

# Clinical importance of the presence of giant cells in temporal arteritis

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## ABSTRACT

**Background:** The clinical significance of giant cells seen on temporal artery biopsy in temporal arteritis is unknown.

**Aim:** To help define the prognostic value of the presence of giant cells in temporal arteritis.

**Methods:** The clinical course of all patients with biopsy proven temporal arteritis from 1994 to 2004 was reviewed. The 92 patients were divided into those with giant cells (GC) (n = 76) seen on biopsy and those with no giant cells (NGC) (n = 16). Clinical findings were compared between groups. An additional analysis combined results with a previous study at the same institution to compare occurrence of blindness.

**Results:** The GC group had a higher proportion of polymyalgia rheumatica (PMR) (36.8%) compared to the NGC group (12.5%) (p = 0.059). There was no significant difference in patient age, sex, sedimentation rate, or presenting symptoms. The length of time treated with corticosteroids and relapse rate was nearly identical for both groups. When combining data with the previous study, in the GC group 21/109 (19%) developed blindness, while only 2/34 (6%) became blind in the NGC group (p = 0.11).

**Conclusion:** The presence of giant cells is not a significant factor in determining treatment or clinical progression of temporal arteritis. However, results showed the GC group to have three times the occurrence of blindness and PMR compared to the NGC group. Although the differences were not significant, this analysis suggests an association with giant cells and more aggressive disease.

The clinical significance of giant cells seen on temporal artery biopsy in temporal arteritis is unknown. Giant cells are not required in the histopathological diagnostic criteria for temporal arteritis.<sup>1</sup> Gilmore first suggested naming the syndrome giant cell arteritis due to the uniform presence of multinucleated giant cells.<sup>2</sup> A study by Morgan and Harris in 1978 reviewed 10 cases of non-giant cell temporal arteritis and suggested a worse prognosis and greater mortality in these patients.<sup>3</sup> However, many of the cases reviewed had systemic vasculitis in addition to disease of the temporal artery.

Temporal artery biopsy specimens which contain a necrotising vasculitis are often reported by pathologists as not having giant cells present. These patients are still treated clinically as having temporal arteritis, but the prognosis and clinical manifestations associated with patients without giant cells are uncertain.

There is speculation as to whether giant cells are missed by either skip lesions<sup>4</sup> or sampling techniques. Variability can exist in the length of artery

taken at biopsy and whether both left and right temporal arteries are biopsied.<sup>5</sup> In addition, pathological assessment can vary in the number of samples sectioned from the tissue for evaluation. Individual pathologists can vary as well with their interpretation of the disease.

The goal of our study was to compare clinical differences between temporal arteritis patients with and without giant cells. Based on previous studies in our clinic we hypothesised that giant cells were associated with a more aggressive disease process.<sup>6</sup>

## METHODS

### Patients and study design

Our study protocol was reviewed and approved by the institutional research review board at the Geisinger Medical Center. We reviewed the clinical course of all patients (n = 92) with biopsy proven temporal arteritis from 1994 to 2004 at the Geisinger Medical Center. Biopsies were performed by the Departments of Ophthalmology and Mohs Surgery. Bilateral temporal artery biopsies were not performed on all patients. Artery segments taken at biopsy were 2.5 cm in length on average.

The 92 patients were divided into two groups: those with giant cells reported on their biopsy pathology report and those without giant cells noted (n = 28). A pathologist then reanalysed the biopsy specimens reporting no giant cells; in half of them, giant cells were discovered. The corrected specimens were then regrouped into those with giant cells and those without giant cells. This was a retrospective review of available slides. All sections on the available slides were reviewed for the presence or absence of giant cells based on the H&E morphology. A standardised protocol for sectioning level thickness or number of sections was not part of the study. Immunohistochemistry was not used.

A study similar to this one was conducted at our institution in 1985. This study also examined the rate of blindness in patients that had giant cells present at pathology compared to those without giant cells present at pathology. In the study similar re-evaluation of biopsy sections was performed and data were regrouped if giant cells were found. This study also found that the rate of blindness was higher, but not statistically different, in the giant cell (GC) group (GC: 9/35, 23%; non-GC: 1/18, 6%; p = 0.11). As an exploratory analysis, we combined the blindness results of the 1985 study with the results of the 2006 study.<sup>6</sup>

**Table 1** Comparison of patients with giant cells (GC) present (n = 76) to those without giant cells present (n = 16)

	Statistic	Giant cell (n = 76)	Non-giant cell (n = 16)	p Value
Demographics				
Age	Mean (SD)	74.6 (7.9)	75.8 (4.8)	0.58*
Sex (females)	No. (%)	47 (61.8%)	11 (68.8%)	0.60‡
Clinical course				
Erythrocyte sedimentation rate	Median (range)	81.5 (24.0–448.0)	70.0 (7.0–110.0)	0.55†
Polymyalgia rheumatica	No. (%)	28 (36.8%)	2 (12.5%)	0.059‡
Hospitalised at diagnosis	No. (%)	10 (13.2%)	3 (18.8%)	0.69§
Blindness	No. (%)	12 (16.2%)	1 (6.3%)	0.45§
Relapses needing treatment	No. (%)	29 (50.9%)	6 (54.6%)	0.99§
Starting steroid dose	Median (range)	60.0 (20.0–1250.0)	80.0 (60.0–1250.0)	0.11†
Length of steroids	Mean (SD)	22.3 (9.2)	22.9 (8.1)	0.84*
Presenting symptoms (yes)				
Headache	No. (%)	52 (68.4%)	11 (68.8%)	0.98‡
Vision	No. (%)	38 (50.0%)	7 (43.8%)	0.65‡
Scalp	No. (%)	19 (25.0%)	2 (12.5%)	0.35§
Jaw	No. (%)	30 (39.5%)	4 (25.0%)	0.28‡
Muscle/joint	No. (%)	21 (27.6%)	4 (25%)	0.99§
Fever	No. (%)	9 (11.8%)	3 (18.8%)	0.43§
Fatigue	No. (%)	11 (14.5%)	2 (12.5%)	0.99§

Note that missing values were present for: erythrocyte sedimentation rate (6 in GC, 1 in non-GC); blindness (2 in GC); relapses needing treatment (19 in GC, 5 in non-GC); starting steroid dose (3 in GC, 1 in non-GC); and length of steroid treatment (19 in GC, 6 in non-GC).

\*Two-sample t-test; †Wilcoxon test; ‡ $\chi^2$  test; §Fisher's exact test.

### Clinical features

A retrospective review of clinical features was recorded and compared between the two groups: giant cells (GC) vs non-giant cells (NGC). Data were compiled from both paper charts and electronic medical records. Demographics, including age and sex, were compared between the two groups. Clinical symptoms at presentation were compared as well as sedimentation rate. Clinical symptoms were subjective as per the patient and included headaches, vision problems, scalp tenderness, arthralgias/myalgias, fever and fatigue. Corticosteroid treatment was assessed by comparing starting dose and length of treatment. Morbidity was assessed by comparing events of blindness, hospitalisations and development of polymyalgia rheumatica (PMR). Relapse was considered to include those events where corticosteroid therapy was reinstated due to return of clinical symptoms or increased sedimentation rate.

### Statistical analysis

Continuous data were compared using a two-sample t-test or, in cases of skewed data, a Wilcoxon rank-sum test. Categorical data was compared using a  $\chi^2$  test or Fisher's exact test, as appropriate. SAS V.9.1 (Cary, North Carolina, USA) was used for data manipulation and statistical analysis. All tests were two-sided and statistical tests resulted in p-values <0.05 were considered significant. Hence, there were no significant differences between the groups.

### RESULTS

Demographics, including age and sex of patients, showed no significant difference between the GC group and the NGC group as shown in table 1. Likewise there were no significant differences in the presenting symptoms between the two groups (table 1). Of note, the GC group had a higher proportion of PMR (36.8%) compared to the NGC group (12.5%) (p = 0.059).

No significant difference was seen in the starting dose of corticosteroids for the two groups. The length of time treated with corticosteroids and the disease relapse rate were nearly

identical for both groups. Both groups averaged 22 months of treatment for their temporal arteritis.

The GC group had three times the occurrence of blindness compared to the NGC group (tables 1 and 2). When combining data with the 1985 study, 19% in the GC group developed blindness, while only 6% became blind in the NGC group (p = 0.11) as shown in table 2.

### DISCUSSION

Some have proposed that non-giant cell temporal arteritis may be a different form of vasculitis separate from giant cell arteritis.<sup>3</sup> Giant cell arteritis may be a form of Takayasu arteritis, and non-giant cell arteritis may be more related to connective tissue associated vasculitis or periarteritis nodosa.<sup>7</sup> This concept would be difficult to confirm and it would be hard to categorise such discrepancies in disease based on giant cells alone. Also, treatment would still be the same regardless of the sub-type of arteritis involved.

Giant cells have long been associated with temporal arteritis. Our study suggests that the presence of giant cells may be associated with more aggressive disease shown in the form of visual loss and PMR.<sup>8,9</sup> Although not significant, our results show a definite increased occurrence of blindness and PMR associated with the finding of giant cells on biopsy. It is possible that with an increased database of patients, a clinical significance would be seen.

Our study also questions whether giant cells are being missed on pathology reports. Giant cells may be excluded by sampling

**Table 2** Exploratory analysis combining results of the 1985 study with the results of the 2006 study comparing occurrence of blindness between those with giant cells (GC) and those without giant cells (NGC)

	GC (n = 109)	NGC (n = 34)	p Value
Number of patients with blindness	21/109 (19%)	2/34 (6%)	0.11*

\*Two-sample t-test.

## Take-home messages

- ▶ The presence of giant cells in temporal artery biopsies is not a significant factor in determining treatment or clinical progression of temporal arteritis.
- ▶ Although not significant, those with giant cells in the study had nearly three times the occurrence of blindness and polymyalgia rheumatica compared to those without giant cells.

error both in the way of skip lesions and tissue sampling for analysis. A study by Klein *et al* found skip lesions in 28% of temporal arteritis patients analysed.<sup>10</sup> One patient had a single focus of inflammation measuring only 330 µm in length in an otherwise normal artery. Perhaps, like skip lesions, giant cells themselves are isolated to certain foci within the temporal artery. Therefore, one limitation of our study was that giant cells may have been present in the NGC group but were missed due to tissue sampling. There are no standard criteria for recommended length of temporal artery biopsy taken. Recommended temporal artery biopsy lengths have varied in guidelines from 2 to 7 cm.<sup>5</sup> Even our institution has varying lengths taken between the Departments of Mohs Surgery and Ophthalmology, with biopsy lengths of 2 and 3 cm, respectively. Current thought is that longer biopsy size is preferred for diagnosis of giant cell arteritis. One study showed a threshold size of 1 cm to be associated with increased diagnostic yield.<sup>5</sup> The length of temporal artery biopsy performed on our patient population was within the current standards. Another limitation is the number of potential transverse sections examined routinely, which could increase or decrease the odds of finding giant cells in the artery. A standardised protocol for sectioning level thickness or number of sections was not part of this study.

Although not statistically significant, the findings of our study suggest that giant cells may represent a more aggressive disease state in temporal arteritis. Therefore if giant cells are present, one may consider more aggressive therapy initially at the time of diagnosis based on the suggested, but not significant, increased chance of blindness. Such therapy could

include pulse dosing of corticosteroids as suggested in previous studies.<sup>11–13</sup> Intravenous pulse dosing of 1 g methylprednisolone daily for three days has produced improvement in vision, whereas previous studies indicated that blindness was irreversible once it had occurred.<sup>11 12</sup> In addition, a recent study showed that intravenous pulse corticosteroid therapy might improve response to therapy and lessen remission rates.<sup>13</sup> Also, our results suggest that giant cells are associated with the development of PMR; a slower corticosteroid taper might therefore be appropriate, as would be the expected treatment for PMR.<sup>14</sup> In conclusion, our study helps to address the clinical importance of giant cells in temporal arteritis.

**Competing interests:** None.

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