Effect of biopsy length on the rate of positive temporal artery biopsies

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ABSTRACT

Objectives. To investigate the relationship between temporal artery biopsy (TAB) length and the diagnostic sensitivity for giant cell arteritis (GCA).

Methods. TAB pathology reports were reviewed for histological findings and formalin-fixed TAB lengths. The patient’s charts were reviewed for clinical data. TAB was considered positive if there was a mononuclear cell infiltrate in the vessel wall. Biopsy-negative GCA was diagnosed when patients fulfilled the American College of Rheumatology classification criteria, in addition to favorable rapid response to steroid therapy. Patients were divided into 3 groups according to the clinical and histological features: Biopsy-positive GCA, biopsy-negative GCA, and no GCA.

Results. 305 TAB reports of 173 individuals were reviewed. When only GCA patients TAB-positive and TAB-negative were considered, TAB in the biopsy-positive patients was significantly longer than in biopsy-negative cases (p=0.008). The rate of positive biopsies was only 19% with TAB length of 5 mm or less, but increased to 71-79% with TAB lengths of 6-20 mm, and to 89% when TAB length was longer than 20 mm. Only 3% of positive biopsies were 5 mm or shorter, compared to 27% of TAB in biopsy-negative GCA cases (p<0.001).

Conclusion. TAB with post-fixation length shorter than 5 mm carries an increased biopsy-negative rate therefore longer TAB length is required for accurate diagnosis. Increasing post-fixation TAB length beyond 20 mm may further increase the rate of positive biopsies, although data were insufficient in that regard.

Introduction

In Western countries giant cell is arteritis (GCA) is the most common form of primary systemic vasculitis in middle-aged and older adults (1, 2). The diagnosis of GCA is suspected on the basis of the clinical presentation and elevation of acute phase reactants. It is customarily confirmed by a temporal artery biopsy (TAB) demonstrating the presence of characteristic inflammation of the temporal arteries. Positive TAB has very high specificity for GCA diagnosis, approaching 100%. However, its sensitivity is lower, in the range of 80-90%, and in some reports it was as low as 60% (3, 4). One of several factors that have been advanced to explain false negative TAB results is the discontinuous or segmental nature of the inflammatory involvement in GCA (5-8), resulting in missing the histological changes in some segments.

The resultant widely accepted consensus is that a longer TAB segments should be excised to maximize the chance of visualizing arterial segments with inflammatory changes. However, the procedure for obtaining longer TAB segments may require longer time and may also leave longer scars. Although it has been recommended that large segments of 2-3 cm, 3-5 cm, or even 4-6 cm be taken (4, 8-14), the TAB length yielding optimal diagnostic sensitivity remains unknown.

Several studies tried to address this question (14-21). However, most of those studies compared biopsy-positive GCA patients to a combined group of patients with biopsy-negative GCA and patients with no GCA. This may make interpretation of the data somewhat difficult. Inclusion of “no GCA” cases may bias the results, as in these cases TAB at any length would always be negative. In contrast, longer TAB in biopsy-negative GCA cases may theoretically result in finding positive segments. We therefore undertook this study of comparing biopsy-positive and biopsy-negative GCA in an attempt to determine the relation between TAB length and diagnostic sensitivity for GCA.
Patients and methods
Consecutive TAB pathology reports, over a period of 10 years (1996-2005) in one medical center, were reviewed for histological findings and lengths of formalin-fixed TAB specimens. The artery was processed routinely according to the commonly accepted approach: it was initially fixed in formalin. Thereafter the specimen was cut into serial 2 mm long slices, followed by paraffin embedding. The slices were cut in step sections and stained with hematoxylin and eosin. Reports had been originally given by 4 different pathologists. All slides were reviewed for this study by a single experienced pathologist. There was agreement in regard to biopsy results in all but 2 cases, which were subsequently excluded.

The patients’ charts were reviewed for clinical data. Ethics approval was granted. Vasculitides other then GCA, which might involve the temporal arteries, were ruled out by initial and follow-up clinical data. Patients on steroid therapy at any dose for 3 days or more prior to the day of the biopsy were not included (n=2). Patients were divided into 3 groups according to the clinical and histological features: biopsy-positive GCA, biopsy-negative GCA, and no GCA.

TAB was considered positive when mononuclear cell infiltrates in the vessel wall, with or without giant cells, were observed. Cases with inflammatory infiltrate confined to the adventitia or involving the vasa vasorum were considered positive. In cases with bilateral positive biopsies, both were included as “biopsy-positive GCA”. When TAB was positive on one side and negative on the other side, the positive biopsy was included under “biopsy-positive GCA” and the negative side was considered as “biopsy-negative GCA”.

Patients with negative TAB were diagnosed as biopsy-negative GCA when the ACR classification criteria (22) were met, GCA symptoms and signs of inflammation improved within 3 days of corticosteroid therapy (40 mg/d of prednisone or more), and no other condition relevant to the patient’s symptoms was diagnosed during a follow-up period of 6 months. Two rheumatologists (GN, GSB) reviewed the medical information and reached consensus on the diagnosis of biopsy-negative GCA. Patients with negative TAB not fulfilling the ACR classification criteria, or with no response to corticosteroid therapeutic trial, or diagnosed with another condition explaining their GCA-like symptoms, were considered “no GCA”.

Results
Three hundred and five TAB reports of 173 individuals were reviewed. Biopsies were performed bilaterally in 132 cases, and unilaterally in 41 patients. Table I shows the rate of positive TAB in relation to the TAB length, and the mean TAB length of each group of patients. Considering all biopsies, the rate of positive TAB was very low (8%) when TAB length was 5 mm or less. However the rate approached 50% when TAB length was 11 mm or more, and exceeded 50% with TAB longer than 20mm (Table I). However, as argued above, inclusion of “no GCA” cases may bias the results, as in these cases TAB at any length would always be negative.

When only GCA patients (TAB-positive and TAB-negative) were considered (Table II), TAB in the biopsy-positive patients was significantly longer than in biopsy-negative cases (p<0.008). The rate of positive biopsies was only 19% with TAB length of 5 mm or less, but increased to 71-79% with TAB lengths of 6-20mm, and to 89% when TAB length was longer than 20mm. Only 3% of positive biopsies were 5 mm or shorter, compared to 27% of TAB in biopsy-negative GCA cases (p<0.001).

Discussion
The optimal size of a TAB is still debated (8). Several studies approached

<table>
<thead>
<tr>
<th>Table I. Temporal artery biopsy (TAB) lengths comparing biopsy-positive GCA, biopsy-negative GCA, and no GCA.</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>TAB length (mm)</strong></td>
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<tr>
<td>----------------------</td>
</tr>
<tr>
<td>Biopsy-positive GCA, n (%)</td>
</tr>
<tr>
<td>Biopsy-negative GCA, n (%)</td>
</tr>
<tr>
<td>No GCA, n (%)</td>
</tr>
<tr>
<td>All, n (%)</td>
</tr>
</tbody>
</table>

*p<0.01 compared to the other groups.

<table>
<thead>
<tr>
<th>Table II. Temporal artery biopsy (TAB) lengths of biopsy-positive GCA compared to biopsy-negative GCA.</th>
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<tbody>
<tr>
<td><strong>TAB length (mm)</strong></td>
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<tr>
<td>----------------------</td>
</tr>
<tr>
<td>Biopsy-positive GCA, n (%)</td>
</tr>
<tr>
<td>Biopsy-negative GCA, n (%)</td>
</tr>
<tr>
<td>All, n (%)</td>
</tr>
</tbody>
</table>

*p=0.008 compared to biopsy-negative GCA.
Temporal artery biopsy length in GCA / G.S. Breuer et al.

Table III. Mean lengths of positive and negative temporal artery biopsies (TAB): published series.

<table>
<thead>
<tr>
<th>Author (Ref.)</th>
<th>Positive/Negative (n)</th>
<th>Mean length positive TAB (mm)</th>
<th>Mean length negative TAB (mm)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Kent (14)</td>
<td>8/62</td>
<td>22</td>
<td>13</td>
<td>0.1</td>
</tr>
<tr>
<td>Roth (15)</td>
<td>7/11*</td>
<td>12</td>
<td>17.2*</td>
<td>NS</td>
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<tr>
<td>Taylor-Gjeeve (16)</td>
<td>38/98</td>
<td>20.7</td>
<td>16.9</td>
<td>0.058</td>
</tr>
<tr>
<td>Sudlow (17)</td>
<td>50/135</td>
<td>10.6</td>
<td>8.6</td>
<td>&lt;0.005</td>
</tr>
<tr>
<td>Albertini (18)</td>
<td>7/28</td>
<td>22</td>
<td>22</td>
<td>NS</td>
</tr>
<tr>
<td>Chakrabarty (19)</td>
<td>20/100</td>
<td>9</td>
<td>10</td>
<td>NS</td>
</tr>
<tr>
<td>Mahr (20)</td>
<td>223/1297</td>
<td>13.4</td>
<td>13.3</td>
<td>0.72</td>
</tr>
<tr>
<td>Gabriel (21 )</td>
<td>172/563</td>
<td>36.3</td>
<td>37.1</td>
<td>NS</td>
</tr>
<tr>
<td>Current</td>
<td>108/48*</td>
<td>12.7</td>
<td>10.1*</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

*Negative TAB were biopsy-negative GCA.

References
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