Does This Patient Have Temporal Arteritis?

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Context Clinicians must be able to confidently diagnose temporal arteritis (TA), since failure to make a correct diagnosis may lead to irreversible visual loss as well as inappropriate evaluation and treatment of headache, fatigue, and other potential presenting symptoms. The diagnostic value of particular signs and symptoms among patients with suspected TA is unknown.

Objective To determine the accuracy of historical features, physical examination, and erythrocyte sedimentation rate (ESR) in diagnosis of TA.

Data Sources We performed a MEDLINE search of English-language articles published between January 1966 and July 2000 and a hand search of bibliographies of retrieved articles, previous reviews, monographs, and textbooks.

Study Selection Studies that provided detailed clinical information on patients who had been referred for temporal artery biopsy. Of 114 studies retrieved, 41 met our inclusion criteria; 21 included both biopsy-positive and biopsy-negative patients and formed the core of our review.

Data Extraction Both authors independently reviewed each study to determine eligibility, abstracted data using a standardized instrument, and classified study quality using predetermined criteria.

Data Synthesis The prevalence of TA in the general population is less than 1%. However, in our 21 core studies, 39% of patients referred for temporal artery biopsy had positive results. The only 2 historical features that substantially increased the likelihood of TA among patients referred for biopsy were jaw claudication (positive likelihood ratio [LR], 4.2; 95% confidence interval [CI], 2.8-6.2) and diplopia (positive LR, 3.4; 95% CI, 1.3-8.6). The absence of any temporal artery abnormality was the only clinical factor that modestly reduced the likelihood of disease (negative LR, 0.53; 95% CI, 0.38-0.75). Predictive physical findings included temporal artery beading (positive LR, 4.6; 95% CI, 1.1-18.4), prominence (positive LR, 4.3; 95% CI, 2.1-8.9), and tenderness (positive LR, 2.6; 95% CI, 1.9-3.7). Normal ESR values indicated much less likelihood of disease (negative LR for abnormal ESR, 0.2; 95% CI, 0.08-0.51).

Conclusions A small number of clinical features are helpful in predicting the likelihood of a positive temporal artery biopsy among patients with a clinical suspicion of disease; the most useful finding is a normal ESR, which makes TA unlikely.

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CLINICAL SCENARIOS

Case 1

A 74-year-old woman has the recent onset of daily bitemporal headache but is otherwise well. Her general physical examination results are normal and the erythrocyte sedimentation rate (ESR) is moderately elevated at 64 mm/h. You wonder whether additional history or physical examination findings will modify your suspicion of possible temporal arteritis (TA) or whether the historical features alone warrant proceeding to temporal artery biopsy.

Case 2

A 53-year-old man has a 1-month history of fever and fatigue and reports a single episode of transient partial loss of vision in 1 eye. You believe that TA is among the diagnostic considerations but suspect that he is too young for this diagnosis. You wonder if additional history, physical examination, or laboratory testing will change the probability of TA sufficiently to alter your decision about the role of temporal artery biopsy rather than pursuing diagnostic evaluation for carotid artery stenosis or other considerations first.

WHY IS THIS AN IMPORTANT QUESTION TO ANSWER WITH A CLINICAL EXAMINATION?

When faced with a patient with headache, fatigue, or other possible presenting symptom of TA, clinicians must be able to correctly and confidently establish the diagnosis so as to prevent irreversible visual loss and to minimize the inappropriate evaluation and treatment of alternative diagnoses. While headache is the most common reason for clinical suspicion of TA, no single type of headache or other clinical presentation is specific for TA and the disorder is among the diagnostic considerations for many symptom complexes in older individuals. Our review will analyze the diagnostic value of these varied symptoms and signs in predicting the likelihood of TA among patients for whom there is a clinical suspicion of disease.

The first known report of a patient with TA was by Hutchinson in 1890.[1] His

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case was that of man who was referred due to "red streaks on his head" that were painful and prevented him from wearing his hat; these proved to be swollen temporal arteries, which over time became firm and pulseless. It was not until 1932 that Horton and colleagues[2] described the first 2 cases of pathologically confirmed TA; both patients had fever, weakness, anorexia, weight loss, anemia, leukocytosis, and painful, tender temporal arteries. Thus, many of the characteristic features of this newly described disease were present in these first few patients. Interestingly, headache was absent. In 1937, headache was recognized as a common feature,[3] and in 1938 visual loss was first reported.[4] In the modern era, however, clinicians are unlikely to see patients with such advanced disease and the full array of untreated symptoms.

The mortality of patients with treated TA, over follow-up periods as long as 12 years, is the same as for age-matched individuals without TA. For example, Matteson and colleagues[5] studied 205 of the patients with TA who formed the initial cohort for the development of the American College of Rheumatology classification criteria. During a mean of 7 years of follow-up, the survival for patients with giant cell arteritis was nearly identical to that of age-matched controls; the standardized mortality ratio was 1.03. Other authors have also observed that no excess mortality exists among patients with TA over time periods ranging from 4.5 to 12 years.[6-8] Unrecognized (and therefore untreated) patients may have a higher mortality but no such natural history studies of untreated patients exist in the modern era.

While preventing death may not be among the benefits of early diagnosis of TA, timely diagnosis and treatment will prevent visual loss. A prompt decision regarding further evaluation (including referral for temporal artery biopsy) and early initiation of treatment are the primary rationales for improving the clinical prediction of the diagnosis. In addition, clinicians may avoid an extensive evaluation for other causes of symptoms by establishing a proper diagnosis. Since systemic corticosteroids have been the standard therapy for TA for decades, few studies have determined the long-term incidence of visual loss among untreated patients. Several studies, however, have demonstrated a substantial reduction in the incidence of visual loss after institution of corticosteroid therapy. Even among patients with complete unilateral visual loss, prompt recognition and corticosteroid therapy will decrease the risk of visual loss in the contralateral eye.

Aiello and colleagues[9] reviewed the Mayo Clinic experience of 245 patients diagnosed with TA who had a complete ophthalmologic examination at the time of diagnosis or early in the course of treatment. The estimated 5-year probability of developing visual loss after initiating corticosteroid therapy was 1%; that of additional visual loss in patients who already had visual loss was 13%. These observations, and others, emphasize the importance of the early diagnosis and treatment of TA and of the clinical examination in identifying patients at risk for catastrophic visual outcomes.[10-12]

Estimates of the prevalence of TA have been fairly constant. Using population data from Olmsted County, Minnesota, Salvarani and colleagues[13] estimated the age-adjusted incidence for individuals aged 50 years or older to be 24.2 per 100 000 women and 8.2 per 100 000 men. In another report, prevalence estimates increased by age and were 200 per 100 000 individuals aged 50 years and older, and 1100 per 100 000 individuals aged 85 years and older.[14] These findings are similar to those observed in a Swedish population study where the average annual incidence of TA among individuals older than 50 years was 22.2 per 100 000 and the incidence increased with age.[15] In this study of 665 patients with TA proven by biopsy, only 1 patient was younger than 50 years. Other investigators have reported similar incidences.[16,17] That TA is predominantly a disease of older individuals has importance due to the aging of our society. In the US 2000 census (http://factfinder.census.gov/home/en/sf1.html), 35 million individuals (12.4% of the population) were aged 65 years or older and 9 million (3.3% of the population) were aged 80 years or older; these proportions are expected to increase in the coming years.

The relatively low prevalence of TA does not diminish its importance to clinicians due to the morbidity resulting from overlooking this disorder. In fact, the higher prevalence of TA (1.5%) in 1 large autopsy series suggests that the disorder may be either unrecognized or clinically occult in many cases.[18] The visual prognosis of occult TA is, of course, unknown, and series that describe the frequency of signs and symptoms include only patients with clinically evident TA.

Pathophysiology

The clinical manifestations of TA are a direct consequence of local (or "arteritic") and systemic inflammatory disease. Localized arterial inflammation, particularly in the smaller branches of the external carotid artery, cause endovascular damage, vessel stenosis, and occlusion, ultimately leading to tissue ischemia or necrosis. Examples of localized arteritic symptoms include jaw claudication, due to involvement of the masticatory muscles, and visual loss due to involvement of the ophthalmic or posterior ciliary arteries. The particular cytokine profile may contribute to the ischemic and prominent constitutional features, such as malaise, fever, or weight loss.[19,20]

How to Elicit the Signs and Symptoms

The myriad signs and symptoms in patients with TA require familiarity with the most common ones, recognizing that many patients will demonstrate few symptoms and have a normal physical examination. Headache, jaw claudication, visual complaints, polymyalgia rheumatica (PMR), and constitutional features in a patient older than 55 years are among the most common symptoms. A high index of suspicion will lead the clinician to pursue these features,

as they may not be part of routine history taking. Headache quality (typically severe and throbbing; less often sharp, dull, or burning), location (may be diffuse or localized, but is bitemporal in half of cases), and onset (typically acute) are key features to assess; however, the headache of TA is often nonspecific in character.[21] Headache may actually be due to scalp tenderness, reported by the patient as pain when combing the hair or putting on a hat. The headache is a new headache that is either recent in onset or different from previous headaches among patients with a history of chronic headaches. The duration of the headache before seeking medical attention is commonly 2 to 3 months. Jaw claudication refers to pain in the proximal jaw near the temporomandibular joint that develops only after a brief period of chewing, especially food requiring vigorous mastication, such as steak or a bagel.

Clinicians must distinguish jaw claudication from other causes of jaw pain in elderly persons, such as disorders of the temporomandibular joint (in which pain begins right away with chewing) or ill-fitting dentures. Visual complaints commonly include sudden monocular blindness, but clinicians should ask patients about a stuttering onset of visual loss, amaurosis fugax, a field cut, or diplopia. As an inflammatory polyarthritis with tendon or bursal involvement, PMR typically causes abrupt onset of morning stiffness involving the neck, shoulders, and hips with referred pain to the proximal arms and thighs; this explains the prominent myalgias.[22] While neoplasm and infection may be highly suspected in the older patient with fever, anorexia, weight loss, and malaise, systemic inflammatory disease such as TA may also cause these symptoms.

The physical examination is frequently unremarkable in patients with TA, but the detection of certain abnormalities may increase the suspicion of disease. The patient's temperature and general appearance are important first steps. Abnormalities of the temporal arteries, including tenderness, reduced or absent pulsation, erythema, nodularity, or swelling may be detected by light palpation just anterior and slightly superior to the tragus of the ear; following the pulse anteriorly along the temples and comparison with the contralateral side help detect findings that may be remarkably focal. Scalp tenderness, usually near the temporal arteries, may also be evident by light palpation. The scalp and tongue should be inspected for ischemic or necrotic skin changes. The funduscopic examination, ideally with pupillary dilation, may reveal a pale or swollen disc (evidence of ischemic optic neuropathy)[23] or retinal artery occlusion, while visual field testing may demonstrate a field cut. Joint examination may reveal reduced range of motion in the shoulder or hip due to pain or more distal synovitis, particularly of the wrist.

METHODS

Search Strategy and Quality Review

We performed a MEDLINE search of English-language articles published between January 1966 and July 2000. Search terms included *temporal arteritis*, *giant cell arteritis*, *clinical features*, *diagnosis*, *diagnostic tests*, *sensitivity and specificity*, *medical history taking*, *physical examination*, *signs and symptoms*, and *erythrocyte sedimentation rate*. We identified additional references by the use of a previously published search strategy in The Rational Clinical Examination series.[24] This strategy combined 10 exploded MeSH headings *(physical examination, medical history taking, professional competence, "sensitivity and specificity," reproducibility of results, observer variation, "diagnostic tests, routine," decision support techniques, Bayes theorem, mass screening)* and 2 text-word categories ("sensitivity and specificity," and "physical examination"), and intersected with *temporal arteritis*. We identified additional articles, including those predating MEDLINE, through a hand search of the bibliographies of retrieved articles, previous reviews, monographs, and textbooks. Both authors independently reviewed all retrieved articles to determine their eligibility for our review and included only those articles where agreement existed that the study had met our inclusion criteria. We sought no unpublished studies.

The purpose of our review is to determine the value of individual clinical features in predicting the likelihood of positive results from temporal artery biopsy. Eligible studies were, therefore, those in which the authors provided a detailed list of clinical features for patients suspected of or confirmed to have TA. We excluded articles with limited data on clinical features and those with fewer than 7 patients with positive temporal artery biopsy results. Many early studies classified patients as having TA based on either the authors' own clinical criteria alone or on the presence of positive biopsy results. When a study considered both groups of patients as having TA, we required that at least 90% of included patients had undergone temporal artery biopsy and had a positive result.

We classified each article by the pathologic criteria used to determine the presence of positive biopsy results and by the referral source for recruitment of patients. In some cases, authors published clinical data on the same or overlapping series of patients in more than 1 article. In these cases, if we could not determine with certainty that no overlap existed between the patients in these studies, we excluded all studies except for the report with the largest number of patients. Of 114 studies retrieved using our search strategy, 41 were eligible for our review. Twenty-one studies included patients with both positive and negative temporal artery biopsy results; these form the core of our review.

We determined if the authors required any predetermined published clinical criteria for patient inclusion, such as the American College of Rheumatology criteria[25] for the diagnosis of TA, or other criteria. When studies used such criteria to classify patients as having TA with positive biopsy results or TA with negative biopsy results, we considered a positive biopsy result to be the true reference standard and considered

only those patients with such results to have the disease. In our analysis, we included only those clinical features that were cited by at least 2 studies.

We classified the quality of evidence in each study by 2 separate methods (TABLE 1). First, we developed our own criteria that included consecutive vs nonconsecutive samples, inclusion of patients with only positive biopsy results or with both positive and negative results, and the requirement of positive biopsy results for all patients labeled as having TA. In addition, we graded the quality of each study using a classification scheme for levels of evidence adapted from that previously developed for The Rational Clinical Examination series.[26] In this scheme of levels I through VI, the highest levels of evidence we found were in level III studies.

Statistical Methods

Sensitivity was defined as the proportion of patients with TA who had the particular sign or symptom; specificity was the proportion of patients without TA who did not have the particular sign or symptom. We calculated likelihood ratios (LRs) when authors reported clinical findings of patients suspected of having TA both with positive and negative temporal artery biopsy results. The positive LR is the increase in the odds of having TA when the sign or symptom is present and is defined as sensitivity / 1–specificity. The negative LR is the decrease in the odds of having TA when the sign or symptom is absent and is defined as 1–sensitivity / specificity. Summary measures for these dichotomous data and for the data reported on a continuous scale (eg, hemoglobin) were obtained using a random effects measure that gives broad 95% confidence intervals (CIs).[27,28] Uncertainty in these measures is reflected in the broad 95% CIs around the estimates.

RESULTS

Precision and Accuracy

Twenty-one studies that met our inclusion criteria included patients with both positive and negative temporal artery biopsy results and form the basis of our review (TABLE 2). These studies reported clinical findings on a total of 2680 patients, 1050 of whom had positive temporal artery biopsy results. The overall prevalence (prior probability) of positive biopsy results among patients with a clinical suspicion of TA in these studies was 39%. All but 4 of the studies were retrospective chart reviews. 11 of the studies were of the highest quality (study quality 1) based on our predetermined criteria, and 19 of the studies included all patients who had a temporal artery biopsy during the study period.

Precision of the History and Physical Examination for TA

No study that met our inclusion criteria evaluated the precision (ie, interobserver or intraobserver variation) of the history and physical examination for the diagnosis of TA. Most of the studies cited in this review are retrospective chart reviews and did not use standardized instruments for eliciting signs and symptoms across different observers. We therefore restrict our discussion to the accuracy of clinical findings.

Table 1. Predetermined Criteria for the Quality of Evidence in Primary Studies

Study Quality		Level of Evidence	
Score	Criteria	Level*	Definition
1	Study includes consecutive patients referred for biopsy, including patients with both negative and positive results. No application of established clinical criteria for temporal arteritis exists as an inclusion criterion. Patients require biopsy confirmation to be classified as having temporal arteritis.	I	Independent, blind comparison of sign or symptom results with a gold standard of anatomy, physiology, diagnosis, or prognosis among a large number of consecutive patients suspected of having the target condition.
2	Study includes consecutive patients referred for biopsy. Patients are classified based on both the presence of predefined established clinical criteria for temporal arteritis and on biopsy results.	II	Independent, blind comparison of sign or symptom results with a gold standard among a small number of consecutive patients suspected of having the target condition.
3	Study of a nonconsecutive sample of patients referred for biopsy. All patients meet predefined established clinical criteria for temporal arteritis. The authors consider patients with negative biopsy results to have temporal arteritis if they meet established clinical criteria for temporal arteritis.	III	Independent, blind comparison of signs and symptoms with a gold standard among nonconsecutive patients suspected of having the target condition.
4	A series of consecutive patients with temporal arteritis proven by biopsy. No controls or patients with negative biopsy results.	IV	Nonindependent comparison of signs and symptoms with a gold standard among "grab" samples of patients who obviously have the target condition plus, perhaps, normal individuals.
5	A random sample of patients with a clinical diagnosis of temporal arteritis. No use of established clinical criteria. Patients do not require biopsy confirmation to be classified as having temporal arteritis.	V	Nonindependent comparisons of signs and symptoms with a standard of uncertain validity (which may even incorporate the sign or symptom result in its definition) among "grab" samples of patients plus, perhaps, normal individuals.
6	A "grab" series of patients with temporal arteritis having a particular feature or features of interest. For example, all patients may have visual loss.	VI	Nonindependent comparison of signs and symptoms with a gold standard among "grab" samples of patients who obviously have the target condition plus, perhaps, normal individuals.

*Expanded grading scheme adapted from that previously published.[26]

Accuracy of History Taking for the Diagnosis of TA

Among the studies that included data on patients both with positive and negative temporal artery biopsy results, 14 historical features were cited by at least 2 studies (TABLE 3). A limitation of our approach is that authors reported some findings much more frequently than others. However, our review incorporates the full extent of the published experience and presumably these reports include all of the major clinical features. Only 2 historical features had LRs of sufficient power to be useful to clinicians. Jaw claudication had the highest positive LR (4.2). This is consistent with the traditional clinical teaching that jaw claudication, while somewhat insensitive, is a relatively specific feature for TA. When we pooled the sensitivity data from all eligible studies, including those studies that reported only patients with positive temporal artery biopsy results,[20,25,53-71] jaw claudication was present in only 34% of patients with disease (TABLE 4).

More surprising was the finding that diplopia was the next most predictive historical feature, with a positive LR of 3.4. While the presence of diplopia substantially increases the likelihood of disease, the absence of diplopia does not significantly modify the probability of disease (negative LR=0.95) due to its low sensitivity (9% among all studies). We derived this value from 5 studies that evaluated this feature; previous reviews and textbooks have not emphasized the importance of diplopia. No other historical feature had a positive LR exceeding 2. This includes features often thought to be useful to

Table 2. Characteristics of Studies That Include Patients With Both Positive and Negative Temporal Artery Biopsies*

Study, y	Study Quality/ Level of Evidence†	Study Type	No. of Patients	Positive Biopsy Results, No. (%)	Referral Source‡	Pathologic Criteria Used to Establish Positive Biopsy Results§	Comments
Gabriel et al,[29] 1995	1/III	Retrospective	525	172 (32.8)	All	Achkar et al[30]	
Hayreh et al,[31] 1997	1/III	Prospective	363	106 (29.2)	All	Author	
McDonnell et al,[32] 1986	1/III	Retrospective	250	42 (16.8)	Specialty	Author	
Hall et al,[33] 1983	1/III	Retrospective	134	46 (34.3)	All	Not stated	
Fernandez-Herlihy,[34] 1988	1/III	Retrospective	107	29 (27.1)	All	Author	Omitted group C patients with equivocal biopsies
Chmelewski et al,[35] 1992	1/III	Retrospective	98	30 (30.6)	All	Author	
Fauchald et al,[36] 1972	1/III	Retrospective	94	61 (64.9)	All	Not stated	Comparison group patients all had PMR
Stuart,[37] 1989	1/III	Retrospective	75	14 (18.7)	All	Allsop and Gallagher[38]	
Kent and Thomas,[39] 1990	1/III	Retrospective	70	8 (11.4)	All	Not stated	
Roth et al,[40] 1984	1/III	Retrospective	51	7 (13.7)	All	Not stated	
Bevan et al,[41] 1968	1/IV	Retrospective	37	28 (75.7)	All	Author	Arteritis and giant cells pooled as biopsy positive
Duhaut et al,[42] 1999	2/III	Prospective	292	207 (70.9)	All	McDonnell et al[32]	All patients >50 y old, ESR >40 mm/h, response to 72 h of corticosteroids
Baldursson et al,[43] 1994	2/III	Retrospective	133	127 (95.5)	All	ACR	
Gonzalez et al,[44] 1989	2/IV	Retrospective	21	10 (47.6)	All	Not stated	All patients met clinical criteria for GCA
Genereau et al,[45] 1999	3/III	Retrospective	37	19 (51.4)	All	ACR	
Vilaseca et al,[46] 1987	3/IV	Retrospective	103	45 (43.7)	All	Allsop and Gallagher[38]	
Gur et al,[47] 1996	3/IV	Retrospective	39	30 (76.9)	Specialty and PCP	Banks et al[48]	All patients met ACR criteria for GCA
Brittain et al,[49] 1991	5/IV	Prospective	31	15 (48.4)	Not stated	Not stated	
Hedges et al,[50] 1983	5/V	Retrospective	91	28 (30.8)	All	Author	Patients excluded if adequate chart documentation of history taking was absent
Skaug et al,[51] 1995	6/III	Retrospective	98	13 (13.3)	Specialty	Not stated	All patients had eye complaints
Dixon et al,[52] 1966	6/IV	Prospective	31	13 (41.9)	Specialty	Author	All patients had PMR

*PMR indicates polymyalgia rheumatica; ESR, erythrocyte sedimentation rate; ACR, 1990 American College of Rheumatology criteria for the diagnosis of giant cell arteritis[25]; GCA, giant cell arteritis; and PCP, primary care practices.
†See Table 1 for definitions.
‡All indicates all patients referred for biopsy; specialty, rheumatology or ophthalmology or other specialty practice; and not stated, referral source not stated by authors.
§Author indicates author's own explicitly stated criteria; and not stated, no pathologic criteria stated for a positive temporal artery biopsy.

clinicians, including fever, PMR, visual loss, and temporal headache. The negative LR of all 14 historical features was near 1. In other words, the absence of any particular feature on history taking did not rule out TA or make the disorder substantially less likely. Patients with positive temporal artery biopsy results had a mean duration of symptoms of 3.5 months before diagnosis; this was 1.5 months (95% CI, 0.4-2.5 months) shorter than those with negative biopsy results. This emphasizes the relatively acute onset of symptoms of biopsy-proven TA and the fact that the longer the duration of symptoms, the less likely the temporal artery biopsy results will be positive.

Table 3. Likelihood Ratios for Symptoms Among Patients With Suspected Temporal Arteritis*

Symptom/References	No. of Patients With Data on Variable†	Positive LR (95% CI)	Negative LR (95% CI)
Anorexia[34,37,39,41,42,46]	674	1.2 (0.96-1.4)	0.87 (0.75-1.0)
Weight loss[31,34,36,37,39,41,42,46,47]	1417	1.3 (1.1-1.5)	0.89 (0.79-1.0)
Arthralgia[33,34,37,39,40,44,46,52]	582	1.1 (0.86-1.4)	1.0 (0.92-1.1)
Diplopia[33,34,42,50,51]	703	3.4 (1.3-8.6)	0.95 (0.91-0.99)
Fatigue[31,33,37,39,41,42,44,46]	1095	1.2 (0.98-1.4)	0.94 (0.86-1.0)
Fever[29,31,34-37,40-42,46,47]	1708	1.2 (0.98-1.4)	0.92 (0.85-0.99)
Temporal headache[36,42]	386	1.5 (0.78-3.0)	0.82 (0.64-1.0)
Any headache[29,31-35,37,39-47,50,51]	2475	1.2 (1.1-1.4)	0.7 (0.57-0.85)
Jaw claudication[29,31-35,37,39,40,42,44-46,50-52]	2314	4.2 (2.8-6.2)	0.72 (0.65-0.81)
Myalgia[31,36,39,40,46]	681	0.93 (0.81-1.1)	1.1 (0.87-1.3)
Polymyalgia rheumatica[29,34,35,37,39,40,42,44,45,47,50]	1383	0.97 (0.76-1.2)	0.99 (0.83-1.2)
Unilateral visual loss[32,50]	341	0.85 (0.58-1.2)	1.2 (1.0-1.3)
Any visual symptom[29,32-37,39-42,44-47,51,52]	2083	1.1 (0.93-1.3)	0.97 (0.9-1.0)
Vertigo[34,36,44]	212	0.71 (0.38-1.3)	1.1 (0.93-1.2)

*LR indicates likelihood ratio; CI, confidence interval.
†Includes only studies that report results for patients with both positive and negative biopsy results.

Accuracy of the Physical Examination for the Diagnosis of TA

Findings on physical examination were more likely to influence the probability of positive temporal artery biopsy results than were historical features (TABLE 5). The presence of synovitis made positive temporal artery biopsy results significantly less likely (positive LR=0.41). The absence of any temporal artery abnormality was the only finding on either the history or physical examination that made disease substantially less likely (LR=0.53). Surprisingly, scalp tenderness, a finding often thought to be specific for TA, did not perform well as a predictor of positive biopsy results. Among patients in whom TA was suspected, the frequency of scalp tenderness was similar in patients with and without the disease (positive LR=1.6).

Abnormal findings on examination of the temporal artery increased the probability of positive biopsy results and predicted disease to a greater extent than any other variable. Beading, prominence, or enlargement of the temporal artery all conferred positive LRs of greater than 4. A tender temporal artery also conferred an increased probability of positive biopsy results (LR=2.6). An absent temporal artery pulse showed a trend toward a useful positive LR; the value of 2.7 was, however, not statistically different from 1. The LRs for "any temporal artery abnormality" may underestimate their power. If eligible studies did not list clinical features separately for each patient, it was not possible to determine if specific temporal artery abnormalities overlapped; in such cases, we made the most conservative calculation as to the actual number of patients with any temporal artery abnormality.

Likelihood ratios approaching 1 suggest that, among patients with a clinical suspicion for TA, the feature was equally common among those with positive biopsy results as among those with negative results. These data do not, however, imply that the cited clinical features are uncommon in TA. We separately determined the sensitivity of physical examination features among all studies, including those that included only patients with positive biopsy results (TABLE 6). In each of our cited studies, physicians referred patients for a temporal artery biopsy when they believed the diagnosis to be sufficiently likely to justify a biopsy. These patients represent a selected sample who often manifested several clinical features of interest, including those analyzed in this review. Patients who lacked features commonly considered suggestive of TA were presumably less likely to have a temporal artery biopsy. This verification bias makes the value of those few findings with the highest and lowest LRs even greater, since they help predict biopsy results among those patients with a significant clinical suspicion of disease.

Table 4. Sensitivity of Symptoms Among All Patients With Positive Temporal Artery Biopsy Results*

Variable	No. of Studies	Sensitivity (95% CI)
Anorexia	12	0.35 (0.23-0.48)
Weight loss	19	0.43 (0.35-0.53)
Arthralgia	13	0.30 (0.21-0.40)
Diplopia	14	0.09 (0.07-0.13)
Facial pain	4	0.17 (0.12-0.23)
Fatigue	19	0.39 (0.28-0.52)
Fever	26	0.42 (0.33-0.52)
Temporal headache	8	0.52 (0.36-0.67)
Any headache	32	0.76 (0.72-0.79)
Jaw claudication	35	0.34 (0.29-0.41)
Myalgia	8	0.39 (0.23-0.56)
Polymyalgia rheumatica	30	0.34 (0.28-0.41)
Unilateral visual loss	11	0.24 (0.14-0.36)
Bilateral visual loss	7	0.15 (0.07-0.27)
Any visual symptom	35	0.37 (0.30-0.44)
Vertigo	4	0.11 (0.05-0.19)

*Includes results of all eligible studies, including those that reported clinical features for patients with positive biopsy results only. CI indicates confidence interval.

Temporal arteritis is more common among women than men, and among white than African American persons. The LRs do not reflect this observation, perhaps because referring physicians incorporated this knowledge into their decisions about which patients to refer for biopsy. However, if one pools

the data from all eligible studies, including those that reported only patients with positive temporal artery biopsy results, TA was 2.1 times more common in women than men (Table 6). Temporal arteritis among African American patients in published reports is restricted largely to small case series,[66] and white patients constituted 86% of all patients with positive biopsy results.

Among patients referred for biopsy, the average age of those with positive results was 73 years; this was only 3.8 years (95% CI, 2.1-5.4) older than the average age of patients with negative results. Age was, however, a valuable criterion for predicting the likelihood of TA. Reviewing data for all eligible studies, including those that reported only patients with positive biopsy results, 26 studies provided sufficient data to determine the age range of patients with biopsy-proven TA. Only 2 patients among a total of 1435 patients were younger than 50 years; this resulted in a sensitivity of 99% for the criterion of age older than 50 years. This suggests that clinicians should only consider TA as a diagnostic possibility in a person younger than 50 years if multiple characteristic or high-probability features are present.

Table 5. Likelihood Ratios for Signs, Demographic, and Laboratory Data Among Patients With Suspected Temporal Arteritis*

Variable/References	No. of Patients With Data on Variable†	Positive LR (95% CI)	Negative LR (95% CI)
Signs and Demographics			
Optic atrophy or ischemic optic neuropathy[40,50]	142	1.6 (1.0-2.5)	0.8 (0.58-1.1)
Any funduscopic abnormality[29,35,50,52]	745	1.1 (0.8-1.4)	1.0 (0.92-1.1)
Scalp tenderness[31,33-35,52]	923	1.6 (1.2-2.1)	0.93 (0.86-1.0)
Synovitis[29,37,46,52]	734	0.41 (0.23-0.72)	1.1 (1.0-1.2)
Beaded temporal artery[42,52]	323	4.6 (1.1-18.4)	0.93 (0.88-0.99)
Prominent or enlarged temporal artery[36,39,42,44,52]	508	4.3 (2.1-8.9)	0.67 (0.5-0.89)
Tender temporal artery[36,39-42,50-52]	755	2.6 (1.9-3.7)	0.82 (0.74-0.92)
Absent temporal artery pulse[41,52]	68	2.7 (0.55-13.4)	0.71 (0.38-1.3)
Any temporal artery abnormality[29,31-33,37,43,46]‡	1559	2.0 (1.4-3.0)	0.53 (0.38-0.75)
Male sex[29,31-37,40-43,45-47,49-52]	2565	0.83 (0.72-0.96)	
White Race[32,35,37,40,50]	565	1.1 (0.99-1.2)	
Laboratory Data			
Anemia[31,32,34,35,37,46,47,49]	1057	1.5 (0.82-2.9)	0.79 (0.6-1.0)
ESR abnormal[32,37,42,46,49-51]	941	1.1 (1.0-1.2)	0.2 (0.08-0.51)
ESR >50 mm/h[35,47,49,50]	259	1.2 (1.0-1.4)	0.35 (0.18-0.67)
ESR >100 mm/h[35,49,50]	220	1.9 (1.1-3.3)	0.8 (0.68-0.95)

*LR indicates likelihood ratio; CI, confidence interval; and ESR, erythrocyte sedimentation rate.
†Includes only studies that report results for patients with both positive and negative biopsy results.
‡Includes only abnormalities that are not classified more specifically by the cited studies. The true incidence of any abnormality is presumably higher but cannot be calculated from the primary data.

Table 6. Sensitivity of Signs, Demographic, and Laboratory Features Among All Patients With Positive Temporal Artery Biopsy Results*

Variable	No. of Studies With Data on Variable	Sensitivity (95% CI)
Signs and Demographics		
Optic atrophy or ischemic optic neuropathy	4	0.29 (0.10-0.57)
Any funduscopic abnormality	6	0.31 (0.14-0.54)
Scalp tenderness	13	0.31 (0.20-0.44)
Beaded temporal artery	3	0.16 (0.07-0.28)
Prominent or enlarged temporal artery	6	0.47 (0.40-0.54)
Tender temporal artery	13	0.41 (0.30-0.52)
Absent temporal artery pulse	6	0.45 (0.26-0.66)
Any temporal artery abnormality	16	0.65 (0.54-0.74)
Male sex	40	0.32 (0.29-0.35)
White race	11	0.86 (0.62-0.97)
Laboratory Data		
Anemia	22	0.44 (0.34-0.54)
ESR abnormal	24	0.96 (0.93-0.97)
ESR >50 mm/h	14	0.83 (0.75-0.90)
ESR >100 mm/h	10	0.39 (0.29-0.50)

*Includes results of all eligible studies, including those that reported clinical features for patients with positive biopsy results only. CI indicates confidence interval.

Accuracy of the Laboratory Evaluation for the Diagnosis of TA

While the primary purpose of this analysis was to determine the operating characteristics of the history and physical examination in diagnosis, clinicians usually obtain an ESR before determining which patients have sufficient likelihood of TA to justify a referral for biopsy. We, therefore, chose to evaluate the test characteristics of the ESR. The mean value for patients with disease was 88 mm/h; that for patients without disease was a mean of 10 mm/h lower (95% CI, 4-25). This difference was not statistically significant.

Results of the ESR measurement were a valuable guide to clinicians; a low or normal level was more likely to rule out disease than a high value was likely to rule in disease. Previously, Miller and colleagues[72] had determined normal ESR values among 27912 adults without apparent disease and suggested defining the upper limit of normal ESR as either age/2 (for men) or as (age + 10)/2 (for women). In our source studies, authors most commonly did not define "normal" ESR; it was not possible to determine if these normal values were adjusted for age. With this caveat, a normal ESR made TA unlikely; the negative LR for abnormal ESR was 0.2 (Table 5). When we separately analyzed the

pooled data from all studies, only 4% of patients with positive temporal artery biopsy results and data on ESR had a normal value. If one uses a less strict cutoff point, even an ESR of less than 50 mm/h substantially reduces the probability of disease (LR=0.35) This value is lower than the negative LR of any finding on history or physical examination.

In contrast to clinical lore, a high ESR was less useful in identifying those with TA among all patients referred for biopsy. This likely relates to the verification bias inherent in patient selection for the eligible studies, as referring physicians would have had knowledge of the ESR before recommending a biopsy. While an ESR of greater than 100 mm/h conferred a positive LR of 1.9, this value is less than the most highly predictive values in the history and physical examination. In contrast, mean ESR values were similar for both patients with and without positive temporal artery biopsy results.

Anemia was present in 44% of patients with biopsy-proven TA. This finding was present in a similar number of patients who had negative biopsy results. Mean hemoglobin levels were similar between patients with positive and negative biopsy results (11.6 vs 12.4 g/dL, respectively); the lack of anemia was not helpful in ruling out disease.

ARE THESE CLINICAL FEATURES EVER NORMAL?

The presence of particular findings in the history and physical examination in patients with negative temporal artery biopsy results does not imply that these findings are "normal" or common in patients without disease. Rather, it suggests that other conditions that clinicians may initially confuse for TA have overlapping clinical features. The frequency of such findings in randomly selected individuals of the same age would likely be lower than the frequency among patients in this review with negative biopsy results.

Several studies have followed patients with negative biopsy results to determine their ultimate or correct diagnoses. Chmelewski and colleagues[35] reported the outcomes of 98 patients undergoing temporal artery biopsies over a 5-year period at their institution. Among the 68 patients with negative biopsy results, 15 proved to have neurologic disorders (including migraine, stroke, and optic neuropathy), 14 had PMR, 10 had other rheumatologic disorders (including vasculitis other than TA, rheumatoid arthritis, and CREST [calcinosis, Raynaud disease, esophageal dysmotility, sclerodactyly, telangiectasia] syndrome), and 4 had fever of unknown origin. Miscellaneous diagnoses included sinusitis, endocarditis, amyloidosis, and malignancy. In another biopsy series, Roth and colleagues[40] studied 33 patients with a clinical suspicion of TA but negative biopsies. The most common diagnoses, in descending order, were joint disease (degenerative or rheumatoid), malignant lymphoma, arteriosclerotic carotid artery disease, diabetes mellitus, and ischemic optic neuropathy.

In our first clinical scenario, the history of bitemporal headache and a modestly elevated ESR would be among those factors that may lead a clinician to suspect TA. In this setting, one would seek the potential additional history of jaw claudication or diplopia, and determine the presence of a prominent, tender, or beaded temporal artery. If present, these factors would substantially increase the likelihood of positive temporal artery biopsy results.

In the second scenario, TA is among the diagnostic considerations for transient partial monocular visual loss in the setting of a constitutional illness. The history in this case is sufficiently compelling to justify a temporal artery biopsy. Given the high prior probability and the poor performance of historical and examination features in excluding disease, an otherwise normal history and physical examination would not sufficiently reduce the likelihood of TA to avoid the need for a temporal artery biopsy. A normal ESR would, however, reduce the likelihood of disease by a factor of 0.2 and should prompt consideration of alternative diagnoses.

THE BOTTOM LINE

Available data suggest that many of the clinical features commonly found in patients with the disease are unhelpful in predicting the likelihood of positive temporal artery biopsy results. Our study evaluates the predictive value of clinical features among patients who are already clinically suspected of having the disease, as determined by the clinicians who referred them for biopsy. While we could not determine, from the primary studies, the factors that went into the decision to refer for biopsy, certain clinical features modified the likelihood of disease among these patients. It is likely that these same clinical factors would be useful to consider at initial evaluation, even before the decision to proceed to biopsy. In addition, the verification bias inherent in this analysis makes the significance of our results greater, since they help to predict biopsy results even among patients who have a higher prior probability of disease than do unselected patients with any particular clinical feature.

When taking a history in a patient with possible TA, jaw claudication and diplopia substantially increase the probability of positive biopsy results (positive LRs=4.2 and 3.4, respectively). No historical findings help rule out the diagnosis by their absence. Among physical examination findings, synovitis makes the diagnosis of TA less likely, while beaded, prominent, enlarged, and tender temporal arteries each increase the likelihood of positive biopsy results. Beaded, prominent, or enlarged arteries confer the highest positive LRs of any clinical or laboratory feature and substantially increase the probability that a patient with suspected TA will have positive biopsy results. While these findings increase the chance of having TA, they are variably sensitive, from 16% (beaded temporal artery) to 65% (any temporal artery abnormality).

The results of tests of ESR alter the likelihood of positive biopsy results. A normal ESR (LR=0.2) or ESR less than 50 mm/h (LR=0.35) each make posi-

tive biopsy results unlikely, but setting the ESR threshold at 100 mm/h is less efficient, as patients with an ESR less than 100 mm/h have an LR (0.8) that only slightly lowers the likelihood of disease. Among patients clinically suspected of disease, those with an ESR greater than 100 mm/h have a modestly increased likelihood of biopsy-proven TA (LR=1.9)

The clinician faced with a patient who may have TA has a difficult challenge. The goal is to rule out other morbid conditions that may mimic TA, to avoid unnecessary evaluation, and to quickly and correctly identify and treat patients who do in fact have the disorder. Given the extreme difference in prevalence of TA between the general population (<1%) vs those referred for temporal artery biopsy (39%), we infer that clinicians are adept at identifying patients at high risk for disease. Many clinicians choose to treat patients they have referred for biopsy with corticosteroids, in the absence of contraindication, pending biopsy results. While this strategy would appear particularly wise in the presence of a factor that we have shown predicts likelihood of disease, this approach deserves further study.

Our review of clinical series of patients with suspected TA does not allow a determination of the predictive value of selected combinations of clinical and laboratory features. In addition, it is not possible to determine from our data whether certain combinations of features would sufficiently increase the likelihood of disease that a clinician should treat presumptively for TA and not perform a biopsy at all. The morbidity of a prolonged course of corticosteroids, however, is such that most clinicians would favor confirmation of disease by biopsy even if the clinical probability is high.

Our analysis demonstrates that a limited number of clinical features substantially modify the probability of the diagnosis of TA among patients suspected of having the disease. Ultimately, the clinician must integrate multiple clinical factors in order to optimize diagnostic and therapeutic strategies for patients with suspected TA.

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Every idea is an incitement. . . . Eloquence may set fire to reason.
—Oliver Wendell Holmes (1841-1935)