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Research Letter

Duration of Steroid Therapy and Temporal Artery Biopsy Positivity in Giant Cell Arteritis: A Retrospective Cohort Study

To the Editor:

Giant cell arteritis (GCA) is the most common large-vessel vasculitis that primarily affects older individuals.[1] Prompt diagnosis and treatment with empiric glucocorticoids (GCs) is important because GCA can lead to ischemic complications, including visual loss.[1,2]

Temporal artery biopsy (TAB) is commonly used to assist in the diagnosis of GCA. Historically, TAB has been the preferred diagnostic test for GCA; however, literature estimates vary, with sensitivities of TAB ranging from 24% to 77%.[3,4] This heterogeneity has been suggested to be due partly to the attenuation of biopsy findings due to GC exposure prebiopsy and skip lesions in the disease.[3] As such, the 2021 American College of Rheumatology Guidelines for GCA management recommend that a TAB should be completed within 14 days of GC initiation.[2] Data, however, are conflicting regarding how long biopsies remain positive. A prospective study by Maleszewski et al in 2017 included 40 individuals with biopsy-proven GCA who were randomly allocated to receive a second biopsy either 3, 6, 9, or 12 months after their initial diagnosis and treatment, and found that 44% of TABs continued to demonstrate arteritis 1 year after starting GCs.[2,5] And although temporal artery ultrasound has demonstrated better performance, data more compellingly indicate that findings often normalize with treatment.[6]

The aim of our study was to investigate how duration of GC exposure affected TAB positivity in a cohort of patients with suspected GCA.

This study was completed using secondary analysis of de-identified data from research that has received approval from the Hamilton Integrated Research Ethics Board. Data were derived from 2 sources: a previously reported trial[7] (ethics approval 06-2732) and a GCA research database (ethics approval 15-403-D). Written and informed patient consent regarding publication of material was obtained.

We extracted data from 2 cohorts: the McMaster GCA Database (n = 52) and individuals enrolled in the prospective trial of Rhéaume et al (n = 171).[7] Both cohorts consisted of individuals referred to rheumatologists in Hamilton, Ontario, Canada, for a possible diagnosis of GCA and who underwent a TAB. A diagnosis of GCA was made clinically, without criteria, using all available materials, including clinical evaluation, inflammatory markers, TAB, and imaging.

Individuals were stratified by weeks of GC treatment before TAB; those who received ≥ 6 weeks of therapy were pooled due to low numbers. The effect of GC therapy duration on TAB positivity was assessed using 2 methods: a 2-sided Cochran-Armitage trend test and multivariable logistic regressions using duration of GC therapy as both a categorical and nonpooled continuous variable, controlling for age, sex, and biopsy length. Sensitivity analyses were performed only on those diagnosed with GCA; we excluded individuals who underwent biopsy after 6 weeks, as biopsies performed at this time may not have been purely diagnostic.

The cohort contained 223 individuals, including 48 (21.5%) who were TAB-positive and 175 (78.5%) who were TAB-negative. Of the total cohort, 118 (52.9%) individuals were diagnosed with GCA, including all individuals who were TAB-positive. Of the 70 (40%) TAB-negative patients with GCA, 36 (51.4%) were diagnosed by magnetic resonance angiography and 34 (48.6%) on clinical grounds alone (Table 1). Patient age, sex, receipt of pre-TAB GCs, and TAB length were similar between groups. TAB-positive individuals were more likely to experience vision loss, jaw claudication, and constitutional symptoms, and have an elevated erythrocyte sedimentation rate and/or C-reactive protein. Forty-six (95.8%) TAB-positive cases and 152 (86.9%) TAB-negative cases received GCs before undergoing TAB (P = 0.81); 25 patients did not receive GCs. Fewer TABs were performed with longer duration of therapy (P < 0.01; Table 2). The Cochran-Armitage trend test did not demonstrate a temporal trend between weeks of treatment and TAB positivity (P = 0.11). Adjusted multivariable logistic regression similarly found that duration of GC exposure as a continuous variable was not predictive of biopsy positivity (odds ratio

Table 1. Characteristics of cohort stratified by TAB status.

	TAB Positive, n = 48	TAB Negative, n = 175	*P*
Age, yrs, mean (SD)	73.5 (9.5)	70.7 (10.6)	0.11
Female sex	35 (72.9)	123 (70.3)	0.72
Received GC prior to TAB	46 (95.8)	152 (86.9)	0.81
Duration of GC exposure pre-TAB, days, median (IQR)	15 (11-29)	15 (9-26)	0.27
Length of TAB, cm, mean (SD)	4.4 (2.3)	3.9 (2.7)	0.36
Positive temporal artery MRA	39 (95.1)	49 (29.7)	< 0.01
Headache	41 (85.4)	147 (84)	0.81
Vision loss	17 (35.4)	27 (15.4)	< 0.01
Other visual changes	28 (58.3)	81 (46.3)	0.13
Scalp tenderness	25 (52.1)	72 (41.1)	0.18
Temporal artery tenderness	19 (39.6)	74 (42.6)	0.71
PMR symptoms	10 (20.8)	47 (26.9)	0.4
Jaw claudication	34 (70.8)	30 (17.1)	< 0.01
Weight loss	11 (22.9)	15 (8.6)	< 0.01
Any constitutional symptoms	21 (43.8)	41 (23.4)	< 0.01
CRP, mg/L, mean (SD)	41.0 (19.4-65.1)	7.9 (2.7-23.0)	< 0.01
ESR, mm/h, mean (SD)	57.0 (37.0-91.1)	32.0 (12.0-57.0)	< 0.01
Final diagnosis of GCA	48 (100)	70 (40)	

Values are expressed as n (%) unless indicated otherwise. CRP: C-reactive protein; ESR: erythrocyte sedimentation rate; GC: glucocorticoid; GCA: giant cell arteritis; MRA: magnetic resonance angiography; PMR: polymyalgia rheumatica; TAB: temporal artery biopsy.

Table 2. TAB positivity and GCA diagnoses stratified by duration of GC treatment pre-TAB.

Duration of GC Treatment Pre-TAB, wks	TABs Performed, n	Positive TABs, n	TAB Positivity Rate, %	GCA Diagnoses, n	Patients Diagnosed With GCA by TAB, %
All	223	48	21.5	118	40.7
0	57	8	14	23	34.8
1	46	11	23.9	28	39.3
2	45	10	22.2	25	40
3	26	6	23.1	8	75
4	21	4	19	10	40
5	10	3	30	8	37.5
≥ 6	18	6	33.3	16	37.5

GC: glucocorticoid; GCA: giant cell arteritis; TAB: temporal artery biopsy.

1.00, 95% CI 0.99-1.01) nor was it as a class variable (data not shown). Two sensitivity analyses were performed: one considered patients ultimately diagnosed with GCA and the other excluded biopsies that were performed after 6 weeks or more of GC exposure. Both demonstrated results similar to those of the original analysis (data not shown).

The results of this analysis indicate that GC therapy does not affect TAB positivity to at least 6 weeks. These findings are consistent with those of Maleszewski et al[5] and suggest that GCs do not necessarily ameliorate vascular pathologic changes; the results also support similar conclusions in several studies.[4,8] The increased prevalence of cranial manifestations in TAB-positive individuals may be influenced by referral bias from clinicians selecting patients experiencing such symptoms for TAB; it is also possible that TAB is both diagnostic and prognostic, where TAB positivity suggests more severe disease.[9]

There are several limitations to this study. There was no standardized diagnostic algorithm for GCA used nor a standardized histological TAB evaluation, which can be affected by GC use but would not necessarily affect clinical diagnosis.[10] Information concerning cumulative GC dosing was not available due to the nature of the data. Additionally, the small sample size, pooling of data at 6 weeks, and retrospective nature of the study make generalization of results difficult, particularly for longer courses of GCs.

These results suggest that the recommendation of obtaining a TAB within 14 days of GC initiation appears unnecessarily conservative. TAB utility is not diminished despite prior steroid use and should not be avoided due to concerns of false negatives.

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