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CASE REPORT

Antineutrophil Cytoplasmic Antibody–Associated Vasculitis Masquerading as Giant Cell Arteritis

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Abstract
The triad of temporal artery tenderness, monocular vision loss, and raised inflammatory markers is suggestive of giant cell arteritis (GCA). We encountered a 76-year-old woman who presented with acute right eye vision loss, temporal tenderness, jaw claudication, and markedly raised inflammatory markers, all suggestive of GCA. After a negative right temporal artery biopsy, serologic work-up revealed elevated proteinase 3 and myeloperoxidase titers. Pathology from a renal biopsy pursued for work-up of acute kidney injury demonstrated pauci-immune glomerulonephritis, leading to a diagnosis of granulomatosis with polyangiitis (GPA). This case underscores the importance of acknowledging and avoiding anchoring bias early in the diagnostic process.

Background
Giant cell arteritis (GCA) is one of the most common idiopathic systemic vasculitides in the United States, occurring most commonly in patients aged 70 to 79 with a lifetime risk of 1% in women and 0.5% in men (1). This disease has several potentially devastating complications, including vision loss and aortitis if not appropriately treated. While most systemic vasculitides present heterogeneously, GCA tends to have a pathognomonic presentation. The American College of Rheumatology-European Alliance of Associations for Rheumatology (ACR-EULAR) major criteria for the diagnosis of GCA include age 50 years or older, a positive temporal artery biopsy or temporal artery halo sign on ultrasonography, an erythrocyte sedimentation rate (ESR) of 50 mm/hour or greater or C-reactive protein (CRP) level greater than or equal to 10 mg/L, and sudden visual loss (2). Recent case reports have shown an increasing amount of overlap between GCA and other vasculitides, most commonly antineutrophilic cytoplasmic antibody (ANCA)-associated vasculitis (AAV) (3). Given GCA and AAV have varying organ involvement and different treatment courses, it is important to distinguish between the 2 in a clinical setting. In this case, we present a patient with bilateral temporal tenderness and vision loss who was initially presumed to have GCA but was ultimately diagnosed with AAV.

Objective
We present this case of atypical AAV presentation leading to an initial diagnosis of GCA to highlight the importance of completing a thorough review of the past medical history and clinical presentation in order to pursue appropriate additional work-up when considering alternative diagnoses.

Case Report
A 76-year-old woman with a history of type 2 diabetes mellitus, hypertension, hyperlipidemia, and recent hearing loss presented to the emergency department with acute right eye vision loss. The patient also reported scalp tenderness (with brushing her hair), bilateral temporal tenderness, jaw pain (worse with chewing food), fatigue, and poor appetite. She did not report

Table 1. Pertinent Laboratory Values on Admission

Tests	Values	Reference Range
Leukocyte count ($10^9/L$)	32.8	4.0–10.5
Hemoglobin level (*g/dL*)	11.1	11.5–15.0
Hematocrit (*%*)	34.5	34.0–44.0
Platelets ($10^9/L$)	678	150–400
Sodium (*mmol/L*)	128	136–145
Potassium (*mmol/L*)	3.3	3.5–5.1
Chloride (*mmol/L*)	93	98–107
CO_2 (*mmol/L*)	22	21–31
Glucose (*mg/dL*)	184	85–125
BUN (*mg/dL*)	52	7–25
Creatinine (*mg/dL*)	4.6	0.6–1.2
CRP level (*mg/dL*)	17.9	0.0–1.0
ESR (*mm/h*)	129	0–30

BUN = Blood urea nitrogen; CO_2 = Carbon dioxide; CRP = C–reactive protein; ESR = Erythrocyte sedimentation rate.

any eye pain, prior diagnosis of uveitis, morning stiffness affecting her joints, shoulder or hip pain, fevers, epistaxis, hemoptysis, hematuria, dyspnea, neurologic deficits, or prior history of kidney disease.

On presentation, examination revealed tenderness of the bilateral temporal regions, bilateral jaw, and center of the forehead. Neurologic examination showed intact extraocular movements bilaterally. However, her vision was limited to light perception in the right eye. No other gross neurologic deficits were noted. The remainder of the examination was unremarkable.

Pertinent laboratory results displayed in Table 1 were consistent with leukocytosis, microcytic anemia, acute kidney injury (AKI) and elevated ESR and CRP levels. Magnetic resonance imaging (MRI) of the brain was suspicious for optic perineuritis bilaterally. An orbital MRI was notable for an abnormal T2 signal within the distal right infraorbital optic nerve with evidence of fat stranding suggestive of right-sided optic neuropathy. The brain MRI also revealed extensive bilateral middle ear effusions.

The patient was evaluated by ophthalmology. Examination revealed a pale optic nerve, flat macula with retinal whitening and cotton wool spots, and attenuated vessels in the right eye. The findings were consistent with central retinal artery occlusion (CRAO). The examination of the left eye was unremarkable. Based on her history, examination findings, and MRI results, GCA was highest on the differential diagnosis. Ophthalmology advised immediate initiation of pulse dose steroid therapy for the treatment of vision loss (presumed to be secondary to GCA) and recommended doing an urgent temporal artery biopsy (TAB). After our rheumatology team evaluated the patient and confirmed that the patient had no prior history of chronic kidney disease (CKD), we recommended further rheumatological and renal work up to better explain patient's AKI and recent hearing loss. Rheumatologic laboratory results are summarized in Table 2. Serum and urine protein electrophoresis did not reveal any evidence of monoclonal gammopathy.

Table 2. Rheumatologic Laboratory Results

Tests	Values	Reference Range
ANA	Negative	NOT DETECTED (<1:40)
ANCA titer	320	–
Myeloperoxidase Ab, IgG (*U/mL*)	55	0–19
Serine Protease, IgG (*U/mL*)	189	0–19
C3 protein (*mg/dL*)	98	65–175
C4 protein (*mg/dL*)	29	13–39
SS-A (Ro)(ENA) Ab, IgG (*units*)	2	0–19
SSB (La)(ENA) Ab, IgG (*units*)	5	0–19

Ab = antibody; ANA = antinuclear antibody; ANCA = antineutrophilic cytoplasmic antibody; ENA = extractable nuclear antigens; IgG = immunoglobulin G; SS-A = Sjögren syndrome-A antibody; SS-B = Sjögren syndrome-B antibody.

The right TAB revealed moderate intimal hyperplasia with small foci of calcification but no evidence of an inflammatory infiltrate or multinucleated giant cells. The patient continued to exhibit worsening renal function. Further investigation with a kidney biopsy was pursued, which demonstrated focal necrotizing, crescentic glomerulonephritis compatible with an ANCA-associated process. Immunofluorescence showed no staining of immune-complex deposits. Taken together, a definitive diagnosis of ANCA-associated vasculitis (likely granulomatosis with polyangiitis [GPA]) was made. The patient continued to receive prednisone, 1 mg/kg of body weight per day after completing pulse dose steroid therapy and rituximab therapy for induction treatment of AAV was started.

Discussion

Our 76-year-old patient presented with sudden vision loss, scalp tenderness, temporal artery tenderness, and elevated inflammatory markers. She fulfilled 5 out of 10 of the ACR-EULAR GCA classification criteria and had a total score of 12, making this a likely possibility. A 2020 meta-analysis studying the diagnostic accuracy of physical symptoms and laboratory tests for GCA reported a likelihood ratio (LR) for similar symptoms as varying between 1.40 for raised ESR (95% CI, 1.22–1.60) to 3.25 for scalp tenderness (CI, 2.49–6.64) (4). The patient did not exhibit limb claudication, which is a highly specific symptom for GCA (6.01) (4). Given the potential devastating complication of permanent vision loss in the setting of CRAO, the decision was made to pursue preemptive treatment with pulse steroids while awaiting a biopsy-confirmed diagnosis. Apart from visual symptoms, the patient also presented with hearing loss and AKI, which are unusual for GCA.

While CRAO may be seen in several rheumatic diseases, it has also been reported in patients with cryoglobulinemia, GPA, and other vasculitides (5, 6). In cases of GPA, the pathophysiology of retinal vasculitis is thought to be secondary to ANCA autoantibodies causing the neutrophils to bind to endothelium and release mediators that injure the vessel wall (7). In addition to the retinal circulation, GPA-induced vasculitis has also been known to involve the choroidal circulation and affect the posterior ciliary arteries (8).

During our literature review, we found several reported cases citing CRAO as the presenting symptom in patients with small vessel vasculitis, including eosinophilic GPA (9) and GPA (10). In the GPA case report, the patient was younger and presented with pulmonary involvement (cough), highlighting the variable presentation seen in vasculitides. A previous case report also found an association between optic perineuritis and GPA (11). AAV can also cause vision loss due to inflammation of the parenchyma or orbital involvement (12). The majority of these case reports involved patients with eosinophilic GPA.

Contrary to large vessel vasculitis, AAV, specifically GPA, often manifests with nasal, otologic, oropharyngeal, pulmonary, and renal involvement as a consequence of endothelial damage to the vasculature and granuloma formation (13). The pathognomonic finding on renal biopsy is pauci-immune crescentic necrotizing glomerulonephritis. Otologic involvement may lead to sensorineural hearing loss. Although not well defined, some have hypothesized it is due to granulomatous lesions pressing on the nerve or the deposition of immune complexes in the immune complexes in the cochlea (13).

In our patient, blindness secondary to GCA was an emergent concern. However, the constellation of central nervous system along with renal and otologic involvement, in the setting of serologic positivity, suggested another systemic process, and a renal biopsy confirmed GPA. This case highlights the importance of keeping GPA on the differential of CRAO, even though it's more rare. Confirming GPA guided the team to administer biologics, such as rituximab. These therapy options were overlooked during the initial encounter. This further emphasizes the pitfall of anchoring bias, which may prevent us from formulating a thorough differential diagnosis and providing the appropriate therapy.

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