

Diplopia as the Presenting Symptom in Giant Cell Arteritis

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Abstract

Patients with acquired cranial nerve palsies commonly present to primary eye care clinics and are associated with a variety of etiologies. While microvascular ischemia is the most common association in older adults, cranial nerve palsies can be associated with other more insidious etiologies, like giant cell arteritis (GCA). This case report describes an uncommon presentation of GCA with ocular involvement and emphasizes the importance of broadening a diplopia differential diagnosis list.

KEY WORDS:

cranial nerve palsy, diplopia, giant cell arteritis, temporal arteritis

INTRODUCTION

Giant cell arteritis (GCA), also known as temporal arteritis, is one of the most visually devastating ocular emergencies. It is the most common systemic vasculitis in adults over age 50 and typically affects women more than men.¹ As a systemic vasculitis with diverse manifestations, it may present to a large array of health care providers including primary care, urgent care, rheumatology, neurology, and optometry or ophthalmology.²

GCA primarily targets medium to large arteries and has a predilection for branches of the internal and external carotid arteries. If it affects the temporal artery, classic temporal headache ensues. When the ophthalmic, central retinal, and posterior ciliary arteries are involved, ocular signs and symptoms may occur.³ Other non-cranial vessels that can have GCA include the aorta, subclavian, axillary and proximal brachial arteries, which cause a variety of nonspecific symptoms.³

Dysregulation between the immune system and vasculature creates an immune response and inflammatory infiltration within these arteries.³ The pathogenesis involves lymphocytes and histiocytes forming multinucleate giant cells which damages the elastic lamina.² This response within the vascular smooth muscle layer causes hyperplasia and eventual occlusion.²

If one of the ophthalmic branches becomes occluded, there is a potential for severe consequences, including irreversible blindness. Since an estimated 50% of GCA patients have a sentinel ocular event, it is important to be able to recognize all the signs and symptoms.⁴

When GCA presents as unilateral optic disc edema and decreased vision, it is rarely missed by eye care providers. However, there are other more insidious presentations that are challenging to diagnose. This report describes a case with diplopia as the presenting symptom in biopsy-proven GCA.

CASE REPORT

A 79-year-old white male presented to the eye clinic with intermittent horizontal diplopia in the right gaze for four weeks. His ocular history was unremarkable. His medical history included bladder carcinoma, hypertension, paroxysmal supraventricular tachycardia, and Meniere's disease. He first sought care at an emergency department about three weeks previously, where he underwent a computed tomography scan which showed no evidence of an acute intracranial process including no signs of an intracranial hemorrhage, cortical infarct, or mass.

His visual acuity was 20/20 in the right eye and 20/20 in the left eye. Pupils were round and reactive to light with no afferent pupillary defect in either eye. Multiple gaze cover testing revealed orthophoria in the primary and left gazes and 15 prism dioptres esotropia in the right gaze, confirming a right abducens nerve deficit. The fundus examination was normal in both eyes without optic disc edema or signs of ocular ischemia.

Upon further questioning, the patient volunteered that he had a significant headache and tenderness across the right temple. This prompted further questioning about GCA-related symptoms, which revealed that he suffered from jaw claudication and recent malaise. He denied recent amaurosis fugax or transient ischemic attack symptoms.

The patient was diagnosed with a presumed cranial nerve six palsy with strongly suspected GCA. He was immediately transferred to the emergency department for diagnostic testing including the inflammatory markers erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP), and a complete blood count. Both ESR and CRP were significantly elevated. The CBC revealed a normal platelet count and below-average values for red blood cell count, hemoglobin, and hematocrit, indicating an underlying anemia. The laboratory findings with values and reference ranges are shown in Table 1.

Table 1: Laboratory test results and reference ranges. Abnormal results are underlined.

Diagnostic Test	Value	Reference Range [†]
Inflammatory markers		
Erythrocyte sedimentation rate	52 millimetres per hour	0-10
C reactive protein	42.8 milligram per liter	0.00-9.99
Complete blood count		
White blood cell count	6.26 cells per microlitre	3.6-11.0
Red blood cell count	4.16 million per cubic millimetre	4.47-5.83
Hemoglobin	12.5 grams per decilitre	13.6-17.4
Hematocrit	38.8%	40-51
Mean corpuscular volume	93.3 femtolitres	80-96
Mean corpuscular hemoglobin	30.0 picograms per cell	27-31
Mean corpuscular hemoglobin concentration	32.2 grams per decilitre	31.5-36.5
Red cell distribution width	13.0%	11.2-15.8
Platelet count	257 cells per microlitre	150-400

[†]Reference range used by Louis Stokes Cleveland Veterans Affairs Medical Center laboratory

Based on the elevated inflammatory markers, underlying anemia and symptoms, he was diagnosed with suspected GCA and started on 60 mg oral prednisone while in the emergency department. He was referred for a temporal artery biopsy with ophthalmology and a baseline examination with the neurology department. Ophthalmology performed a biopsy one week after diagnosis which showed focal lymphohistiocytic infiltrate associated with giant cells within the medial layer of the vessel wall, confirming the diagnosis. At his one-week follow-up with neurology, he reported significant improvement in the diplopia. Since he was asymptomatic and responded well to prednisone, neurology referred him to rheumatology for long-term management and tapering of prednisone. Four years later, he is asymptomatic, has not had any complications, and is no longer taking prednisone.

No identifiable health information was included in this case report.

DISCUSSION

Diplopia in older adults is associated with a large differential diagnosis list which includes restrictive causes, neuromuscular conditions, decompensated strabismus or phorias, and cranial nerve palsies.⁵ Of third, fourth, and sixth cranial nerve palsies, the sixth nerve is the most commonly affected.⁶ For a sixth nerve palsy, such as in this case, the differential diagnosis includes microvascular ischemia, intracranial neoplasm, elevated intracranial pressure, aneurysm, infarction, inflammation, or trauma.^{6,7} Presumed microvascular ischemia is the most common cause of isolated cranial nerve palsies in those over age 50.⁶

Systemic vasculopathies such as diabetes mellitus, hypertension, hypercholesterolemia, coronary artery disease and history of myocardial infarction, stroke or smoking all contribute to microvascular ischemia.⁶ In older adults with an acquired ocular motor mononeuropathy, the presence of one or more of these risk factors is significantly associated with a presumed microvascular etiology.^{6,8} However, these same risk factors are often found in patients with other causes of diplopia, as seen in the patient discussed in this case, which can complicate diagnosis and management.^{6,8} Up to 17% of cranial nerve palsies are caused by other identifiable etiologies.⁶ Since other causes may be life-threatening, early detection and intervention are critical to improve outcomes.

When diplopia is the only neurologic symptom in a patient with a sixth nerve palsy and vascular risk factors, the chance of a non-microvascular etiology is low and the patient is often monitored for resolution.^{6,7} However, any additional neurologic symptoms should warrant further investigation and possible early neuroimaging.⁶ Clinicians must remember to probe further into patient history to ensure that critical symptoms which could indicate a less common cause are not missed. In a cohort of 109 patients with acquired ocular motor mononeuropathies, Tamhankar et al. found that 60% reported a headache or eye pain in association with diplopia, but the presence or absence of pain did not predict the etiology of the palsy.⁶ Therefore, additional questions about neurologic symptoms like paresthesia, dysarthria, ataxia, vertigo, or hemiparesis, and GCA symptoms can help to detect other causes.⁷

Diplopia as the presenting symptom of GCA is uncommon, and occurs in only 5-15% of patients.^{5,9} The exact pathophysiology is unknown, but it is theorized that intermittent ischemia to the cranial nerves, brainstem, or extraocular muscles can cause motility dysfunction.^{5,9} This can present as an isolated or multiple cranial nerve palsies, or internuclear ophthalmoplegia.⁹ Diplopia can be difficult to assess because the presentation can be transient due to the intermittent nature of an occlusive vasculitis.⁹ Diplopia can also be difficult to assess if monocular vision loss has occurred. Monocular vision loss is a more common ocular symptom in GCA; therefore, there may be no diplopia at the time of presentation.^{9,10}

Limited information is available about how often vision loss occurs in GCA patients with a concurrent cranial nerve palsy. Ross et al. retrospectively studied the clinical presentations of GCA patients who presented with diplopia. Of 27 total patients, seven had ischemic optic neuropathies.⁵

GCA causes a variety of symptoms including scalp tenderness, jaw claudication, neck pain, temporal or occipital headache, asthenia, malaise, myalgia, stiffness in the shoulders or limb girdles, limb claudication, weight loss, and fever.² Jaw claudication and neck pain are strong predictors, increasing the odds of biopsy-positive GCA by 9- and 3.4-fold, respectively.¹¹

Ocular symptoms include blurred or loss of vision, amaurosis fugax, diplopia, and ocular pain.⁴ Amaurosis fugax occurs in 10-30% of GCA patients; therefore, all patients above age 50 presenting with amaurosis fugax should have both ESR and CRP testing in addition to the recommended stroke evaluation.^{1,9,12}

Patients with diplopia should undergo a dilated fundus examination at initial presentation to evaluate for other signs of ocular ischemia or optic nerve involvement in addition to careful extraocular motility evaluation and cover test in multiple gazes. The classic sign of GCA with ocular involvement is an arteritic anterior ischemic optic neuropathy, which occurs in about 80% of patients.^{1,9} Other ocular signs associated with GCA include a central retinal artery occlusion, cilioretinal artery occlusion, posterior ischemic optic neuropathy, choroidal ischemic lesions, ocular ischemic syndrome, and cotton wool spots.^{1,4,9} A patient with one of these presentations and concurrent GCA symptoms should prompt further investigation.

If GCA is suspected, emergent diagnostic testing should include the inflammatory markers ESR and CRP, along with a CBC that includes a platelet count.^{2,4,13} Clinical criteria most strongly associated with GCA are a CRP value greater than 2.45 milligrams per deciliter and ESR greater than or equal to 47 millimeters per hour; CRP is more sensitive than ESR.^{11,13} Older studies have shown that, when combined, ESR and CRP provide a 99.2% sensitivity and 97% specificity for detecting GCA.¹¹ However, more recent literature has shown a lower sensitivity of 86.9% and specificity of 84.1%.¹³ Also, ESR and CRP values can be normal in a subset of GCA patients.^{1,13}

A CBC in GCA patients may reveal thrombocytosis, anemia, elevated white blood cell count, low hemoglobin, or hematocrit due to the underlying systemic vasculitis.⁴ An elevated platelet count has been shown to be a strong predictor for a positive temporal artery biopsy, but normal values do not rule out GCA, as seen in this patient.¹⁴

While helpful for diagnosis, these laboratory findings are not specific to GCA; temporal artery biopsy (TAB) is still considered the diagnostic gold standard.²⁻⁴ Other noninvasive diagnostic techniques including color Doppler ultrasound, magnetic resonance imaging with angiography, and computed tomography angiogram have also been inves-

tigated for use in GCA diagnosis.^{2,3} Unlike TAB, which remains positive for two to six weeks following corticosteroid initiation, these other imaging modalities are not as sensitive once treatment has started.² Therefore, TAB remains the standard of care. However, the role of imaging in GCA diagnosis is likely to increase with newer technologies.³

Systemic corticosteroids are the first-line treatment for GCA.²⁻⁴ Typically, patients without vision loss are started on oral prednisone and those with vision loss are started on intravenous methylprednisolone followed by oral prednisone.² Steroids are then slowly tapered with blood inflammatory marker values used as guidelines, but there is no evidence-based regimen for tapering.²⁻⁴ Due to the high rate of adverse side effects associated with corticosteroids, other treatments aimed at reducing cumulative corticosteroid use have been researched, including immunosuppressive and biological agents.³ Tocilizumab, an interleukin-6 receptor alpha inhibitor, is a newer treatment that has been shown to provide glucocorticoid-free remission in GCA patients.^{3,15} However, recent literature revealed that about half of GCA patients have a relapse within months of discontinuing tocilizumab.¹⁶ Other steroid-sparing treatments are being studied. These include azathioprine, ustekinumab, cyclophosphamide, dapsone, and leflunomide.²

Diplopia as the presenting symptom of GCA is rare.⁵ Patients with diplopia associated with GCA will most likely have other signs or symptoms, and diplopia alone is not a statistically significant predictor of biopsy-proven GCA.^{5,10} Patients with diplopia are more likely to have biopsy-proven GCA if they are older or have jaw claudication, vision loss, and elevated ESR, CRP, and platelet levels.¹⁰

GCA should be ruled out in older adults with diplopia by performing symptom screening and dilated eye examination. A clinician should have a high level of suspicion for GCA if diplopia is accompanied by systemic symptoms like jaw claudication, neck pain or signs of ocular ischemia. ●

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