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Case Report

Biopsy-Negative Giant Cell Arteritis Presenting as Stroke Mimic with Vision Loss and Complex Vascular Disease

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Abstract: A man in his 60s with multiple vascular comorbidities presented with sudden, painless vision loss in one eye. Although he had a high risk for atherosclerotic events, initial evaluation for stroke was negative for acute ischemia, but found to have markedly elevated inflammatory markers. Accordingly, giant cell arteritis was investigated and Ophthalmologic findings and fulfillment of the 2022 American College of Rheumatology/European Alliance of Associations for Rheumatology classification criteria supported the diagnosis of giant cell arteritis, despite a negative temporal artery biopsy. Management included high-dose glucocorticoids and delayed tocilizumab initiation due to the need for multiple vascular surgeries. Vision loss was irreversible, but systemic symptoms resolved and vascular interventions were successful. This case highlights the diagnostic and management complexities of biopsy-negative giant cell arteritis in patients with severe atherosclerotic vascular disease, emphasizing the importance of clinical judgment and established classification criteria when imaging and biopsy results are inconclusive.

Keywords: Giant Cell Arteritis; Temporal Arteritis; Vision Loss; Atherosclerosis; Biopsy-Negative; Stroke Mimic; Tocilizumab; Glucocorticoids

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1. Introduction

Giant cell arteritis (GCA) is the most prevalent systemic vasculitis in patients over 50 years of age. Its peak incidence occurs in the seventh and eighth decades of life [1]. GCA affects medium and large arteries, particularly the branches of the carotid artery. It can result in serious ischaemic complications, including irreversible vision loss [2-8]. The main diagnostic criteria are laboratory evidence of inflammation, clinical features, and temporal artery biopsy. However, biopsies may be negative in up to 44% of cases, often due to segmental vascular involvement [skip lesions] [9-12]. Recent guidelines, including the 2022 ACR/EULAR criteria [13], include imaging modalities such as color Doppler ultrasound (CDUS), PET-CT, or CTA/MRA, allowing for diagnosis without biopsy confirmation [14-17]. Management is more complex in patients with atherosclerotic comorbidities and necessitates precise coordination of immunosuppression and surgical intervention. This case report presents a complex diagnostic challenge of biopsy-negative GCA in a patient with extensive vascular disease, demonstrating the importance of clinical judgment when traditional diagnostic methods yield inconclusive results.

2. Case Presentation

A man in his 60s presented to the emergency department with acute, persistent vision loss in his right eye. His past medical history included hypertension, hyperlipidemia, type 2 diabetes mellitus, coronary artery disease (status post bypass), ischemic cardiomyopathy with cardiac pacemaker, severe bilateral carotid artery disease, peripheral arterial disease, prior renal artery stenting, and long-standing tobacco. He

reported several prior episodes of transient blurry vision in the same eye over the previous month, each resolving spontaneously.

On examination, his blood pressure was 133/69 mmHg. There was no scalp tenderness, and bilateral carotid bruits were present. Vision in the right eye was limited to the perception of hand movements and colors. A right relative afferent pupillary defect was found. There were no other focal neurological deficits. A stroke code was activated.

2.1. Investigations

Laboratory tests revealed significantly elevated inflammatory markers, with an erythrocyte sedimentation rate of 88 mm/hr and a C-reactive protein of 228 mg/L. Additional laboratory findings are summarized in Table 1.

Table 1. Key Laboratory Findings on Admission

Laboratory Test	Patient's Result	Reference Range	Units
Erythrocyte Sedimentation Rate (ESR)	88	<20*	mm/hr
C-reactive Protein (CRP)	228	<5	mg/L
White Blood Cell Count (WBC)	10.2	4.0-11.0	$\times 10^9$/L
Hemoglobin	11.1	13.5-17.5	g/dL
Platelet Count	366	150-450	$\times 10^9$/L
Creatinine	1.32	0.7-1.3	mg/dL
Sodium	130	135-145	mEq/L
Potassium	5.2	3.5-5.0	mEq/L

** Approximate reference range for males >50 years; varies by laboratory and method.*

Non-contrast computed tomography of the head revealed no acute hemorrhage or infarction. Computed tomography angiography of the head and neck demonstrated severe bilateral proximal internal carotid artery stenosis (approximately 70%) but no acute large vessel occlusion. A prior carotid ultrasound (seven weeks earlier) had shown similar findings.

Ophthalmologic examination confirmed arteritic ischemic optic neuropathy in the right eye. Findings included trace optic disc edema, a cup-to-disc ratio of 0.3, and a few retinal hemorrhages (Figure 1). A temporal artery biopsy performed five days after presentation was negative for vasculitis; this result was noted in the context of potential segmental involvement ("skip lesions") [11, 12].

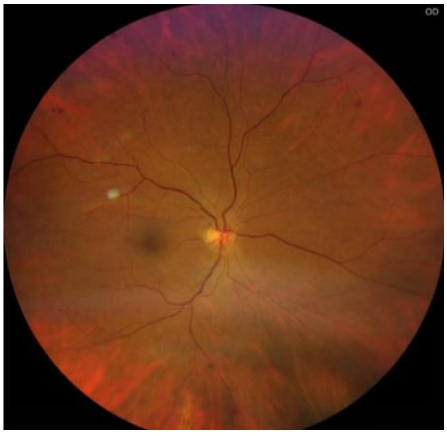

Figure 1. Funduscopic image of the patient's right eye at presentation demonstrating trace optic disc edema and scattered retinal hemorrhages consistent with arteritic ischemic optic neuropathy.

2.2. Differential Diagnosis

Based on the presentation of acute vision loss and a significant history of vascular disease, acute ischemic events were highly suspected. However, the focus shifted to vasculitis due to negative imaging for an acute occlusion, the absence of other neurological deficits, and elevated inflammatory markers.

A diagnosis of giant cell arteritis (GCA) was strongly supported by findings of arteritic ischemic optic neuropathy, jaw pain, and morning stiffness. The temporal artery biopsy was negative, but this result was interpreted in the context of high clinical suspicion and the known risk of segmental involvement ("skip lesions"). The diagnosis was established based on the clinical picture and fulfillment of the 2022 ACR/EULAR criteria [13] (Table 2). Although the patient's severe atherosclerotic disease complicated differentiation from large-vessel vasculitis, the acute ophthalmologic and systemic features were most consistent with GCA.

Table 2. 2022 ACR/EULAR Classification Criteria for Giant Cell Arteritis

Criterion	Max Points	Patient Status & Score
Absolute Requirement: Age ≥ 50 years	N/A	Met
Additional Clinical Criteria		
Morning stiffness in shoulders/neck	+2	Met [+2]
Sudden visual loss	+3	Met [+3]
Jaw or tongue claudication	+2	Met [+2]
New temporal headache	+2	Not Reported [0]
Scalp tenderness	+2	Not Reported [0]
Abnormal examination of the temporal artery[1]	+2	Not Reported [0]
Laboratory, Imaging, and Biopsy Criteria		
Maximum ESR ≥ 50 mm/hour or maximum CRP ≥ 10 mg/liter[2]	+3	Met [+3] (ESR 88, CRP 228)
Positive temporal artery biopsy OR halo sign on ultrasound[3]	+5	Not Met (Biopsy Neg, US N/R) [0]
Bilateral axillary involvement[4]	+2	Not Reported [0]
FDG-PET activity throughout aorta[5]	+2	Not Reported [0]
Total Score		10
Classification Threshold		≥ 6

Abbreviations: ACR, American College of Rheumatology; CRP, C-reactive protein; ESR, erythrocyte sedimentation rate; EULAR, European Alliance of Associations for Rheumatology; FDG-PET, Fluorodeoxyglucose positron emission tomography; GCA, Giant Cell Arteritis; N/A, Not Applicable; N/R, Not Reported; US, Ultrasound.

Definitions:
[1] Abnormal exam = Temporal artery showing absent/diminished pulse, tenderness, or hardness/cord-like appearance.
[2] ESR/CRP values prior to initiation of vasculitis treatment.
[3] Positive if *either* definitive vasculitis on temporal artery biopsy *or* halo sign (homogeneous, hypoechoic wall thickening) on temporal artery ultrasound is present.
[4] Bilateral axillary involvement defined via imaging (angiography, CT, MR, catheter-based, US halo sign, or PET uptake).
[5] Abnormal FDG uptake (greater than liver) throughout descending thoracic and abdominal aorta on PET.

2.3. Treatment

High-dose intravenous methylprednisolone (250 mg every 6 hours for three days) was initiated for arteritic ischemic optic neuropathy, followed by an oral prednisone taper starting at 80 mg daily. Despite a negative temporal artery biopsy, corticosteroids were continued based on strong clinical evidence for giant cell arteritis.

For secondary prevention related to extensive vascular comorbidities and cerebrovascular risk, the patient received dual antiplatelet therapy (aspirin and clopidogrel) and high-dose atorvastatin. Tocilizumab (162 mg subcutaneously weekly) was approved as adjunctive, steroid-sparing therapy but was postponed until after planned vascular surgeries.

Non-pharmacological interventions included transcarotid artery revascularization for severe right internal carotid stenosis, followed by bilateral lower extremity arteriography, left iliac angioplasty with stenting, and right femoral-popliteal bypass for progressive peripheral arterial disease.

2.4. Outcome and Follow-up

The patient was discharged eight days later on dual antiplatelet therapy, high-dose atorvastatin, and a prednisone taper, with follow-up arranged. He underwent a previously scheduled transcarotid artery revascularization for severe right internal carotid stenosis seven days after presentation. The procedure did not improve vision. At a rheumatology follow-up 3.5 weeks post-presentation, his left eye vision was stable and systemic symptoms had resolved.

The patient later developed worsening bilateral lower extremity claudication and an ischemic ulcer on the right heel. Imaging revealed an occluded distal right superficial femoral artery stent, multiple critical stenoses in the left superficial femoral artery, and moderate bilateral iliac artery stenoses. He underwent bilateral lower extremity arteriography, left iliac angioplasty with stenting, and a right femoral-popliteal bypass.

On follow-up three months later, the patient's right eye vision was still severely impaired, but left eye vision was stable. There was a complete resolution of systemic symptoms, including jaw pain, night sweats, and morning stiffness. Following lower extremity revascularization procedures, claudication symptoms improved, and glycemic control allowed discontinuation of insulin.

The prednisone taper continued as scheduled, and tocilizumab was initiated after the patient recovered from vascular surgery. Ongoing post-discharge management consisted of regular rheumatology and vascular surgery follow-up. Surveillance concentrated on monitoring for clinical relapse of giant cell arteritis, in particular as the prednisone dose was tapered to lower levels where relapse likelihood increases [18]. Routine monitoring consisted of assessing clinical symptoms and inflammatory markers. However, as tocilizumab can suppress these markers regardless of disease activity, placing greater emphasis on clinical evaluation was necessary, with vascular imaging considered if progression of large-vessel involvement was clinically suspected [19, 20]. At the most recent follow-up, approximately seven months after presentation the patient was alive and stable.

3. Discussion

This case highlights the diagnostic and management complexities of biopsy-negative giant cell arteritis (GCA) in a patient with severe atherosclerotic vascular disease. The diagnosis was established based on clinical features, markedly elevated inflammatory markers, and fulfillment of the 2022 ACR/EULAR criteria [13] (Table 2), despite a negative temporal artery biopsy—a limitation attributable to segmental vascular involvement ("skip lesions") [9-12].

A central challenge in this case was the inability to obtain definitive imaging evidence of vasculitis after biopsy. Immediate initiation of high-dose glucocorticoids was required to prevent further irreversible vision loss [21-24], but this rapid steroid administration is known to significantly reduce the sensitivity of vascular ultrasound for detecting the "halo sign"—a key feature supporting GCA diagnosis. Literature shows that ultrasound sensitivity drops from as high as 89% pre-treatment to as low as 29% after even short steroid exposure, with notable declines seen after just 2–10 days of therapy [25-29]. In our patient, by the time GCA was suspected and treatment initiated, the window for a sensitive temporal artery ultrasound had already closed.

Advanced imaging options were also limited. MRI was contraindicated due to a non-MRI-compatible cardiac pacemaker. PET/CT, while valuable for assessing large-vessel involvement in GCA, was not pursued because the clinical picture and laboratory findings were already highly suggestive of GCA, and the urgency of treatment outweighed the potential incremental value of imaging confirmation. Furthermore, the accuracy of PET-CT is best preserved if performed before substantial steroid exposure [30], which was not possible in this case. The presence of severe atherosclerosis posed a significant interpretive challenge for any vascular imaging, including PET/CT. Both GCA and atherosclerosis can result in increased FDG uptake, with grade 2 uptake being common in both, while grade 3 uptake is more specific to GCA aortitis [31]. In elderly patients with significant atherosclerosis, PET/CT may have limited specificity for distinguishing vasculitis from atheromatous changes [32]. Similarly, atherosclerosis can produce false-positive halos and increased wall thickness on ultrasound, further complicating differentiation from vasculitic changes [18, 28, 33, 34].

Thus, the limitations in this case—absence of confirmatory vascular imaging and negative biopsy—were due to urgent clinical need, patient-specific contraindications, and the confounding impact of advanced atherosclerosis. These constraints required reliance on clinical judgment, laboratory data, and established classification criteria to guide diagnosis and management. Research has shown that clinical diagnosis based on the ACR criteria—including age, new headache, temporal artery abnormality, and elevated ESR—remains highly predictive, even when imaging findings are uncertain or confounded by atherosclerosis [35]. Other reports highlight that when imaging suggests both possibilities (vasculitis and atherosclerosis), clinical presentation and systemic inflammatory markers are decisive in guiding the final diagnosis [36].

Multidisciplinary planning was essential for this patient, particularly regarding the timing of immunosuppressive therapy and vascular interventions to balance disease control and perioperative risk. Management followed established guidelines recommending prompt high-dose glucocorticoid therapy for vision-threatening GCA [21-23]. While visual loss is often irreversible, early high-dose steroids aim to mitigate the risk of progression or contralateral involvement [24]. Tocilizumab was used as a steroid-sparing agent after critical vascular procedures, in line with evidence from the GiACTA trial [37, 38]. Ongoing monitoring relied on clinical assessment, as laboratory markers may be suppressed by biologic therapy [19, 20].

5. Conclusions

Diagnosis of biopsy-negative giant cell arteritis requires integrating clinical features, elevated inflammatory markers, and established classification criteria (such as the 2022 ACR/EULAR criteria), even in the absence of positive biopsy findings.

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