucleated giant cells (arrow)



to 15% of those with GCA may still have a normal ESR.<sup>19</sup> In patients who have the signs and symptoms of GCA yet a normal ESR value, a temporal artery biopsy should still be performed.<sup>19</sup> An elevated CRP value is also very likely in those with GCA. The CBC values may show mild normochromic normocytic anemia, normal leukocytes and differential count and an elevated platelet count.<sup>9</sup>

If the patient's laboratory findings are positive, oral prednisone should be initiated. If the patient also has ocular symptoms, they should be referred to an ophthalmologist or neuro-ophthalmologist. If there are no ocular complications referral to a rheumatologist or neurologist is indicated. Also, a temporal artery biopsy needs to be obtained within one week. A number of different surgical specialists can usually perform the biopsy. These would include surgeons specializing in ophthalmology, otorhinolaryngology, general or vascular surgery, plastics, oromaxillofacial or neurosurgery.

The definitive test for GCA is a temporal artery biopsy. The likelihood of a positive temporal artery biopsy is 1.5 times greater with an ESR of 47-107mm/hr, 5.3 times greater with a CRP greater than 2.45mg/dL and 4.2 times greater with a platelet count over 400,000/ $\mu$ L.<sup>20</sup> If all three of these lab values are elevated, the likelihood of a positive temporal artery biopsy is eight times greater.<sup>20</sup> It is also suggested that there is a higher predictive power for a positive temporal artery biopsy if both CRP and platelets are elevated when compared to an elevated ESR alone.<sup>20</sup>

A color-duplex ultrasonography can be useful in assessing vascular inflammation. The accessible large arteries and the superficial temporal artery can be examined to look for the characteristic "halo sign" noted on ultrasonography.<sup>11</sup> This "halo sign" is a hypochoic ring around the arterial lumen that shows the edematous thickening of the arterial wall due to inflammation.<sup>11</sup> While ultrasonography is noninvasive and may seem efficient, difficulties arise due to differences in criteria, technical equipment and the evaluation of different vessels.<sup>11</sup> Ultrasonography is thus used to supplement laboratory values and a temporal artery biopsy.

In addition, angiography of the aortic arch and its branches may serve to diagnose large-vessel involvement. Magnetic resonance angiography as well as magnetic resonance imaging of the cranium and chest can show the presence of increased aortic wall thickness and edema.<sup>21</sup> Increased thickness and edema are thought to suggest vascular inflammation, as is the hallmark of GCA. It has been suggested that imaging such as these may help to both diagnose and monitor the disease. Although the temporal artery biopsy is still the gold standard for diagnosis, these noninvasive modalities are helpful in monitoring GCA.<sup>21</sup>

## TEMPORAL ARTERY BIOPSY

In suspected cases of GCA, a temporal artery biopsy should be performed on the side ipsilateral to any vision loss or ipsilateral to the most symptoms.<sup>2</sup> Due to potential vision loss, a physician should not wait for the biopsy results to initiate treatment. The biopsy is performed under monitored conscious sedation.<sup>2</sup> The portion of the frontal branch of the temporal artery to be excised is palpated, its course confirmed with ultrasonography, and then it is marked using a marking pen. A local anesthetic is injected along either side of the vessel markings. A #15 Bard-Parker blade is used to make the initial dermal incision, following the skin markings. Blunt dis-

section is performed to isolate the vessel. Cautery is applied as necessary to maintain hemostasis. When the artery has been localized, the patient is checked for ischemia by compressing the vessel. Titanium clips are used to clamp both the distal and proximal ends of the artery before it is excised (Figure 7). A specimen should be at least 5mm in length with the optimal length being 15mm, as skip lesions that contain no inflammation, may occur.<sup>2,22</sup> Also, there is a disagreement rate of approximately 23% between the right and left temporal arteries, so a negative biopsy result does not necessarily rule out the disease.<sup>1</sup> The subcutaneous tissue is closed with dissolvable 4-0 chromic suture. The incision is sealed with tissue adhesive and butterfly closures. A pressure dressing is then applied. The pressure dressing is removed in 24 hours.

## TREATMENT

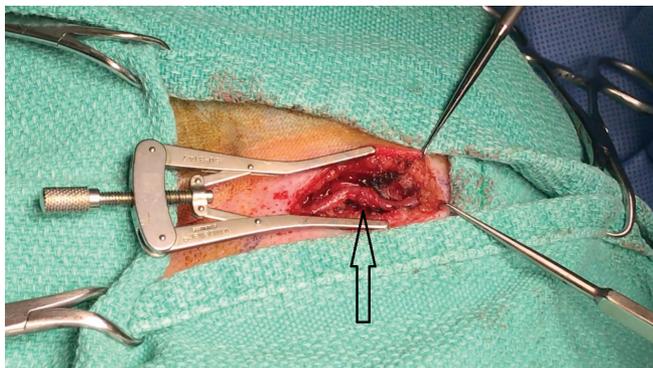
The traditional treatment for GCA is high dose oral steroids (100mg prednisone daily) and should be prescribed immediately after the diagnosis of GCA is suspected. In many cases, this will be able to provide complete symptomatic relief within 24-48 hours.<sup>21</sup> However, if vision loss is the presenting symptom, intravenous methylprednisolone 1-2g for three to five days is the recommended initiating treatment, followed by high dose oral steroids.<sup>6</sup> The physician should monitor both ESR and CRP levels every two to three weeks to assess treatment progression. If laboratory values suggest the disease is resolving, the steroids should be slowly tapered.<sup>1</sup> If the temporal artery biopsy is found to be negative, steroids should be stopped, and the patient should be investigated by the primary care physician for other causes of symptoms. If the temporal artery biopsy is found to be negative but the patient continues to present with persistent and significant signs and symptoms of GCA, the temporal artery on the opposite side should be biopsied. There are no known suggested osteopathic practices or principles for the treatment of GCA.

A new treatment, tocilizumab, was approved by the FDA in May 2017 for the treatment of GCA. Tocilizumab is an interleukin-6 receptor antagonist.<sup>23</sup> It was first approved for the treatment of adult rheumatoid arthritis in patients who have used at least one disease-modifying antirheumatic drug that was unable to provide necessary relief. When used in patients with GCA, those who received subcutaneous tocilizumab administered with oral prednisone had improved treatment outcomes over patients taking oral prednisone and placebo.<sup>23</sup> Sustained remission at week 52 occurred in 56% of the patients treated with tocilizumab weekly and in 53% of those treated with tocilizumab every other week, as compared with 14% of those in the placebo group that underwent a 26-week prednisone taper and 18% of those in the placebo group that underwent a 52-week prednisone taper.<sup>23</sup> Sustained remission was defined as an absence of symptoms of GCA, normal ESR and CRP laboratory tests, and tapering the use of oral prednisone.<sup>23</sup>

The key to a good prognosis in GCA is prompt proper therapy and management.<sup>21</sup> With treatment, a life expectancy similar to the general population is expected for most patients who have not had visual symptoms.<sup>24</sup> Those with vision loss from GCA usually will not recover their vision.<sup>25</sup> The goal of treatment is to stabilize and preserve vision in the unaffected eye.<sup>2</sup> Relapses of GCA are common with about one-third of patients having symptoms return.<sup>26</sup>

**FIGURE 7:**

Surgical image of temporal artery (arrow) before excision



Patients should be treated with the dose of oral prednisone given before relapse or a higher dose.<sup>27</sup> While relapses are most likely to occur within the first 18 months of treatment, they may also occur later.<sup>26</sup>

**CONCLUSION**

Giant cell arteritis is a chronic vasculitis that although often has visual symptoms, may present to the primary care physician first. It is important to be familiar with the signs and symptoms of this disease as initiating early treatment is essential for visual stability and to maintain a high quality of life. The most common symptoms are new onset headache, temporal pain, scalp tenderness, and jaw claudication.<sup>1</sup> When GCA is suspected, an inflammatory laboratory work-up should be immediately ordered including ESR, CRP and a full CBC. Also, a temporal artery biopsy should be ordered as it is still the gold standard for confirmation of the disease. As long as treatment is initiated right away, most patients experience remission of their symptoms.

View temporal artery biopsy video [bit.ly/ofp\\_video](http://bit.ly/ofp_video)

**AUTHOR DISCLOSURES**

No relevant financial affiliations.

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