Temporal artery biopsy in the diagnosis of giant cell arteritis: Bigger is not always better

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ABSTRACT

Objective: Accurate early giant cell arteritis (GCA) diagnosis can be established through temporal artery biopsy (TAB). We herein investigate the relationship between specimen length and positive TAB result in a tertiary-care hospital in Germany during a 8-year period. Secondarily, we studied the relationships of specific epidemiological and laboratory parameters with positive TABs.
Method: We retrospectively reviewed the medical records of all patients with suspected GCA, who underwent TAB in our institution.
Results: The total sample consisted of 116 patients with a mean age of 76.1 (SD 7.7) years. Mean specimen length post-fixation was 0.94 cm (SD 0.49). The TAB(+) group consisted of 64 patients (55.2%). The specimen length was comparable in the two groups (0.96 cm vs 0.91 cm, p = 0.581). Twenty six TAB(+) patients (41%) had a post-fixation specimen longer than 1 cm, comparable with the respective percentage in the TAB(−) group (42%, p = 1). All laboratory tests performed were statistically significantly different in the two groups.
Conclusion: We conclude that TAB length is not associated with the TAB diagnostic yield in patients with clinical suspicion of GCA.

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1. Introduction

Giant cell arteritis (GCA), also known as temporal arteritis or Horton disease, is a granulomatous vasculitis targeting large- and medium-sized arteries. It can progress as a sight-threatening condition with potentially devastating complications, i.e. irreversible visual loss, if not diagnosed and treated promptly. The American College of Rheumatology (ACR) developed in 1990 a five-point scoring system, based on epidemiological, routine clinical and laboratory parameters, to help identify individuals at higher risk for GCA.[1]

Accurate early GCA diagnosis can be established through temporal artery biopsy (TAB), the widely accepted tool for this purpose. Histological examination typically reveals granulomatous inflammation with giant cells located at the junction between the intima and media.[2] Although treatment should not be delayed in anticipation of the biopsy result,[3] histological diagnosis is a central component of GCA management. A negative biopsy can protect the patient from prolonged unnecessary corticosteroid treatment. On the other hand, a negative biopsy result does not rule out GCA, as it can occur in up to 30% of cases.[4]

The issue of the TAB specimen length has been discussed in the literature but remains controversial. GCA is a segmental disease and this is reflected in the histological findings, which can range from inflammation of the adventitia and internal elastic lamina to transmural involvement. Thus, it is suggested that bigger specimens could minimize false-negative results.

The British Society of Rheumatology (BSR) recommends a minimum TAB length of 10 mm and an optimum length of 20 mm.[5] A multicenter study of 1520 TAB specimens considers a length of 5 mm sufficient to establish the diagnosis with accuracy,[6] whereas Kaptanis et al. report no clear benefit in harvesting specimens longer than 6 mm post fixation.[3] Another retrospective multicenter

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study of 966 biopsies sets the cut-off point for higher rate of positive results at 7 mm, recommending a specimen length of approximately 10 mm to eliminate discrepancies.[7]

We herein investigate the relationship between specimen length and positive TAB result in a tertiary-care hospital in Germany during a 8-year period. Secondarily, we studied the relationships of specific epidemiological and laboratory parameters with positive TABs.

2. Methods

2.1. Surgical technique

In our hospital, most TABs are primarily performed in the operating room by surgical trainees under consultant supervision. The superficial temporal artery is palpated and then outlined with a marking pen. In cases of non-palpable artery, a Doppler probe is used to locate it in the preauricular region and trace it to the temporal region. Subsequently, lidocaine 1% is locally infiltrated and a 2–3 cm incision is made through the skin and superficial dermis. Dissection is continued with scissors until the artery, lying on the superficial temporal fascia, is exposed. The vessel is then dissected from the surrounding tissue and ligated prior to division with 3/0 Polyglactin ties. The resected artery is fixed in formalin. The subcutaneous tissue is closed with 3/0 Polyglactin sutures and skin closure is accomplished by means of several 5/0 Prolene sutures.

2.2. Histology

The obtained specimens were controlled histologically after fixation in 10% formalin. The slides were stained with H&E and van Gieson, a special stain for better depiction of the elastic fibers. Microscopically, in positive specimens, a partial destruction of the wall by accumulation of inflammatory cells, including multinucleated giant cells of Langhans or foreign body type, was observed. Inflammation was centred at the intimal-medical junction with consequent fragmentation, degeneration and dissolution of the internal elastic lamina. The presence of perivascular inflammation in the absence of inflammatory changes in the vessel wall was a diagnostic criterion to exclude temporal arteritis.

2.3. Data collection

We retrospectively reviewed and analyzed the medical records of all patients with suspected GCA, who underwent TAB from January 2009 to December 2016 in our institution. Insufficient samples and patients with systemic vasculitis other than GCA were excluded from the study. Patients were divided into two groups based on histopathological diagnosis, i.e. positive or negative for GCA. Both groups were compared in terms of preoperative parameters, including demographics, i.e. gender, age, as well as blood test results, i.e. erythrocyte sedimentation rate (ESR) in the first and second hour, C-reactive protein and platelets.

2.4. Statistical analysis

Continuous data are presented in mean − standard deviation form. Categorical variables were compared using the two-tailed Fisher's exact test, and continuous ones using the two-tailed Student's t-test. A p-value of less than 0.05 was considered statistically significant. Multivariate analysis using logistic regression was employed to identify potential independent determinants of a positive TAB result. Data analyses were performed using SPSS 23 (IBM Corp., Armonk, N.Y., USA).

3. Results

One hundred eighteen patients were referred with a clinical suspicion of GCA and underwent TAB in our institution over the study time period. Two of them did not meet the inclusion criteria and were excluded from the study (one specimen with no dimension recorded and one insufficient sample). The total sample consisted of 116 patients, 49 male (42.2%) and 67 female (57.8%). No patient was bilaterally operated. Overall mean age was 76.1 (SD 7.7) years. The youngest patient was 57 years old and the oldest 92. Mean ESR was 53.4 (normal range <30 mm/h, SD 31.2) after the first hour and 71.5 (SD 28.3) after the 2nd h. Mean CRP was 4.5 mg/dl (normal range <0.5 mg/dl, SD 6.26) and mean platelet count was 354 (normal range 150−350 $10^3/\mu L$, SD 133). Mean specimen length post-fixation was 0.94 cm (SD 0.49) whereas the other two dimensions had a mean length of 0.25 cm (SD 0.19 and 0.09) (Table 1).

No demographic differences were observed between the two groups. The TAB(+) group consisted of 64 patients (55.2%), whereas 52 biopsies were negative for GCA (44.8%, TAB(−) group). No specimen was classified as insufficient or indeterminate. The mean age of patients in the TAB(+) group was 76.9 years (7.7) vs. 75.2 (7.8) in the TAB(−) group (p = 0.25). The TAB(+) group consisted of 40 women (62.5%) and 22 men (37.5%) and the TAB(−) group consisted of 27 women (52%) and 25 men (48%, p = 0.25). All laboratory tests performed, were statistically significantly different in the two groups. Mean ESR after the first hour was 60.5 (31.5) in the TAB(+) group vs 44.6 (28.8) in the TAB(−) group (p = 0.006), while mean ESR after the 2nd h was 77.3 (26.2) in the TAB(+) group vs 64.5 (26.2) in the TAB(−) group (p = 0.015). Mean CRP was also significantly elevated in the TAB(+) group (5.53 vs 3.23 mg/dl, p = 0.049), although ESR elevation was higher, and platelet count was significantly lower in the TAB(−) group (297 vs 381, p = 0.001). The specimen length was comparable in the two groups (0.96 cm vs 0.91 cm, p = 0.581). All parameters mentioned above are summarized in Table 2. Twenty six TAB(+) patients (26/64, 41%) had a post-fixation specimen longer than 1 cm, comparable with the respective percentage in the TAB(−) group (22/52, 42%, p = 1).

The t-test for equality of means demonstrated that there was a significant difference in mean ESR after the first hour (p = 0.006), CRP (p = 0.049) and platelet count (p = 0.001) between the TAB(+) and TAB(−) groups. Moreover, performing a t-test for equality of variances demonstrated that the SD of all values, except for the ESR after the second hour, did not differ significantly among TAB(+) and TAB(−) cases. Logistic regression indicated that a five-variable model, consisting of age, specimen length post-fixation, ESR after the first hour, CRP and platelet count, can predict outcome in 70% of cases (compared to 55.2% in the null model). Only platelet count was statistically significant in multivariate logistic regression (Table 3).

Table 1
Demographics, laboratory tests and biopsy length of the entire cohort. All continuous variables are normally distributed and therefore presented as mean (standard deviation). Categorical variables are presented as absolute (n) and relative (%) frequencies.

Parameter	Value
Age (years)	76.1 (7.7)
Gender (Female)	67 (57.8%)
ESR - 1st hour (mm/h)	53.4 (31.2)
ESR - 2nd h (mm/2 h)	71.5 (28.3)
CRP (mg/dl)	4.5 (6.3)
Platelets (x10^3/μL)	354 (133)
Specimen length (cm)	0.94 (0.5)
Specimen 2nd dimension (cm)	0.25 (0.2)
Specimen 3rd dimension (cm)	0.25 (0.1)
GCA-positive specimens	64 (55.2%)