SCIENTIFIC CORRESPONDENCE

Effect of prior steroid treatment on temporal artery biopsy findings in giant cell arteritis

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Br J Ophthalmol 2002;**86**:530–532

Aim: To examine the effect of up to 6 weeks of corticosteroid treatment on the positive temporal artery biopsy rate in giant cell arteritis (GCA).
Methods: Prospective comparative clinical study of 11 patients meeting the American College of Rheumatology criteria for diagnosis of GCA. Patients underwent temporal artery biopsy within 1 week, at 2–3 weeks, or after 4 weeks of corticosteroid treatment.
Results: Overall, nine of 11 (82%) patients had positive temporal artery biopsies. Six of seven (86%) biopsies performed after 4 or more weeks of steroid treatment were positive.
Conclusion: Temporal artery biopsy is useful several weeks after institution of steroids.

Giant cell arteritis (GCA) is a systemic vasculitis of unknown aetiology, which most commonly affects medium sized arteries resulting in ischaemic events. The superficial temporal, occipital, vertebral, ophthalmic, and posterior ciliary arteries are typically involved resulting in visual disturbance or loss due to amaurosis fugax, ischaemic optic neuropathy, retinal artery occlusion, or cerebral ischaemia. This vasculitis tends to be self limiting over months to several years,[1] but exacerbations and recurrences are seen in some patients and both the disease process and its treatment with steroids are associated with considerable morbidity and mortality.[2 3]

Histological tissue examination is the gold standard in the diagnosis of GCA and has a sensitivity of 24–90% and a specificity of 81–100%.[4–7] A negative temporal artery biopsy (TAB) does not, however, rule out a diagnosis of GCA because of the possibility that a skip lesion (an unaffected segment of artery) may have been examined.[8 9] This has led some clinicians to question the value of this investigation.

Controversy exists regarding whether prior steroid treatment masks the characteristic pathological signs of GCA. It has become generally accepted among clinicians that temporal artery biopsy should be performed within 2 weeks from starting steroid treatment.

Our aim was to determine prospectively the effect of high dose corticosteroid treatment on temporal artery biopsy.

MATERIALS AND METHODS

The joint ethics committee of the Royal Victoria Infirmary and Associated Hospitals Trust gave ethical approval for the study. Family practitioners in the catchment area, neurologists and ophthalmologists in the hospital were invited to refer all new patients with a clinical diagnosis of GCA who had not yet commenced treatment with corticosteroids. Prompt assessment, within 24 hours of referral, of these patients was carried out by one of the investigators (NEFC), a neurologist. Patients were entered into the study if they fulfilled three of the following four American College of Rheumatology Criteria (1990) for the diagnosis of GCA[4]:

(a) new onset headache

(b) age over 50 years

(c) clinically abnormal temporal artery

(d) raised erythrocyte sedimentation rate (ESR).

After obtaining informed consent, the patients were initially randomised to undergo biopsy before and within 1 week, at 2–3 weeks, and at 4–6 weeks after commencing a standardised regimen of high dose corticosteroid treatment. Corticosteroid treatment was started by the assessing investigator (NEFC). If the patient had presented with acute visual loss, corticosteroids were started by the ophthalmologist and the patient was also reviewed by the neurologist. The number of patients who met the entry criteria was very low: five patients were entered in the study between April 1997 and April 1999. Many patients did not meet the entry criteria because of the vague nature of their symptoms and signs which is typical of this disease. Others were excluded because they had risk factors for corticosteroid treatment or when the referring doctor did not want to delay temporal artery biopsy for other reasons.

Subsequently recruited patients were biopsied after 4 weeks of steroid treatment and a further six patients were recruited.

All patients had baseline examination, investigations including full blood count and ESR and a chest *x* ray.

A standardised corticosteroid treatment regimen used was based on the current practice in our hospital and was as follows:

(1) No visual involvement:

Prednisolone orally 60 mg daily for 7 days then

50 mg daily for 7 days, then,

40 mg daily for 7 days then further gradual reduction in treatment was according to symptoms and other markers of disease activity.

(2) With visual involvement:

Intravenous hydrocortisone 200 mg immediately and prednisolone orally 80 mg daily for 3 days followed by the above regimen.

All the biopsies where carried out while the patients were on steroids with reduction of steroids following the standardised regimen and clinical response. No patient was on less than 40 mg of prednisolone by the time of their biopsy. The temporal artery biopsies were processed and cut at 4–5 μm thickness. At least three levels of 4–5 μm were made. From each paraffin block, three haematoxylin and eosin stain slides and one elastic stain slide were routinely processed. The slides were passed through the routine pathology reporting system and subsequently reviewed by a pathologist assigned to this project (SOT).

Table 1 Study patients

	Patient										
	1	2	3	4	5	6	7	8	9	10	11
Age (years)	77	69	81	80	79	90	68	68	71	65	80
Sex	F	F	F	F	M	F	F	F	M	F	M
Headache	+	+	+	+	+	+	+	+	+	+	+
Tender temporal artery	+	+	+	+	+	+	+	+	+	+	+
Jaw claudication	+	+	–	–	–	+	+	+	+	+	–
Visual loss	–	–	–	+	+	+	–	+	–	–	+
Amaurosis fugax	–	–	–	–	–	–	–	–	–	+	–
Diplopia	–	–	–	–	–	–	–	–	–	–	+
AION	–	–	–	+	+	+	–	–	–	–	–
CRAO	–	–	–	–	–	–	–	–	–	–	+
Others	–	–	–	–	–	–	–	Pale disc	ARMD	–	–
Systemic symptoms	+	+	+	+	+	+	–	+	–	–	+
ESR (mm/h)	46	40	110	104	82	97	24	65	82	30	80
Artery biopsy length (mm)	13	17	25	10	15	5	4.5	2.5	33	4	7
Duration of steroid (days)	0	4	17	18	25	30	32	36	36	37	45
Result	+	+	–	+	+	+(H)	+	+(H)	+	A	+

AION = anterior ischaemic optic neuropathy, CRAO = central retinal artery occlusion, ESR = erythrocyte sedimentation rate, +H = healed giant cell arteritis, A = atherosclerosis, ARMD = age related macular degeneration.

Four major features were assessed to determine the presence of active GCA. These were foreign body/Langerhans' giant cells in the intima and media, lymphocytes and histiocytes in the media, reduplication/fragmentation of the internal elastic lamina, and intimal thickening caused by oedema and fibrocellular proliferation. Healed GCA was diagnosed in the presence of intimal fibrosis, media scarring with eccentric and segmented disruption of the internal elastic lamina or chronic media inflammation with neovascularisation. However, if one or more of these features were absent, healed arteritis or atherosclerosis was considered (Table 2).

RESULTS

The patients' ages ranged between 65 and 90 years (mean 75). Eight patients were female and three male. All patients were subsequently confirmed to have GCA clinically on the basis of their presentation, response to steroid treatment, and clinical course. The length of biopsies ranged from 0.25 cm to 3.3 cm, with an average of 1.2 cm. The presenting clinical features of the recruited patients and the biopsy results are summarised in Table 1. The histological features are summarised in Table 2. Repeat biopsy in negative cases was not performed as the patients' symptoms had resolved on treatment. There is only about 2–3% increase in yield of a positive biopsy on contralateral biopsy.[10] Overall, nine of 11 (82%) biopsies were positive. Three of four (75%) were positive within 2 weeks of starting steroid treatment and six of seven (86%) after 4–6 weeks of treatment.

DISCUSSION

Temporal artery biopsy is a day case procedure associated with low morbidity.[11 12] However, the described presence of unaffected segments of involved arteries (skip lesions)[13] and the possibility that an artery is not involved in a particular patient have resulted in a significant false negative rate of up to 25% on biopsy.[6 14 15] Although many continue to advocate TAB for all patients suspected of having GCA,[6 16] the real possibility of a false negative result has led others to suggest limiting biopsy to specific groups of patients.[7 13 17 18]

The reassurance of having confirmed the diagnosis with a positive temporal artery biopsy irrespective of when it is carried out, is often greatest when there is an inadequate response to treatment or a complication of corticosteroid treatment. Biopsies are usually performed within 1 or 2 weeks of commencing corticosteroids despite the conflicting results of the handful of published studies (all retrospective) which have looked at the effect of steroid treatment on positive temporal artery biopsy rates in patients with GCA.

Allison and Gallagher[19] retrospectively compared the percentage of positive biopsies in 61 patients who received no steroid treatment, 51 patients who had been on steroids for less than 1 week, and 20 patients for more than 1 week. All patients were clinically diagnosed and managed as GCA cases. 82% of the untreated patients had a positive biopsy result compared to 60% of patients who received corticosteroids for 1 week or less before biopsy, and 10% of patients who received steroid therapy for more than 1 week before biopsy. They suggested that an increase in the percentage of false negative

Table 2 Histopathological features of the biopsies

Patient	GC	L&H in M	REL	IT	Other features	Artery biopsy length (mm)	Assessment of activity
1	+++	++	++	++	Adventitial chronic inflammation, side branch vasculitis	13	Active
2	+++	++	++	+++	Fibrinoid degeneration, adventitial chronic inflammation	17	Active
3	–	–	–	–	–	25	Negative
4	+	++	++	+++	Adventitial chronic inflammation	10	Active
5	+	++	+++	++	Adventitial chronic inflammation, side branch vasculitis	15	Active
6	0	+	++	++	Focal media scarring, calcification	5	Healed
7	+	+++	++	++	–	4.5	Active
8	0	0	++	++	Media calcification	2.5	Healed
9	++	+	++	++	Adventitial chronic inflammation	33	Active
10	0	0	0	+	–	4	Arteriosclerosis
11	+	++	++	++	–	7	Active

GC = Giant cells, L&H in M = lymphocytes and macrophages in media, REL = replication of elastic lamina, IT = intimal thickening.

biopsies occurs within days of corticosteroid treatment. The mean length of biopsy specimens was 7.9 mm in the untreated group and 6.2 mm in the treated group. The authors speculated that larger specimens may have revealed evidence of more residual foci of active inflammation or healed arteritis. The average formalin fixed, length of the biopsy specimens in our series was longer at 12.35 mm. Although our numbers are much smaller, seven of nine (78%) of our patients biopsied after 2 weeks of corticosteroid treatment and five of six (83%) of those biopsied after 4 weeks showed evidence of active arteritis. One of our smallest biopsies (4 mm) also yielded one of the two negative results, perhaps the result of the presence of skip lesions. Achkar *et al*[20] and Chmelewski *et al*[21] reviewed records of patients who had undergone temporal artery biopsies. In keeping with the results presented here, both studies showed no difference in positive biopsy rates between patients biopsied before treatment and those who had received steroids at any dose for any period up to 2 weeks. The proportion of "atypical" biopsies was shown to increase with the duration of steroid use. The proportion of positive biopsies was low in Achkar's study presumably due to the inclusion of patients with varying degrees of clinical likelihood of GCA.

McDonnell *et al*[18] retrospectively reviewed the temporal artery biopsies of 237 consecutive patients and found that specimens showed features of active arteritis after a mean of 7 days of corticosteroid treatment and healed arteritis after a mean of 82 days. The longest treatment to biopsy interval among patients with active arteritis was 45 days compared to an average of 82 days in patients with healed arteritis. There have also been individual case reports in the literature of positive biopsy results up to 6 months after steroid treatment.[18 22–24]

Overall, our study yielded a high positive temporal artery biopsy rate of nine of our 11 patients (82%) in those commenced on steroid therapy. Of the six patients in our study with a positive biopsy after 25 days or more of corticosteroids, four showed features of active arteritis and two features of healed arteritis. The longest steroid to biopsy interval was 45 days. This biopsy despite clinically adequate response to treatment still showed features of active arteritis with presence of giant cells.

To our knowledge this is the only prospective study performed to examine the effect of corticosteroid treatment on positive and false negative temporal artery biopsy rates in GCA. Owing to the prospective design, we only included patients who had a clinically definite diagnosis of GCA. We used a standardised corticosteroid regimen at entry, so that differences in positive biopsy rate were less likely to be due to differences in treatment. Although small in number, our results would suggest that late temporal artery biopsy is of value in the diagnosis of GCA. A negative result obtained after up to a month of steroid treatment should suggest the possibility of an alternative diagnosis in the same way as a negative biopsy at presentation. A much larger, multicentre, randomised study is necessary to determine this with sufficient statistical significance. As far as we are aware, there are no published studies other than that of Gallagher to suggest that the positive biopsy rate is significantly affected by up to 4 weeks of corticosteroid treatment.

Corticosteroid treatment should be commenced immediately in patients with a strong clinical suspicion of GCA. From our findings, we have the impression that biopsy after 4 weeks of corticosteroid treatment does not significantly alter the diagnostic yield. Temporal artery biopsy should be performed at presentation in patients with known contraindications to steroid treatment or where there is diagnostic doubt. Where there is difficulty obtaining prompt temporal artery biopsy, those with a definite clinical diagnosis of giant cell arteritis can undergo a therapeutic trial of corticosteroids followed by late biopsy.

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Accepted for publication 10 December 2001

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