Temporal Arteritis

A Cough, Toothache, and Tongue Infarction

David B. Hellmann, MD

Temporal arteritis, the most common form of systemic vasculitis in adults, is a panarteritis that chiefly involves the extracranial branches of the carotid artery. The condition is illustrated in this article by the case of a 79-year-old woman with a dry cough, toothache, tongue infarction, and vision loss. The mean age of onset is 72 years and the disease rarely occurs in persons younger than 50 years. The most common presenting manifestations are headache, jaw claudication, polymyalgia rheumatica, and visual symptoms. Eighty-nine percent of patients have an erythrocyte sedimentation rate greater than 50 mm/h. However, about 40% of patients present with atypical manifestations, including fever of unknown origin, respiratory tract symptoms (especially dry cough), and large artery involvement. Familiarity with such unusual manifestations of temporal arteritis facilitates early diagnosis and treatment, thereby reducing the risk of vision loss.

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CASE PRESENTATION

DR HELLMANN: My patient, Professor R, who is a 79-year-old woman, was well until she developed a disorder that eventually produced blindness in her right eye. Although most of the common presenting features of temporal arteritis (TA) are familiar to general internists and family physicians, the many disguises of this condition may challenge the diagnostic skills of any experienced physician. Learning to see through these disguises is crucial to early diagnosis and the prevention of visual loss. Professor R, please tell us how your illness began.

PROFESSOR R: All my troubles began the month my husband and I were moving from our home into a retirement community. Before that, I was completely healthy, playing tennis, swimming, and hiking. I am now a professor emeritus and still perform research on iconography of libraries in the 17th and 18th centuries. It keeps me interested, traveling, and visiting libraries in Europe. My husband and I have been doing all sorts of exciting things and I have never been in a hospital except for a broken arm. The month we sold our house I was under a great deal of stress. Moving from a house into a 2-bedroom apartment, I had to give up a lot, especially my own library of 2000 books. So, I was so tired that I began to take naps for the first time. I thought the tiredness would go away but after 2 to 3 weeks I also developed a cough.

DR HELLMANN: Did you bring up anything when you coughed?

See also Patient Page.

PROFESSOR R: No, it was dry. I saw a physician who gave me some pills but the cough persisted. Two months later I continued to cough and felt exhausted. Since it was winter, we thought that if we got away for a week to Hawaii I would get better. The afternoon before we left for Hawaii I awoke from a nap and could not see out of my right eye. It was all black. I could not reach a physician so I told my husband, "Let's just go. By the time we get back I'm sure I'll be seeing fine again." And we went on our trip.

DR HELLMANN: Did your vision get better?

PROFESSOR R: No, it never did.

DR HELLMANN: Did you experience a headache or any other symptoms, aside from the fatigue, cough, and visual loss?

PROFESSOR R: I never had a headache. But after I started coughing and before I had the eye problem, I did develop a toothache. I could not quite determine which tooth or teeth hurt. My mouth just hurt all over. Then I developed a burning sensation on the left side of my tongue. Between my toothache and tongue pain, I could not eat very well and lost 20 pounds during the week we were away. When we returned from Hawaii, my first visit was to the dentist. He found nothing wrong with my teeth. It was actually an ophthalmologist who first suspected the correct diagnosis because of my blindness and other symptoms; the eye doctor tested my sedimentation rate and then immediately admitted me to the hospital.

DR HELLMANN: That is right, the erythrocyte sedimentation rate (ESR) was 115 mm/h. Results of the other tests performed at that time, including a complete blood cell count, serum chemistries, and a chest radiograph, were normal. She was treated with intrave-

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nous methylprednisolone in high doses and underwent a right temporal artery biopsy. The biopsy showed granulomatous inflammation with multinucleated giant cells, rupture of the internal elastic lamina, and luminal narrowing. These findings were diagnostic of temporal arteritis. One day after the biopsy, Professor R was discharged taking prednisone, 60 mg/d.

I saw Professor R for the first time 1 week later. Her vital signs were normal. She had minimal light perception in the right eye with a relative afferent pupillary defect. That is to say, her pupils constricted less when I shone a light in the right eye than when I shone the light in the healthy left eye. The right optic disc was pale. The right temporal artery was surgically absent while the left—barely pulsatile—was hard and stiff. An ischemic ulcer the size of a jellybean was present along the left lateral surface of the tongue. The peripheral pulses were palpable and symmetrical, and there were no bruits in the carotid, subclavian, axillary, abdominal aortic, or femoral artery regions.

DISCUSSION

Professor R's presentation is instructive because it emphasizes some of the unusual ways in which TA can present. When it presents atypically, as it did in Professor R, it may not be diagnosed before the development of blindness, the most feared complication of TA. Knowing the disguises that TA can wear affords physicians the best chance of diagnosing and treating TA before the development of blindness.

Definition, Epidemiology, and Pathogenesis

Temporal arteritis is the most common form of systemic vasculitis in adults. The disease is defined as a panarteritis that preferentially involves the extracranial branches of the carotid artery.[1-6] Aging is the single greatest risk factor for the disease: TA virtually never occurs before the age of 50 years, and the annual incidence rises steadily thereafter, from 1.54 of 100 000 people in the sixth decade of life to 20.7 of 100 000 people in the eighth decade.[1,3] The average age of onset of TA is 72 years. Perhaps as a result of the aging population in this country, greater recognition of the disease on the part of physicians, or both, the incidence of TA has been rising in some populations.[1] Temporal arteritis has been reported in all groups, but appears especially common in people of Scandinavian or Northern European heritage.[1,2] Certain genes (ie, *HLA-DR4* haplotypes 0401 and 0404/8, which are contained in the *HLA-DRB1* locus) have been associated with an increased risk of developing TA.[7] Although the cause of TA is unknown, the disease appears to be T-cell dependent and antigen driven.[8]

Classic Manifestations

The classic manifestations of TA are headache, jaw claudication, polymyalgia rheumatica (PMR), and visual symptoms (TABLE).[4-6,9] Headache is the most common feature, occurring eventually in more than 70% of patients. Although the headache often causes a deep aching pain over the temporal area, the headache can be extremely variable in location, intensity, and quality. Quite often, the only distinctive feature of the headache is that it is new. Even if the patient has experienced migraines or tension headaches for years, he/she will note that this headache is different. Alternatively, the patient may say, "I am 72 and have never had headaches until now." Some patients develop inflammation of the occipital artery, causing pain at the base of the skull. These symptoms are easily mistaken for cervical spine disease.

Jaw claudication is the occurrence of pain in muscles of the face caused by protracted chewing.[9] This symptom results from ischemia and is essentially angina of the muscles of mastication. In contrast to temporal mandibular joint disease, jaw claudication does not produce pain with the initiation of chewing or with the chewing of soft foods. Rather, jaw claudication is induced by the chewing of tougher foods such as meat. I emphasize, however, that only about half of the patients with jaw pain from TA provide a classic description of claudication. Many report merely a vague sense of discomfort in or around the jaw that may be unrelated to chewing. One of my other patients had a diffuse mandibular discomfort that she attributed to her face-lift, even though that surgery had taken place months earlier and had healed without difficulty. A sense of dental discomfort, as described by Professor R, is another common variant of jaw claudication. I have also seen patients with TA present with pain in the sinus region or in the ear. Some were treated with antibiotics for sinusitis or otitis despite the absence of any physical findings to support those diagnoses. Given the variability in presentation of the headaches and jaw claudication associated with TA, the diagnosis should be considered whenever anyone older than 50 years complains of persistent unexplained pain above the neck.

Table. Classic Symptoms and Findings in Temporal Arteritis*

	Frequency, %
Symptoms	
Headache	77
Jaw claudication	51
Constitutional symptoms	48
Polymyalgia rheumatica	34
Visual symptoms	29
Findings	
Fever	26
Abnormal temporal artery	53
Erythrocyte sedimentation rate >40 mm/h	94

*Data derived from Machado et al.[5]

Polymyalgia rheumatica is defined as pain and stiffness in the shoulders, neck, and hip girdle areas and is worse in the morning and improves as the day goes on. Because of the pain, a patient may have trouble combing hair, putting on a coat, or standing up from the toilet. It has been said that getting out of bed is to PMR what making a fist is to rheumatoid arthritis. While most patients with PMR believe the pain is associated with weakness, they always say that pain is the predominant feature. (This contrasts with polymyositis and other forms of inflammatory myopathy, in which weakness is the major complaint). Magnetic resonance imaging studies have demonstrated clearly that the pain of PMR results from inflammation of bursae in the shoulder and hip regions, and to a lesser extent

Box. Atypical Manifestations of Temporal Arteritis

- Respiratory tract symptoms
  - Dry cough
  - Sore throat
  - Tongue pain
  - Choking sensation
- Fever of unknown origin
- Large artery involvement
  - Upper and lower extremity claudication
  - Thoracic or abdominal aortic aneurysm
- Peripheral nervous system features
  - Mononeuritis multiplex (especially of the brachial plexus)
- Central nervous system features
  - Stroke
  - Transient ischemic attacks
  - Dementia
  - Hallucinations
- Syndrome of inappropriate antidiuretic hormone
- Tumorlike lesions
  - Breast mass
  - Ovarian mass
- Microangiopathic hemolytic anemia

by synovitis of the nearby joints.[10] These findings help explain why patients most commonly localize the discomfort to the tissues rather than to joints.

Visual symptoms, including loss of vision and diplopia, develop in about one third of patients (Table).[4-6,9] Blindness is the most worrisome complication because it is usually irreversible. Blindness usually results from an anterior ischemic optic neuropathy, which in turn is caused by occlusion of the posterior ciliary artery, a branch of the ophthalmic artery. The posterior ciliary artery is the main source of blood flow to the optic nerve head.[11] Blindness is almost never the first symptom of TA. Therefore, there is almost always a window of opportunity to make the diagnosis and prevent visual loss. When blindness occurs, it develops an average of 5 months after the onset of TA. Unfortunately, our patient developed this complication only 2 months after the beginning of her symptoms. In patients with anterior ischemic optic neuropathy, no disc abnormalities are detectable for the first few hours. Subsequently, the disc swells and becomes pale.[11]

Other common manifestations of TA include weight loss, fever, and arthralgia. Some patients also present with arthritis that can be difficult to distinguish from rheumatoid arthritis.[12] An abnormal temporal artery is found on physical examination in only half of the patients.[4-6,9] Therefore, a normal temporal artery by physical examination does not exclude this diagnosis. Abnormalities of the temporal artery include thickening, enlargement, or the loss of pulsation. Professor R had a thickened, ropy temporal artery. Enlarged temporal arteries are not specific for TA; for example, extensive Paget disease of the skull can be accompanied by increased blood flow to the skull and enlarged temporal arteries.

The most common laboratory abnormalities in TA are a markedly increased ESR (averaging nearly 100 mm/h), a normochromic normocytic anemia, and (in approximately 30% of cases) a mildly elevated alkaline phosphatase.[4-6,9] Although an elevated ESR is usually a reliable companion of TA, approximately 11% of patients present with an ESR of 50 mm/h or less and 4% have an ESR of 30 mm/h or less.[13,14] Recent use of corticosteroids for another condition (eg, asthma), localized arteritis, or inability to express fully inflammatory responses may explain why some patients have a normal ESR despite having active TA.[13,14]

Atypical Manifestations

About 40% of patients with TA do not present with classic symptoms but rather with atypical manifestations (BOX).[3,15-19] The prominence of Professor R's dry cough is noteworthy because respiratory symptoms can be an important manifestation of TA. The respiratory manifestations of TA were highlighted by a Mayo Clinic study showing that about 1 patient in 10 has respiratory symptoms.[20] In 4%, these are the chief complaints.[20] Dry cough, which our patient had, is the most common respiratory manifestation of TA. The cause of the cough is not known. Chest imaging results are normal in these patients. Because TA is a systemic disease, it is possible that cough centers, which are distributed throughout the midbrain, the airways, the diaphragm, and esophagus,[21] become irritated by inflammation in nearby blood vessels. The cough resolves quickly after prednisone is started.

When should dry cough, a very common symptom with many causes, be considered a possible manifestation of TA? First, because TA is so rare before 50 years, a younger person with cough should not be suspected of having the disease. Second, dry cough is never the sole symptom of patients with TA. Cough occurring in the absence of other symptoms is not suggestive of TA. Indeed, some have had classic manifestations, including headache and PMR, which happened to be less troublesome to the patient than the cough. Some patients may not have had classic manifestations of TA but did have other symptoms. Professor R experienced malaise, weight loss, fatigue, and tooth and tongue pain before she developed blindness. Thus, the patient's age and the results of the review of symptoms help identify the patients with cough who warrant further evaluation.

Other respiratory tract symptoms of TA include a sore throat (pharyngitis-like symptoms), tenderness of the ante-

rior neck, tongue pain, hoarseness, and the sensation of choking.[20] Tongue pain results from ischemic damage that may manifest as glossitis, ulceration of the tongue, lingual claudication (tongue pain with talking), or lingual infarction.

Fever of unknown origin is another important manifestation of TA.[18] Temporal arteritis accounts for only 2% of all fevers of unknown origin, but 16% of those occurred in patients older than 65 years.[18] The fever in TA averages 39.1°C and can reach nearly 40°C; about two thirds of patients have rigors and drenching sweats, features that often conjure diagnoses of infection or lymphoma.[18] Of great help in distinguishing the fever of unknown origin of TA from those caused by infection or malignancy is that almost all patients with TA and fever of unknown origin have a normal white blood cell count, at least before starting prednisone.[18]

Large artery involvement is more common among patients with TA than generally appreciated.[22,23] One study of 238 patients with TA noted involvement of the carotid, vertebral, and subclavian arteries in 14% of patients.[22] Such involvement may cause upper extremity claudication, unequal blood pressures in the arms, transient ischemic attacks, or cerebrovascular accidents. Lower extremity involvement that is sufficient to cause claudication is rare but has been reported.[24] To maximize the chance of detecting large artery disease, the physical examination of patients suspected of having TA should include the measurement of blood pressure in both arms, careful palpatation of the bracheal and radial pulses, and auscultation for bruits not only above the carotid but also above and below the clavicle for subclavian disease and above the flexor surface of the upper arm to detect axillary artery involvement.

Even the aorta is involved in a substantial number of patients with TA. A population-based study from Olmsted County, Minnesota, revealed that 18% of patients with TA have aortic involvement, with the most common complication being thoracic aortic aneurysm.[23] Indeed, patients with TA are 17 times more likely than age-matched controls to develop thoracic aortic aneurysms.[23] Although the aneurysms can complicate TA at any time, the mean time to recognition of the aneurysms is 5 to 6 years after the diagnosis of TA. More recent studies using positron emission tomographic scans suggest that as many as one half of all patients with TA develop inflammation of the aorta or its major branches.[25]

Although some patients with aortic involvement by TA are asymptomatic, others develop aortic dissection resulting in aortic regurgitation or sudden death. One of my other patients illustrates this problem. Her disease had been quiescent for 5 years when she suddenly developed severe back pain. The initial evaluation was unrevealing and she was given a tentative diagnosis of a nephrocalcinosis. The next day, the identity of her problem became clear when she developed acute aortic regurgitation. Pathologic studies suggest that aneurysms can result from smoldering inflammation or from weakening of the vessel wall from previous inflammation.[23]

Other atypical manifestations of TA are mass lesions of the breast or ovaries that mimic tumors,[26] the syndrome of inappropriate antidiuretic hormone secretion, microangiopathic hemolytic anemia, peripheral neuropathy, and central nervous system symptoms (Box).[15,16,27,28] Why patients with TA develop different manifestations is not entirely clear. However, evidence suggests that some clinical subsets may involve unique pathologic pathways that are caused by differential expression of inflammatory cytokines.[29] For example, interferon γ, elaborated by T cells, is increased in patients with biopsy proven TA but not in patients who have PMR in the absence of vasculitis.[8,29]

Predicting the Presence of TA

A recent literature review has tried to determine the accuracy of the history, the physical examination, and the ESR in the diagnosis of TA.[30] The analysis focused on patients referred for TA biopsy and determined which features best predicted a positive result. The only clinical features that substantially increased the likelihood of TA among these patients were jaw claudication (positive likelihood ratio [LR], 4.2; 95% confidence interval [CI], 2.8-6.2), diplopia (positive LR, 3.4; 95% CI, 1.3-8.6), and temporal artery beading (positive LR, 4.6; 95% CI, 1.1-18.4). A normal ESR reduced the likelihood of TA (negative LR, 0.2; 95% CI, 0.08-0.51).[30]

These attempts to make the diagnosis of TA evidence-based powerfully underscore the importance of clinical judgment. While TA affects less than 1% of the population, 39% of the patients referred for temporal biopsy had a positive result.[30] It is striking to report how well physicians, analyzing all the data, identify cases of TA, especially when considering the low predictive value of individual clinical variables. A broad consideration of the typical and atypical features of TA may further improve clinical judgment.

Establishing the Diagnosis

To be classified as having TA, a patient must meet 3 of the following 5 criteria established by the American College of Rheumatology: (1) 50 years or older, (2) new-onset localized headache, (3) temporal artery tenderness as decreased temporal artery pulse, (4) ESR of 50 mm/h or higher, and (5) abnormal temporal artery biopsy findings demonstrating mononuclear infiltration or granulomatous inflammation.[31] However, these classification criteria were never meant to serve as diagnostic criteria. Others have demonstrated the limitations of these criteria, including having a positive predictive value of only 29%.[32]

In clinical practice, establishing the diagnosis of TA usually requires a biopsy of the temporal artery. Because skip lesions are believed to occur in TA, diagnosis is facilitated by obtaining large biopsy specimens (>2 cm long) and by examining multiple pathologic sections.[2] The administration of corticosteroids given for less than 2 weeks does not reduce the yield of temporal artery biopsy.[33] Bilateral temporal artery biopsies are not usually needed because they are concordant in 95% to 99% of

cases.[34-36] Patients with large artery involvement are diagnosed by arteriography or magnetic resonance angiography, either of which may demonstrate long segments of smooth stenoses. Temporal artery biopsy is positive in only about half of patients who manifest large artery disease.[37] Duplex ultrasonography has identified abnormalities in 93% of patients with TA but the technique is operator-dependent and the sensitivity and specificity of temporal artery ultrasound outside of a few research centers are unknown.[38,39] It is also too early to tell whether the abnormalities seen on positron emission tomographic scanning will be useful diagnostically. Therefore, unless the patient has large artery disease, which is best diagnosed by angiography, all patients suspected of having TA should undergo temporal artery biopsy.

Approach to Treatment

Because the central goal in managing TA is to prevent blindness, treatment should be initiated immediately whenever the disease is strongly suspected. Most authorities believe that TA requires starting prednisone in the range of 60 mg/d.[2] In contrast, isolated PMR, which is 3 times more common than TA, requires only 10 to 20 mg/d of prednisone at the start of therapy. The rate of tapering prednisone is chiefly determined by the patient's symptoms.

Although prednisone is the cornerstone of therapy, 60% of patients relapse during or after prednisone tapers. In addition, the long duration of prednisone therapy required to treat TA (often >2 years) and the high rate of prednisone adverse effects (weight gain, diabetes, hypertension, and compression fractures) have prompted searches for steroid-sparing agents.[40] A Spanish group conducted a double-masked, placebo-controlled trial showing that the combination of prednisone and methotrexate reduced the need for prednisone slightly.[41] Unfortunately, the modest reduction in prednisone did not achieve detectable reductions in prednisone-related adverse effects.[41] Other investigators have not found that methotrexate is a steroid-sparing agent in TA.[42]

In conclusion, TA is the most common systemic vasculitis in adults. Its classic manifestations are headache, jaw claudication, PMR, and visual symptoms. However, TA can wear many disguises. The case presented emphasizes how dry cough, atypical tooth pain, and tongue infarction can all serve as a warning that a patient may have TA and be at risk of losing vision.

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