Rate of Discordant Findings in Bilateral Temporal Artery Biopsy to Diagnose Giant Cell Arteritis

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ABSTRACT. ***Objective.*** To determine to what extent performing simultaneous bilateral temporal artery biopsies might increase the diagnostic sensitivity in giant cell arteritis (GCA).

Methods. In total 173 consecutive pathology reports of temporal artery biopsies were reviewed for histological findings by a single pathologist. The rate of discordance of biopsy results was calculated in patients with GCA.

Results. Biopsies were performed bilaterally and simultaneously in 132 cases; 51 had positive results. In 38 the biopsy was positive on both sides (concordant results), while in 13 patients only one side was positive (discordant results), reaching a discordance rate of 13/51 = 0.255. Therefore 12.7% of the patients (one-half of the discordance rate) could have been misdiagnosed as biopsy-negative had a biopsy been done only unilaterally in those 51 cases.

Conclusion. These data suggest that performing bilateral temporal artery biopsies increases the diagnostic sensitivity of the procedure by up to 12.7%, compared to unilateral biopsies. (J Rheumatol First Release Feb 15 2009; doi:10.3899/jrheum.080792)

Key Indexing Terms:
TEMPORAL ARTERITIS BIOPSY DIAGNOSIS GIANT CELL ARTERITIS

The diagnosis of giant cell arteritis (GCA) is suspected on the basis of its typical clinical presentation combined with elevated acute-phase reactants[1]. In the majority of cases the diagnosis is confirmed by temporal artery biopsy (TAB) demonstrating characteristic inflammation of the artery. However, the arterial wall inflammation is segmental, and the 2 temporal arteries may be unevenly involved. Therefore, histological signs of inflammation may be missed in TAB performed in arteritis-free segments. As a result, in most studies 10%–20% of TAB are reported as negative in patients with GCA, although the rate may be as high as 40%[2-5].

A negative TAB often makes the diagnosis of GCA uncertain, and necessitates further diagnostic investigations to exclude other medical conditions. A positive biopsy certainly carries significant assurance for both patient and physician, and may ease the acceptance of treatment-related adverse effects. One may assume that by taking bilateral samples the yield of TAB would increase, but previous studies showed a very wide range of discordance rates of bilateral TAB results in patients with GCA, varying from 3% to 45%[6-12]. We undertook this study to determine to what extent performing simultaneous bilateral TAB might increase the diagnostic sensitivity in patients with GCA.

MATERIALS AND METHODS

Consecutive TAB pathology reports over 10 years (1996-2005) at Shaare-Zedek Medical Center (SZMC) were reviewed for histological findings. All arteries were processed routinely according to the commonly accepted approach: the artery was initially fixed in formalin, then the specimen was cut into serial 2–3 mm-long slices, followed by embedding in paraffin. Each slice was then cut transversely, and stained with hematoxylin and eosin.

All slides were reviewed for this study by a single experienced pathologist. TAB was considered positive when a mononuclear cell infiltrate was seen in the vessel wall, with or without giant cells, in association with disruption of the internal elastic lamina. Biopsies were performed either prior to or within 3 days of commencing steroid therapy. The patients' charts were reviewed for clinical data. Approval of the SZMC Ethics Committee was granted for this study.

The rate of discordance of biopsy results was calculated in biopsy-positive patients with GCA who had bilateral TAB. Based on the discordance rate, the rate of biopsy-positive GCA patients that could have been misdiagnosed as biopsy-negative had a TAB been done only unilaterally was calculated. Assuming that the chance of obtaining a TAB from each side was identical, the calculated rate of misdiagnosis as "biopsy-negative" (if only unilateral biopsies are performed) was actually one-half of the discordance rate. It was calculated by a formula assessing the gain in sensitivity of simultaneous bilateral TAB (compared to unilateral TAB). The formula is $[(C + D) - (C + D/2)]/C + D$, where C is the number of patients with positive biopsies on both sides (concordant results), and D is the number of patients with

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Accepted for publication November 27, 2008.

a positive biopsy on one side and a negative biopsy on the other side (discordant results). The formula may be simplified as D/2(C + D).

RESULTS

TAB reports of 173 individuals were reviewed. The common practice at SZMC is to perform bilateral TAB simultaneously; however, some patients agree to biopsy one side only. TAB was performed bilaterally and simultaneously in 132 cases, and unilaterally in 41 cases. Fifty-one of the 132 patients who had bilateral biopsies had positive TAB. In 38 of these 51 patients, TAB was positive on both sides (concordant results), while in 13 patients only one side was positive (discordant results), resulting in a discordance rate of 13/51 = 0.255. TAB was positive on the right side in 7 patients and on the left side in 6 patients. Assuming that the chance of obtaining TAB from each side was identical, a diagnosis of biopsy-positive GCA would have been missed in one-half of these 13 patients. The formula for this group of patients then is [51 – (38 + 13/2)]/51 = 0.127; i.e., that 12.7% of these biopsy-positive GCA patients could have been misdiagnosed as biopsy-negative had a TAB been done only unilaterally.

In some patients the length of the TAB sample was small. It is assumed that the ability to detect inflammation in small samples decreases as a result of the segmental characteristic of the inflammatory infiltrate. Lengths of TAB segments in the 13 patients with discordant results are presented in Table 1. In 8 cases the positive side was longer than the negative side, while in 5 cases the negative side was equal in length or longer than the positive side. A TAB length of 5 mm or less was considered inadequate by a recent study[13]. Excluding cases with segments of 5 mm or less, the discordance rate decreased somewhat to 19%, so that 9.5% of biopsy-positive GCA patients with biopsies longer than 5 mm could still have been misdiagnosed as biopsy-negative had a biopsy been done unilaterally. Lengths of TAB segments in this subgroup were not significantly different between the positive and the negative sides (15.5 ± 7.3 and 12.4 ± 4.7 mm, respectively; p = 0.445, Mann-Whitney test).

Table 1. Lengths of temporal artery segments in 13 patients with discordant biopsy results.

Patient	Negative Side, mm	Positive Side, mm
1	4	7
2	5	8
3	5	10
4	5	35
5	6	17
6	8	7
7	10	10
8	10	15
9	10	23
10	15	8
11	15	15
12	18	30
13	20	15

DISCUSSION

We reviewed 51 cases with biopsy-positive GCA who had simultaneous bilateral TAB. The TAB discordance rate in this group was 25%, suggesting an increase in the diagnostic sensitivity in patients with GCA by up to 12.7% as compared to results from unilateral TAB. It is possible that some of these cases would have been misdiagnosed as "no GCA," resulting in a lost opportunity for the necessary treatment. There are no independent validating criteria to determine whether GCA is present when TAB is negative. The American College of Rheumatology criteria for the classification of GCA[14] may assist in making the diagnosis. However, classification criteria function best in studying groups of patients, and less well when used for diagnosing individual cases. Therefore a positive biopsy result certainly carries significant assurance for both patient and physician regarding the final diagnosis.

Another approach for evaluating the rate of misdiagnosis from unilateral biopsies is to assess the sensitivity of unilateral TAB compared to bilateral TAB when biopsies are performed sequentially (the contralateral side is biopsied only when the first biopsy is negative). This is calculated by the formula suggested by Hall and Hunder[6]. The formula we have suggested is appropriate for evaluating simultaneous, bilateral biopsies rather than sequential biopsies (both bilateral and unilateral).

For the purpose of calculation, we assumed that the chance of obtaining a TAB specimen from each side was identical. In practice, this may not necessarily be true: if a unilateral biopsy is planned, the tendency is to perform it on the symptomatic side and not randomly, when patients present with unilateral signs or symptoms. Thus the discordance rate presented here may be an overestimate. However, in studies reporting sequential biopsies the site of the first biopsy was chosen according to localizing signs or symptoms[15]. Gonzalez-Gay, *et al* report that in 5 of 57 such patients (9%) the diagnosis was made only after contralateral TAB was performed[15]. The first TAB was of sufficient length (3 cm or longer). Using sequential biopsies, Hall and Hunder calculated that 14% of GCA patients were diagnosed only because TAB was performed on the second side[6].

The method described above for calculating discordant TAB rates was applied to analyze other studies[6-12] (Table 2). Those studies differed in their methodologies. Three studies included cases with bilateral negative biopsies as "concordant results," disregarding that these individuals do not have GCA, resulting in a low discordance rate in those studies[10-12]. Such cases were not included in Table 2. In addition, in 3 studies[8,9,11] and in our study both arteries were biopsied simultaneously; in 2 studies[6,7] arteries were biop-

Table 2. Rate of discordant results of temporal artery biopsies in patients with biopsy-positive GCA who had bilateral biopsies. In all studies, only patients who had bilateral biopsies of which at least one side was positive (biopsy-positive GCA) were included here. Patients with unilateral biopsies or with bilateral negative biopsies were excluded from this calculation.

Study	Biopsy Sequence	Biopsy-positive GCA Patients with Bilateral Biopsies, n	Patients with Positive Biopsy on 1 side only, n	Discordance Rate, %*
Hall and Hunder[6]	Sequential	41	12	29
Sorensen and Lorenzen[7]	Sequential	46	7	15
Ponge[8]	Simultaneous	38	17	45
Baldursson[9]	Simultaneous	50	10	20
Boyev[10]	Sequential or simultaneous	33	6	18
Danesh-Meyer[11]	Simultaneous	39	1	3
Pless[12]	Sequential or simultaneous	20	8	40
Current series	Simultaneous	51	13	25

* Assuming that the chance of obtaining a biopsy from each side was identical, a diagnosis of biopsy-positive GCA would have been overlooked in one-half of these cases.

sied sequentially, and 2 studies included biopsies performed either sequentially or simultaneously[10,12]. To make the data in Table 2 more uniform, we included from those studies only patients with biopsy-proven GCA who had bilateral biopsies of which at least one side was positive. Patients with unilateral biopsies or with bilateral negative biopsies were excluded from this calculation. Nevertheless, the range of discordance rates was still wide (3%–45%).

Our data suggest that performing bilateral TAB increases the diagnostic sensitivity in patients with GCA. Whether a long unilateral TAB specimen would be equal in its diagnostic sensitivity to shorter-specimen, bilateral TAB is difficult to determine using our data, as the number of such long unilateral biopsy specimens was very limited. Choosing the simultaneous or sequential approach in a given individual will probably depend on the nature of symptoms and signs of the disease and the pre-test probability of GCA.

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