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CLINICAL VIGNETTE

Giant Cell Arteritis

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Case Report

A 76-year-old woman was “feeling sick” and presented for an urgent care visit. She reported bilateral hip pains, right greater than left, which started 2 weeks ago. She had no recent falls and denied leg and upper extremity pain/tenderness. Past medical history includes bronchiectasis, osteoporosis, and history of breast cancer.

She reported intermittent low-grade fevers but denied chills, cough, or shortness of breath. She had no urinary tract infection symptoms and denied a rash or skin lesions. Appetite was normal with no weight loss. She did report significant fatigue and felt tired all day long. Home COVID test was negative.

Her vital signs were normal with no change in weight. Her hips were non-tender to palpation with normal strength and range of motion. Her gait and balance were normal and the rest of her exam was unremarkable.

Bilateral hip x-rays were normal. Other labs included a normal ESR (14 mm/hr), elevated CRP (5.9 mg/dl), leukocytosis ($10.96 \times 10^3/\mu\text{L}$) and thrombocytosis ($509 \times 10^3/\mu\text{L}$). Metabolic panel was unremarkable. She was referred to rheumatology.

She was seen by rheumatology the next day and reported new symptoms including shoulder pain, night sweats, and right jaw pain. Her history and current symptoms supported diagnosis for Giant Cell Arteritis (GCA). She started prednisone 40 mg daily and urgently scheduled for an temporal artery biopsy with vascular surgery. The patient’s temporal artery biopsy confirmed GCA showing “active arteritis with fibrinoid necrosis and luminal thrombus”. Her prednisone was increased to 50 mg daily (1 mg/kg of body weight), along with *Pneumocystis jirovecii* prophylaxis, calcium and Vitamin D, and provided information on tocilizumab.

Discussion

Giant cell arteritis (GCA) is the most common large vessel, systemic vasculitis in older adults. This inflammatory vasculopathy involves medium and large sized arteries such as the aorta and its major branches. The first documented cases of granulomatous inflammation involved the temporal arteries and were published in 1932 by Horton and colleagues of the Mayo Clinic.^{1,2} “Temporal arteritis” remained the name for this type of vasculitis for many years until it became clear that the vessels

involved and clinical complications are much broader.¹ GCA is the current diagnosis for this systemic process and refers to the multinucleated giant cells found in inflammatory vascular infiltrates.^{1,2}

The vessel wall inflammation leads to luminal occlusion and tissue ischemia. The inflammation is characterized by macrophages, which may fuse to create the “giant cells” and CD4+ T lymphocytes.³ The cranial arteries and the aorta along with its primary and secondary branches are particularly susceptible. Reduced blood flow and ischemia are the source of pain in the affected areas with temporal artery involvement often leading to headache.³

GCA is the most common form of systemic vasculitis, with an incidence of 15-25 cases per 100,000 persons over 50 years old.^{1,4} GCA is more common in Caucasians with northern European ancestry.^{1,3-6} Women are more susceptible than men, and the lifetime risk of developing GCA is approximately 1% for women and 0.5% for men.^{1,2,4} Age is a strong risk factor. GCA is most common in patients over 50 years old and risk increases with advancing age, with a peak incidence in ages 70-80 years old.⁶ With aging of the population, there will be increased future cases of GCA.

Patients with GCA present with a variety of clinical symptoms and signs. The onset is typically subtle developing over weeks to months, though about 20% of patients report sudden onset of symptoms due to vascular and systemic inflammation.² Inflammation of extra-cranial branches of external carotid arteries may result in headaches, scalp tenderness, jaw claudication, tongue pain, visual disturbances, and neurologic symptoms due to cerebrovascular ischemia.^{1,3} The most common symptom of GCA is headache (76%).³ The headache is classically constant, sudden in onset and located in the temporal area.² However, patients may present with constitutional symptoms making the diagnosis more difficult. These include low-grade fever, night sweats, unintentional weight loss, fatigue and malaise.^{1,3} Approximately 15-25% of patients with GCA experience ophthalmologic complications including blurring, diplopia, or vision loss.^{1,2} Additional serious complications may occur with delayed diagnosis including transient ischemic attacks, strokes or aortic aneurysms.³

After the history and physical exam, laboratory should include erythrocyte sedimentation rate (ESR), c-reactive protein (CRP),

comprehensive metabolic panel (CMP) and complete blood count (CBC). Results commonly include an elevated ESR, an elevated CRP, elevation of liver transaminases with reduced albumin, normocytic, normochromic anemia, and thrombocytosis.² There are no highly specific biomarkers for GCA.⁶ Acute phase markers of inflammation – ESR and CRP -- are often significantly elevated.² However, only one acute phase marker may be elevated. In the past, ESR was the main marker to assess for GCA, but about 25% of patients have normal ESR with elevated CRP.²

Temporal artery biopsy is the gold standard for the diagnosis of GCA. Patients should undergo a temporal artery biopsy with assessment of a 1.5 to 2.0 cm in length vascular segment.⁶ The biopsy identifies 85 to 95% of cases but a negative biopsy does not rule out GCA.⁶ Given the potential complications associated with GCA, especially vision impairment and stroke, treatment should start while waiting for the biopsy results and continue with negative biopsy if patients symptoms strongly support the diagnosis.³ Additional studies are now available for diagnosis and subsequent monitoring.¹ Color duplex ultrasonography (CDS) can be used for artery assessment in patients with cranial symptoms. In patients with GCA, the CDS typically shows vascular occlusion, increased intima-media thickness, and the presence of a hypoechoic area around the vessel lumen (halo sign).^{1,3} The halo sign has a pooled sensitivity of 68% and a specificity of 90% for the diagnosis of GCA. However, there are limitations, it requires a well-trained technician, and the inflammation can decrease quickly after starting prednisone.¹ Other tools that used for large-vessel imaging in the diagnosis and subsequent monitoring include computed tomography angiography, magnetic resonance angiography, and fluorodeoxyglucose-positron emission tomography.¹

The American College of Rheumatology's published criteria for the classification of giant cell arteritis in 1990. At least three of the following five criteria must be met to be support a GCA diagnosis: age at onset >50, new onset headache, high erythrocyte sedimentation rate (> 50 mm/hour by the Westergren method), abnormal temporal artery on palpation, and changes consistent with GCA on biopsy.⁷ When patients have at least three of the criteria, the sensitivity is 93.5% and the specificity is 91.2% for GCA.⁷

The standard of treatment for GCA is glucocorticoids. Therapy starts with prednisone at a dose of 1 mg per kilogram of body weight per day. If patients present with visual complications at the time of their diagnosis, methylprednisolone 500 mg to 1 gram daily for 3 days is given before starting prednisone.³ In most patients, high-dose prednisone is followed by rapid improvement of systemic inflammatory signs likely due to the effective suppression of interleukin-6 and the acute phase response.⁶ After the reduction of symptoms and decrease of acute phase reactants (CRP and/or ESR), prednisone can be tapered with a goal of < 10 mg/day.⁶ Patients usually start treatment at 60 mg of prednisone for 3-4 weeks until symptoms resolve, then a slow taper to 10 mg daily and reduce 1 mg every

1-2 months until stopped.³ The goal is to treat for an average of 18 months.

While treatment at the start of diagnosis is effective, there are risks of relapse and complications. A GCA relapse is common, with about 43% of patients experience at least one relapse.³ Relapse symptoms may include ischemic complications, polymyalgia rheumatica, or recurrence of the GCA headache.³ GCA can impact vision and patients with visual symptoms such as blurring, diplopia, or visual loss should be immediately referred to ophthalmology for examination.³ Additional complications include aortic aneurysm, aortic dissection and stroke.³ Aspirin (75 to 150 mg per day) is often prescribed to reduce risk of ischemic complications and cardiovascular events in GCA patients.^{3,6} Also proton pump inhibitors are frequently recommended because of potential toxicity of high dose prednisone and aspirin.

High dose glucocorticoids also increase risk for additional medical conditions. Hypertension, hyperglycemia, and loss of bone mass are common prednisone side effects and require attention and treatment.⁶ Bisphosphonates should be considered to prevent bone loss and osteoporosis. Physical therapy should be considered to improve muscle strength and reduce risk of falls and fractures. Prednisone lowers immunity and patients are at a higher risk for infections such as *Pneumocystis jirovecii* pneumonia. Prophylactic antibiotics are recommended for patients receiving prednisone of 20 mg or more daily.⁶

Aside from prednisone, the treatment options for GCA have been limited. In the past, methotrexate was a potential adjunct to glucocorticoids in patients with large-vessel vasculitis, and remains an option for those at high risk for steroid complications.⁶ Current treatment choices include tocilizumab (a humanized monoclonal antibody against the interleukin-6 receptor) for relapsing or recurrent disease and steroid sparing.³

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