

## Giant cell arteritis presenting as facial swelling

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### ABSTRACT

Facial swelling is commonly ascribed to angioedema and a host of other causes. Temporal arteritis (TA), a disease most often diagnosed in patients over the age of 50 years, frequently presents with nonspecific and often ignored complaints (headache, symptoms of polymyalgia rheumatica, low-grade fever, fever of unknown origin, loss of appetite, depression, joint pains, weight loss, hair loss, and even respiratory symptoms). The diagnosis of TA is highly likely in the presence of new-onset headaches, polymyalgia rheumatica, and a tender, cord-like, or swollen temporal artery. Facial swelling must be appreciated as another presentation of TA, especially when accompanied by other nonspecific symptoms. High clinical suspicion, immediate treatment, and definitive diagnosis by temporal artery biopsy are necessary to prevent the most severe vascular complications of blindness and cerebrovascular accidents. Treatment with corticosteroids is most often successful. Because this treatment is fraught with all the risks of high-dose and prolonged steroid therapy, it should only be initiated in cases of significant clinical suspicion, followed by a timely temporal artery biopsy to confirm the diagnosis. Delay in therapy increases the risk of a vascular catastrophe. Delay in obtaining a temporal artery biopsy after therapy has been initiated decreases the diagnostic sensitivity of the test. Other modalities of immunosuppressive therapy remain either unsuccessful or unproven. Concomitant low-dose aspirin therapy appears to hold promise.

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**Key words:** Blindness, corticosteroid treatment, facial swelling, giant cell arteritis, jaw claudication, ophthalmoplegia, polymyalgia rheumatica, temporal arteritis, temporal artery biopsy

### CASE PRESENTATION

#### Chief Complaint

The patient is an 85-year-old white woman who presents with severe frontal headache, facial pain and swelling, and difficulty swallowing.

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#### History of Present Illness

The patient presented with 3 days of severe frontal headache, facial pain and swelling, and difficulty swallowing. She noted fever to 101.6°F, neck pain, myalgias, weakness, and swelling of her tongue. Swelling of her face, eyelids, and tongue steadily progressed. One day before admission, she experienced nausea and several episodes of vomiting. The patient denied any prior episodes of chronic or severe headaches or angioedema. Over the next 24 hours, there was marked improvement in the facial swelling but no improvement in facial pain, neck pain, or swallowing and worsening of tenderness over the temporal areas. The patient denied any prior episodes of chronic or severe headaches, angioedema, or drug or food hypersensitivity.

#### Physical Examination on Hospital Admission

Vital signs were temperature, 101.6°F; heart rate, 93/minute; respiratory rate, 18/minute; and a blood pressure of 150/80 mm Hg. Her face, eyelids and tongue were markedly swollen. The extraocular movements were intact, but the fundi could not be well visualized. Her head was tender in the temporal regions, but no cords were appreciated. Mild nuchal rigidity and ten-

derness and a thyroid goiter were noted. The remainder of the physical examination was normal.

### QUESTION 1

Which of the following are included in the differential diagnosis of a patient presenting with a painful face with or without swelling?

- A. Angioedema
- B. Submandibular calculi
- C. Infections of the submandibular gland
- D. Osteomyelitis
- E. Muscle contraction headaches
- F. Carotidynia
- G. Trigeminal neuralgia
- H. Giant cell (temporal) arteritis

### QUESTION 2

Which of the following are included in the differential diagnosis of giant cell (temporal) arteritis?

- A. Migraine headache
- B. Carotidynia
- C. Polymyalgia rheumatica (PMR)
- D. Rheumatoid arthritis
- E. Trigeminal neuralgia
- F. Temporomandibular joint disease
- G. Sinusitis
- H. Oral/dental pathology
- I. Autoimmune thyroid disease
- J. Occult malignancy
- K. Causes of sudden blindness

### Discussion of the Differential Diagnosis

Causes of facial swelling include angioedema (chronic idiopathic, acquired, or hereditary angioedema), malignancy, allergic angioedema secondary to food or drug allergy, submandibular calculi or infections, osteomyelitis, Gleich syndrome, malignancy, and sinusitis.<sup>1,2</sup> C1-esterase inhibitor autoantibodies have caused isolated tongue swelling.<sup>3</sup> Angina, temporomandibular joint disease, muscle contraction headaches, carotidynia, trigeminal neuralgia, PMR, and temporal arteritis (TA) (giant cell arteritis [GCA], or cranial arteritis) comprise causes of facial pain. The differential diagnosis for TA/GCA includes all of the aforementioned, multiple myeloma, myalgias from statin therapy, osteoarthritis, rheumatoid arthritis, occult malignancy, and causes of sudden blindness.<sup>1,4,5</sup>

TA/GCA is the most common form of idiopathic large- and medium-sized vessel vasculitis of branches of the aortic arch.<sup>6</sup> GCA has an incidence of 18 cases/100,000 in patients >50 years of age.<sup>5</sup> The disease affects all races but predominates in white people from Scandinavia, Great Britain, and the northern United States.<sup>7</sup> In northern Europe the ratio of women to men is 3:1, and in Spain this ratio is lower.<sup>8,9</sup>

TA/GCA's clinical picture includes new onset of headache (from temporal or occipital artery involvement), a tender and/or nodular temporal artery with decreased pulsation, elevated erythrocyte sedimentation rate (ESR), and a diagnostic temporal artery biopsy.<sup>1,5,6</sup> Rarely, physical examination has revealed cord-like pulseless and thickened facial and occipital arteries.<sup>10</sup> In an older study of 100 patients, the most common initial complaints were headache (60% of patients) and PMR (40–60% of patients).<sup>7,8,11–13</sup> Five to 40% of patients with PMR have occult TA.<sup>14</sup> Synovitis has been reported not infrequently, and arthralgia in the proximal joints is common.<sup>15,16</sup> Respiratory symptoms are infrequent but not rare (9% incidence) and may be the presenting complaint in 4% of patients.<sup>1</sup> Aortic regurgitation, myocardial infarction, and deafness are rare complications.<sup>17</sup>

It should be noted that a normal ESR is found in 5–24% of patients.<sup>1</sup> Biopsies are diagnostic in 80–95% of untreated patients.<sup>1</sup> Steroids reduce their diagnostic value to 78% after <2 weeks of therapy, 65% after 2–4 weeks of therapy, and 40% after 4 or more weeks of therapy.<sup>18</sup> However, most clinicians will start steroid therapy as soon as TA/GCA is suspected and quickly proceed with a temporal artery biopsy.<sup>16,19</sup> Unilateral biopsies have a 4–5% false-negative frequency.<sup>7,12,14</sup> Bilateral temporal artery biopsies are mandatory. In one study, 14% of patients were diagnosed on the innocent-appearing side.<sup>20</sup> Reactive bone marrows, leukocytosis, thrombocytosis, elevated liver enzymes, elevated C-reactive protein, and anemia of chronic disease are well documented in these patients.<sup>12,14,16,21</sup>

In typical cases, the superficial temporal artery will be readily visible, knotty, pulseless, tortuous, thickened, and tender. Hair loss and ischemic scalp ulceration have been reported. Similar findings have been reported in the contralateral upper extremity, neck, and chest arteries.<sup>1</sup> One-half of the patients have eye complaints. Diplopia is caused by vasculitis affecting cranial nerves III, IV, and VI. Thirteen to 50% of untreated patients develop sudden onset of permanent blindness from occlusion of the posterior ciliary artery. Blindness in both eyes is rare. This is often preceded by amaurosis fugax or ophthalmoplegia.<sup>1,5–7</sup>

Significant involvement of large arteries (27% of patients) includes aortic aneurysms or dissection (18%), stenosis of the superior branches of the aortic arch especially the subclavian and axillary arteries (10–15%), and, occasionally, stenosis of the lower aortic vessels (<1%). These patients have a 17-fold increased risk of thoracic aortic aneurysms and a 2.4-fold increased risk of abdominal aortic aneurysms. Symptoms related to these vessels include extremity and jaw claudication (34% of patients with TA) and diffuse mandibular, dental, and sinus pain or discomfort.<sup>5,6,14</sup>

Facial swelling has been infrequently reported as the initial presentation of TA/GCA.<sup>15,22,23</sup> Scalp necrosis, tongue necrosis, other cranial neuropathies, peripheral neuropathies, cerebrovascular accidents, transient ischemic attacks, and cotton-wool exudates secondary to retinal ischemia have been reported. TA/GCA is a well-appreciated cause of fever of unknown origin, anorexia, weight loss, wasting syndrome, depression, headache, and failure to thrive.<sup>5,14,17</sup>

A review of 260 consecutive patients with TA/GCA found 17 patients (6.5%) with head-and-neck swelling. These authors report that facial swelling was often the initial manifestation of disease and transient. Facial swelling was often painful, involved the orbital region and face, especially the lower part of the cheeks and maxillae. The neck was less frequently involved, and rarely the tongue, limb, or forehead. Ear, nose, throat symptoms were observed in 80% of cases (jaw claudication and frank trismus). Two patients had permanent visual impairment and one patient had sudden hearing loss. The swelling either spontaneously disappeared or regressed after steroid therapy. A small number of patients suffered recurrence of their facial swelling.<sup>24,25</sup> A variant of this presentation is hemifacial edema, trismus, and fever. These manifestations disappeared before more typical findings of TA/GCA led clinicians to the diagnosis.<sup>26</sup>

Facial swelling as a result of TA/GCA has preceded anterior ischemic optic neuropathy and is believed to be "an indicator" of anterior ischemic optic neuropathy.<sup>15</sup> The mere sensation of facial puffiness may be an initial manifestation of TA/GCA and a predictor of visual disturbances.<sup>27</sup> Another case of TA/GCA facial swelling was accompanied by glossitis and odynophagia (claudication-like symptoms of the tongue and muscles of deglutition).<sup>12</sup> Even more unusual is TA/GCA presenting as a submandibular mass as the result of facial artery involvement.<sup>22</sup>

Patients must meet three of the following five criteria to be accepted in studies for TA: age of >50 years, new onset of headache (found in 65–75% of TA patients), abnormal temporal artery by physical examination, ESR of >50 mm/hour, and diagnostic temporal artery biopsy. An ESR of <50 mm/hour significantly reduced finding TA by temporal artery biopsy.<sup>14</sup> These criteria distinguish TA from other forms of vasculitis described in Table 1<sup>28–38</sup> with 93.5% sensitivity and 91.2% specificity.<sup>14,39</sup> Jaw claudication alone or with either scalp tenderness or a new headache increased the chances of a positive temporal artery biopsy to >75%.<sup>19</sup>

Early biopsy reveals patchy segmental inflammation with infiltrated macrophages and lymphocytes limited to the elastic lamina or adventitia. This may progress to necrosis of the arterial wall with granulomas containing multinucleated histiocytes, some of foreign body type and some of Langhans' type giant cells. Throm-

bosis occurs and late recanalization has been noted. Bilateral and multiple sections are necessary to confirm the diagnosis.<sup>1,6</sup>

Standard therapy for TA is corticosteroids (equivalent of prednisone, 1 mg/kg per day, for 1 month followed by a 5–10% taper every 2–4 weeks until discontinued or the lowest tolerated dose). Prognosis is good if therapy is begun before visual loss. Visual loss has occasionally reversed.<sup>14</sup> Duration of therapy is usually 2–3 years. Visual loss while on therapy is rare.<sup>5</sup>

In a retrospective study, aspirin appears to reduce the risk of cranial ischemic complications.<sup>39</sup> Alternate-day steroid therapy had a higher failure rate (70%) when compared with once-daily therapy (20%).<sup>40</sup> Aziothioprine, dapsone, cyclophosphamide, infliximab, and methotrexate have not established efficacy.<sup>40–42</sup> There is a case report of the successful treatment with adalimumab of relapsed TA after high-dose steroids had to be tapered.<sup>43</sup>

TCA/GA appears to be a T-cell-mediated disease. The pathogenesis involves activation of the CD4<sup>+</sup> T cells, release of cytokines, activation of macrophages, and production of reactive oxygen intermediates and metalloproteinases. What factor initiates this cascade of inflammatory tissue destruction remains to be determined. The presence of dendritic cells and Toll-like receptors are one avenue of research that is being investigated.<sup>44</sup> Interleukin (IL)-10 promoter gene and myeloperoxidase (MPO) promoter gene polymorphisms (–592 C/A IL-10 promoter gene and –463 G/A MPO promoter gene) are associated with susceptibility to GCA.<sup>45,46</sup>

### Additional History

The patient's medical history was significant for hypertension, hypothyroidism, chronic anxiety, goiter, and T-12 dermatomal zoster 2 months before this illness. She took no over-the-counter medications and denied recent travel, change in medications, or home environment. Her medications included metoprolol, levothyroxine, sertraline, alprazolam, amlodipine, and aspirin.

Alprazolam-induced angioedema must be included as a specific cause of drug-induced angioedema. Alprazolam has been reported to cause allergic reactions and tongue angioedema. One such report implicated the tartrazine dye used in the drug preparation. Other benzodiazepines have caused erythema multiforme and toxic epidermal necrolysis (tetrazepam).<sup>47–51</sup>

### Laboratory and Other Diagnostic Findings

A head CT scan revealed small vessel white matter changes. The initial ESR was 60 mm/hour. Her he-

Table 1 The vasculitides<sup>28-38</sup>

Pathologic Entity and Pathology	Typical Presentation	Unusual Clinical Presentations	Diagnosis	Treatment
<b>Hereditary angioedema (HAE)</b> Autosomal-dominant Prevalence 1:50,000. Type 1 HAE: Low levels of active C1-INH Type 2 HAE: Normal levels of dysfunctional C1-INH Type 3: A recently described HAE exclusively found in women with mutations in coagulation factor XII gene	Subcutaneous nonpruritic swelling without accompanying urticaria; typical symptoms include voice change, respiratory stridor, or asphyxia	May present late in life after treatment with ACE inhibitor treatment Type 2 has presented as food allergy Type 3: Disease triggered by estrogen therapy, oral contraceptives, and pregnancy	Type 1: Low C4 and C1-INH levels and normal C3, CH <sub>50</sub> and C1q serum levels Type 2: Reduced C1-INH activity, normal serum antigen level Type 3: Two different missense mutations identified at the same position in the factor XII gene with normal C1-INH levels	Danazol (an attenuated androgen); antifibrinolytic agents or tranexamic acid; C1-INH concentrate; recombinant transgenic C1-INH; DX-88 (ecallantide, a plasma kallikrein inhibitor); or, icatibant
<b>Acquired deficiency of C1-INH (AAE)</b> Associated with lymphoproliferative or rheumatologic disorders. Type 1 AAE: Antidiotype antibodies against B-cell surface immunoglobulins, resulting in formation of immune complexes. These immune complexes activate C1, which causes consumption of C1-INH Type 2 AAE: Immune blockade of the C1-INH molecule active site by autoantibodies producing a nonfunctional cleaved C1-INH		May present after treatment with ACE inhibitor treatment		

Table 1 Continued

Pathologic Entity and Pathology	Typical Presentation	Unusual Clinical Presentations	Diagnosis	Treatment
<b>ANCA-associated primary vasculitic syndromes</b> See Wegener's granulomatosis, Churg-Strauss syndrome, and microscopic polyangiitis	Cutaneous manifestations: Palpable purpura or infiltrated erythema May involve the small vessels around the temporal artery and present with typical manifestations of giant cell arteritis	Nodular erythema, livedo racemosa, deep ulcers, digital gangrene		
<b>Wegener's granulomatosis</b> ANCA-associated vasculitis; small and medium vessel necrotizing vasculitis and granulomatous inflammation; giant cells present; proliferative GN (pauci-immune)	Triad of upper airway involvement (which is often indolent), lower respiratory tract involvement, and GN; abnormal CXR is very common; ocular, cutaneous and musculoskeletal manifestations are common	Central diabetes insipidus, retro-orbital mass, hearing loss, thyroid, prostate and breast involvement	Tissue biopsy of site with active disease Open lung or thoroscopic biopsy often best Renal biopsy can be supportive but is generally not diagnostic ANCA positivity is most often c-ANCA (anti-PR3 specificity)	Nonsevere or limited disease: Methotrexate Severe or generalized disease: Initial treatment with corticosteroids and cyclophosphamide Once in remission, maintenance therapy with methotrexate or azathioprine
<b>Microscopic polyangiitis</b> ANCA-associated small vessel vasculitis; proliferative GN (pauci-immune); no giant cells	Often has a long prodromal phase RPGN is essentially universal; alveolar hemorrhage and gastrointestinal symptoms are common		GN and pulmonary involvement are absent in classic PAN; p-ANCA (anti-MPO) positivity is present in 60%)	High-dose corticosteroids initially with additional immunosuppressive therapy depending on severity of disease

Table 1 Continued

Pathologic Entity and Pathology	Typical Presentation	Unusual Clinical Presentations	Diagnosis	Treatment
<b>Churg-Strauss syndrome</b> ANCA-associated small vessel vasculitis; giant cells and eosinophilia present; granulomatous inflammation of the respiratory tract	Has prodromal, eosinophilic and vasculitic phases; typically, asthma precedes other symptoms by years; eosinophilia, pulmonary infiltrates, and mononeuritis multiplex are classic; sinusitis, allergic rhinitis, abdominal symptoms, cutaneous manifestations, and cardiac disease are common; cardiac disease is a leading cause of mortality in this disease	Reversible exophthalmos; skull base infiltration with granulomas	Tissue biopsy of site with active disease ( <i>i.e.</i> lung, nerve); has low frequency of ANCA <sup>+</sup> tests; when positive usually p-ANCA (anti-MPO)	Primary treatment is high dose glucocorticoids; in patients with severe or refractory disease, additional agents such as cyclophosphamide or azathioprine are typically used
<b>Takayasu's arteritis</b> Myointimal proliferation with vessel wall thickening and luminal stenosis, or if smooth muscle cell and elastic fiber destruction predominates, aneurysm formation	Most common signs and symptoms are upper extremity claudication, asymmetric blood pressures, and vascular bruits (carotid, subclavian and aortic vessels most often) Systemic symptoms are not as common; signs and symptoms of cerebrovascular insufficiency are very common Abnormal pulmonary imaging studies are common but clinical symptoms present only ~25% of the time; hypertension is present in 40–80% of patients and may be underestimated in patients with subclavian and innominate artery stenosis	Retinopathy, vitreous hemorrhage	Diagnosis is based on clinical findings in the setting of compatible vascular imaging abnormalities	High-dose glucocorticoid therapy (1 mg/kg per day) is the standard for those patients with relapsing disease on prednisone taper or with steroid resistant disease, methotrexate or cyclophosphamide may be added Surgical interventions include bypass, PTCA, aortic root repair or replacement; overall, bypass grafting maintains better patency Disease activity is extremely difficult to assess

Table 1 Continued

Pathologic Entity and Pathology	Typical Presentation	Unusual Clinical Presentations	Diagnosis	Treatment
<b>Giant cell arteritis</b> Large vessel vasculitis; involvement tends to be patchy and rarely affects intracranial arteries; multinucleated giant cells present in ~50% of biopsies	Age of onset $\geq$ 50 year; new onset localized headache; ESR $>$ 50, temporal artery tenderness, jaw claudication, amaurosis fugax, polymyalgia rheumatica, anemia, mononeuritis multiplex, and constitutional symptoms are common Aortic aneurysms can be seen as early or late complications	Nonproductive cough, arm claudication, tumor-like mass in the breast, SIADH, tongue infarction, hearing loss, and Charles Bonnet syndrome (visual hallucinations)	Suspect if patient is $>$ 50 years old, PMR, F/UO, unexplained anemia, new headache, acute visual changes and/or elevated ESR Temporal artery biopsy If temporal artery not clinically involved may need to biopsy other arteries such as occipital or facial	High-dose glucocorticoids and low dose aspirin (81–100 mg/day)
<b>Henoch-Schonlein purpura (IgA-associated vasculitis)</b> Capillary and venule involvement. IgA containing complexes	Purpura, urticaria, abdominal pain, GI bleeding, intussusception, arthritis/arthralgias and GN are common manifestations; often self-limited; frequently recurrent	Venous thrombosis with high levels of factor VIII and homocystein		In absence of renal dysfunction, symptomatic treatment; need to periodically monitor for recurrence until complete resolution of symptoms
<b>(Cutaneous) Leukocytoclastic angitis</b> Postcapillary venules are the vessels most commonly involved Characterized by leukocytolysis (nuclear debris from invading neutrophils)	Generally purpuric lesions that occur in crops and are more pronounced in gravity-dependent areas May have striking dependent edema		Diagnosis is made by skin biopsy	Eliminate underlying precipitant. Treatment options include NSAIDs, colchicine, pentoxifylline, dapsone, and short-term low-dose steroids Compression stockings for edema

Table 1 Continued

Pathologic Entity and Pathology	Typical Presentation	Unusual Clinical Presentations	Diagnosis	Treatment
<b>Central nervous system isolated angitis. Including (1) granulomatous angiitis of the CNS (GACNS) (2) BACNS (3) Atypical PACNS</b>				
Granulomatous medium vessel vasculitis limited to the central nervous system	Decreased cognition (83%), headache (56%), seizure (30%), stroke (14%), and hemorrhage (12%) are most common presentations		Cerebral angiography may be helpful; brain and leptomeningeal biopsy are the gold standard	
Langerhans and foreign-body type multinucleated giant cells often present	Elevated ESR, and CSF protein are common. Three clinical subset: GACNS—male predominant, any age, with long prodromal period and classic histology on biopsy BACNS—more likely female, acute onset of headache or neurologic symptoms, classic angiogram, more often monophasic and benign course			GACNS: Treated with cyclophosphamide and corticosteroids (see treatment for Wegener's) BACNS: Glucocorticoids for ≤6 mo with adjunctive calcium channel blockers
<b>Polyarteritis nodosa</b>	Weight loss, skin nodules, livedo reticularis, hypertension, renal insufficiency, abdominal pain, blood in the stool, myalgia and weakness, neuropathy, testicular pain, and an association with hepatitis B infection are common; many of these are part of the classification criteria for this disease	Breast and uterine involvement; rare vasculitis of the cystic or appendiceal arteries may mimic acute cholecystitis or appendicitis	There is no diagnostic lab test; tissue biopsy and arteriography	High-dose glucocorticoids are the initial mainstay Patients with critical organ involvement (renal or gastrointestinal ischemia, cardiomyopathy or dense neuropathy) usually are treated with an additional immunosuppressive agent such as cyclophosphamide or methotrexate If active hepatitis B or C infection is present, a relatively short course of steroids in conjunction with aggressive antiviral therapy is fairly standard
Medium-sized vessel vasculitis with segmental transmural inflammation of muscular arteries	Unlike the ANCA-associated vasculitides it does not involve veins and granulomatous inflammation does not occur			Atypical PACNS: Treated initially with steroids alone

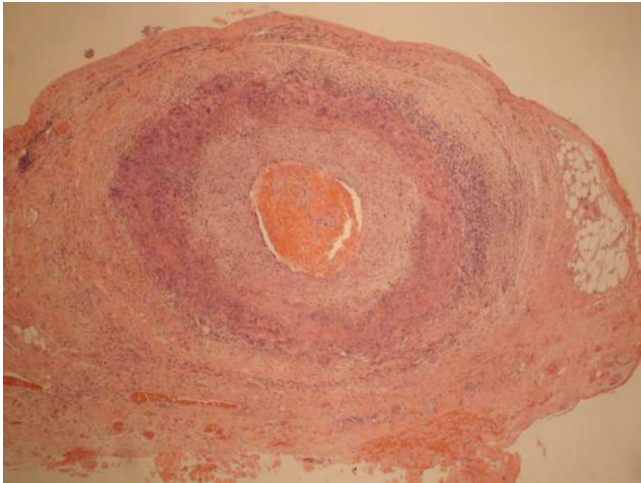


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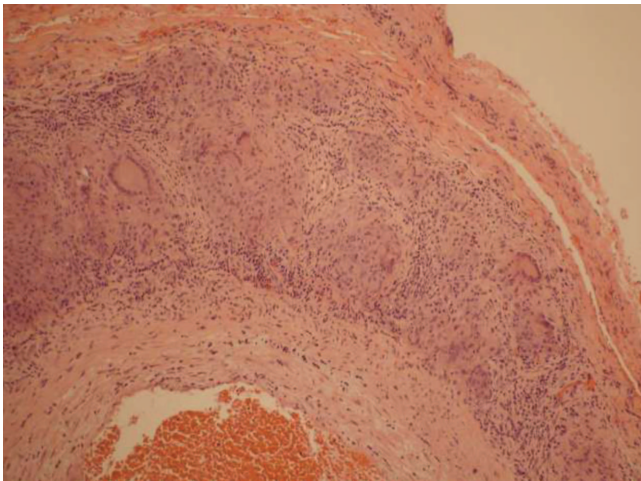
Pathologic Entity and Pathology	Typical Presentation	Unusual Clinical Presentations	Diagnosis	Treatment
<b>Kawasaki Disease (KD)</b> Medium vessel vasculitis	Mucocutaneous lymph node syndrome: Fever, conjunctivitis, mucositis, polymorphous rash, edema/erythema/desquamation of hands and feet, lymphadenopathy Complications include coronary artery aneurysms, MI, heart failure, and arrhythmias	Fusiform aneurysms of brachial arteries Incomplete KD, in which adenopathy is finding most often absent	Clinical	i.v. immune globulin therapy and aspirin
<b>Behcet's disease</b> Necrotizing leukocytoclastic obliterative perivasculitis and venous thrombosis; affects capillaries, veins and arteries of all sizes; immune complex vasculitis	More common in Middle Eastern men, and women from the Far East; recurrent, usually painful mucocutaneous ulcers (oral and urogenital) Ocular disease present in 2/3 (uveitis most common) Vascular disease present in 1/3, especially venous thromboembolic disease CNS disease present in 10–20% Pathergy test positive. Cutaneous disease is common and varies	Renal and peripheral nervous system involvement is less common	On the basis of clinical findings. ICAM-1 levels appear to correlate with disease activity	Severity of the illness usually improves over time; life expectancy is normal Major serious complication is blindness; mucous membrane involvement is treated with topical steroids and thalidomide can be used in more severe cases; colchicine and interferon $\alpha$ can be used Thrombophlebitis is treated with aspirin; uveitis and CNS disease require systemic high dose steroids and azathioprine Anti-TNF may be an alternative treatment for panuveitis and mucocutaneous disease
<b>Cogan's syndrome</b>	Interstitial keratitis with vestibuloauditory symptoms; may be associated with systemic vasculitis especially aortitis with aortic valve involvement			Glucocorticoids are the mainstay of treatment; treat as early as possible with onset of hearing loss; early treatment improves outcome

Table 1 Continued	Pathologic Entity and Pathology	Typical Presentation	Unusual Clinical Presentations	Diagnosis	Treatment
<b>Secondary vasculitides</b>	Infection related; secondary cryoglobulinemic; connective tissue disease related; drug hypersensitivity-related; malignancy related hypocomplementemic urticarial vasculitis; organ transplant related; and, pseudovasculitis (antiphospholipid syndrome, atrial myxoma, endocarditis, Sneddon syndrome)	Secondary cryoglobulinemic vasculitides may involve the small vessels around the temporal artery and present with typical manifestations of giant cell arteritis			

HAE = hereditary angioedema; ANCA = antineutrophil cytoplasmic antibody; C1-INH = C1 esterase inhibitor; ACE = angiotensin-converting enzyme; GN = glomerulonephritis; PR3 = proteinase-3; GN = proteinase-3; GN = glomerulonephritis; CXR = chest x-ray; RPGN = rapidly progressive glomerulonephritis; MPO = myeloperoxidase; PTCA = percutaneous transluminal coronary angioplasty; ESR = erythrocyte sedimentation rate; SIADH = syndrome of inappropriate antidiuretic hormone; PMR = polymyalgia rheumatica; FUIO = fever of unknown origin; GI = gastrointestinal; NSAID = nonsteroid anti-inflammatory drug; BACNS = benign angiopathy of the CNS; PACNS = primary angiitis of the CNS; MI = myocardial infarction; ICAM-1 = intercellular adhesion molecule-1; TNF = tumor necrosis factor.

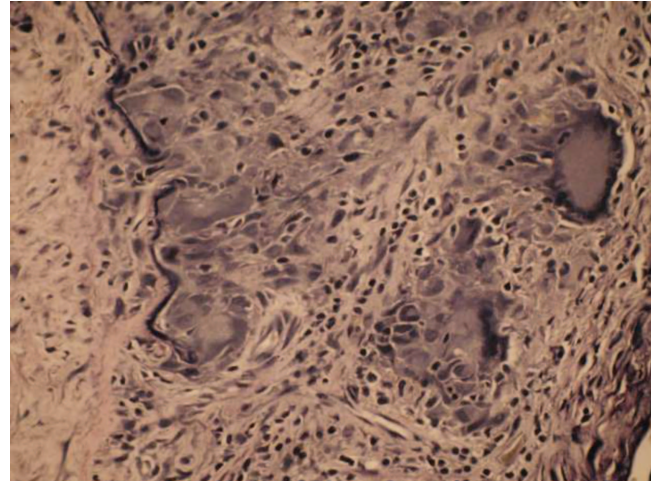


**Figure 1.** Low-power view of hematoxylin and eosin-stained section of the right temporal artery. Extensive transmural inflammatory infiltrate is involving the medium-size artery wall. Multinucleated histiocytes (giant cells) are frequently present in the media and some extending to adventitia where areas of prominent inflammatory infiltrate are present. Foci of medial necrosis (homogenous acellular areas) can be identified. Marked intimal thickening with edema and early fibrosis are seen also.



**Figure 2.** Medium-power view of hematoxylin and eosin-stained section of the left temporal artery. There is marked multinucleated giant cell and epithelioid histiocyte infiltrate, forming occasionally nodular aggregates (granulomata). Some of giant cells are of Langhans' type (peripherally lined nuclei) and some others are of typical foreign body type (random location of multiple nuclei). Other inflammatory cells visible are lymphocytes, neutrophils, and eosinophils, signifying acute and chronic inflammation. Special stains were negative for acid-fast bacilli and fungal microorganisms, in the setting of appropriate controls (not shown).

moglobin was 11.4 gm/dL, (with normochromic normocytic indices). The white blood cell count was 12,400 cells/mm<sup>3</sup> with no eosinophils and a normal



**Figure 3.** High-power view of elastic-stained section of the right temporal artery. Destruction of the wall by granulomatous inflammation is present. A group of giant cells have accumulated on the medial side of intimal-medial junction, closely approaching the internal elastic lamina (dark linear stain), in the process of phagocytosis. There is a disruption of continuity and absence of internal elastic lamina in the other area that is not involved by giant cells and showing early neovascularization. Separately, a prominent giant cell of Langhans' type can be seen. Again, a mixed acute and chronic inflammatory infiltrate is noted.

differential count. Other laboratory tests were normal or negative (cerebral spinal fluid chemistry, culture, cytology, and bacterial antigen survey; TSH; free T<sub>4</sub>; C<sub>3</sub>; C<sub>4</sub>; CH<sub>50</sub>; C<sub>1</sub>q; C<sub>1</sub>-INH; serum IgE; C<sub>1</sub>q binding assay; cryoglobulins; ANA; rheumatoid factor; antimicrosomal antibodies; antithyroglobulin antibodies; and, serum protein electrophoresis). Figures 1–3 show her pathological findings in bilateral temporal artery biopsy specimens.

She was treated with antibiotics, acyclovir, diphenhydramine, and methylprednisolone (40 mg i.v. b.i.d.). Bilateral temporal artery biopsy specimens showed extensive granulomatous inflammation with disruption of the wall architecture.

### Final Diagnosis

The headache, neck, and facial pain gradually improved over the next 5 days. She was discharged on prednisone 60 mg/day. The final diagnosis was TA.

### CONCLUSION

This patient's age, elevated ESR, and tenderness over the temporal areas were significant clues. The biopsy specimens and response to steroid therapy were consistent with TA.

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