Temporal artery biopsy for giant cell arteritis: retrospective audit

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DECLARATIONS

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HS, MS and CM conceived and designed the study; HS, TP and SG collected the data; HS, MS and SG studied and interpreted the data; HS and MS drafted the article; all authors have made a critical revision of the article and all authors have approved the article. HS and MS contributed equally

Summary

Objectives Temporal artery biopsy (TAB) is performed in suspected cases of sight-threatening giant cell arteritis (GCA). We aimed to determine the feasibility of TAB in patients who are suspected of having GCA.

Design, setting and participants A retrospective audit of all patients undergoing TAB at a single teaching hospital between 2005 and 2011, identified from the histopathology database.

Main outcome measures (1) Clinical profile and biochemical criteria associated with positive histology. (2) Proportion of negative histology patients who were commenced on steroid therapy.

Results One hundred and fifty-three TAB were performed (mean age 70.8 years, men:women = 3:2, 110 Caucasian: 43 Asian). Thirty-two biopsies were positive for GCA and 121 were negative. In total, 68 (61%) of 112 negative TAB patients were clinically diagnosed with GCA despite histological findings ($P < 0.001$). Nine out of 153 biopsies were non-arterial. Histologically positive TAB patients were of higher mean age (77.1 [95% CI 74.5–79.7] versus 69.1 [95% CI 66.7–71.6]; $P < 0.001$) and had a higher erythrocyte sedimentation rate (ESR) (60 [95% CI 46.1–73.9] versus 39.8 [95% CI 34.2–45.3]; $P < 0.01$)] than those with negative histology.

Conclusions Raised ESR and higher age may be the most useful indicators of GCA. Many histologically negative individuals were nevertheless clinically diagnosed and managed as GCA.

Introduction

Giant cell arteritis (GCA) is an inflammatory vasculopathy involving large- and medium-sized arteries. It occurs in 2.2 per 10,000 patient years in the UK.[1] GCA occurs in people over the age of 50 years and is more common in women. A higher incidence of the condition is seen in populations from Northern European countries.[2] It can present with common non-specific symptoms such as blurred vision, headache, myalgia and lethargy. More specific signs and symptoms

to the preparation of the manuscript

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of jaw claudication, scalp tenderness and scalp necrosis may also be present. If not treated immediately with steroid therapy, it can lead to irreversible visual loss, stroke and death.

The American College of Rheumatology (ACR) formed a clinical classification criteria for GCA in 1990.[3] Although these criteria have a high specificity and sensitivity, temporal artery biopsy (TAB) may be performed in suspected cases of GCA to aid a definitive diagnosis or to exclude it if the index of suspicion is low. Despite being considered the gold standard test for diagnosis of GCA, it is a procedure not without complications and skip lesions can render the test inconclusive.[4]

We aimed to determine the feasibility of TAB in patients suspected of having GCA in our centre between 2005 and 2011.

Methods

A retrospective review was performed of all patients who underwent a TAB in a single hospital from 2005 to 2011. The patient details were obtained from the histopathology department at University Hospitals Coventry and Warwickshire and these patients were identified on our electronic database. Demographic data, pathology reports, laboratory findings, operation details and clinical letters were viewed to obtain management details.

Erythrocyte sedimentation rate (ESR) was taken to be positive if greater than 50 mm/hour, as recommended by The American College of Rheumatology 1990 criteria for GCA[3] and C-reactive protein (CRP) was taken to be positive if greater than 24.5 mmol/L as directed by previous studies.[5,6] The study was approved by the local hospital audit committee.

Statistical analysis

Statistical calculations were performed using GraphPad Prism 4 (GraphPad Software, La Jolla, CA, USA) software package. A value of $P < 0.05$ was considered statistically significant. D'Agostino and Pearson omnibus normality test was used to confirm non-Gaussian distribution of numerical data. Subsequently, non-parametric analysis was performed using the Mann–Whitney *U* test. Categorical variables were analysed using the Chi-squared test.

Results

Demographics

Between 2005 and 2011, a total of 153 temporal artery biopsies were performed at UHCW NHS Trust for suspected GCA. There was a male: female ratio of 3:2. One hundred and ten subjects were Caucasian and a further 43 were Asian. Mean age at TAB was 70.8 years.

Biopsies were performed by ophthalmologists (13%) and vascular surgeons (87%), at consultant and registrar grade. Non-arterial biopsy was recorded in nine (6%) cases.

Histology

A total of 32 biopsies were histologically positive for arteritis and 112 were negative. Individuals with histologically positive TAB were of significantly higher mean age than those shown to be histologically negative (77.1 [95% CI 74.5–79.7] versus 69.1 [95% CI 66.7–71.6]; $P < 0.001$). Similarly, a greater mean ESR was recorded in individuals exhibiting positive histology (60 [95% CI 46.1–73.9] versus 39.8 [95% CI 34.2–45.3]; $P < 0.01$), with specificity of 83.6% and sensitivity of 63.3% at ESR = 60 mm/hour. Length of arterial biopsy (NB: 9 of the 121 histologically negative biopsies were excluded from this analysis due to non-arterial biopsy), preoperative CRP, gender and ethnicity were not significantly associated with histological arteritis (Table 1). Length of superficial temporal artery biopsied was a mean of 10.9 mm for ophthalmologists and 9.5 mm for vascular surgeons (P = NS; Mann–Whitney *U* test).

Clinical management

Preoperative steroids therapy were commenced for 125 (82%) of the individuals subjected to TAB for a presumptive diagnosis of GCA. Nine percent did not receive preoperative steroids and in a further 9%, there was no recorded data relating to steroid therapy.

Postoperatively, a clinical diagnosis of GCA was made in all individuals found to exhibit histological arteritis. All of these patients received steroids postoperatively.

Of note, 68 (61%) of 112 histologically negative TAB patients were clinically diagnosed with

Table 1
Comparison of histologically positive and negative TAB subjects

	Arteritis, n = 32 (histological)	*Non-arteritis, n = 112 (histological)*	*P value*
Age-years (95%CI)	77.1 (74.5–79.7)	69.1 (66.7–71.6)	$P < 0.001$
Gender (M/F)	21/11	69/52	P = NS
Mean length (mm)	10.5	9.4	P = NS
Ethnicity (Asian/Caucasian)	9/23	34/87	P = NS
ESR – mm/hour (95%CI)	60 (46.1–73.9)	39.8 (34.2–45.3)	$P < 0.01$
CRP – mmol/L (95%CI)	41.9 (26.2–57.6)	31.2 (23.9–38.5)	P = NS

TAB, temporal artery biopsy; NS, not significant

GCA despite the operative findings ($P < 0.001$) and these patients were treated with steroids post-operatively. Alternative clinical diagnoses recorded in the case-notes included trigeminal neuralgia, non-arteritic anterior ischaemic optical neuropathy, polymyalgia rheumatica, migraine, amaurosis fugax and 'unknown aetiology.'

Discussion

In our cohort of 153 consecutive patients undergoing temporal artery biopsy, the significant factors associated with a positive histological diagnosis of GCA were age and ESR. This is in conflict with previous studies which suggest that CRP is more sensitive than ESR in the diagnosis of GCA, such as that by Kernani *et al.* which found that an elevated CRP provided a sensitivity of 87% for a positive biopsy compared with an elevated ESR which had a sensitivity of 86%. This study also found that among GCA patients with a positive biopsy, normal ESR and CRP were observed in 4% of cases.[7] Another study by Hayreh *et al.* found that CRP (>50 mmol/L) was more sensitive (sensitivity 100%) than ESR (sensitivity 97%) and the combination of the two provided the best specificity (97%) in patients with GCA compared with control subjects who were seen in an ophthalmology practice for other conditions.[6] Another study also found that elevated CRP was a better predictor of a positive biopsy than ESR.[5] However, although the latter study included 3001 subjects undergoing TAB (459 with positive biopsy), the frequency of CRP testing was low and only available in 20% of the patients (98 patients with GCA and 493 subjects with a negative biopsy). Ypsilantis *et al.* found that raised ESR was significantly associated with a positive biopsy, but they did not include CRP levels in their study as it was not routinely measured in their patients suspected to have GCA.[8] Our current study therefore suggests that ESR still has an important role to play in the diagnosis of GCA, and may be superior to CRP in predicting a positive TAB and a patient's likelihood of having GCA.

Despite nine out of 153 biopsies being non-arterial, no documented complications were noted in our institution. However, to allow patients to undertake a procedure whereby the risks of infection, bleeding and damage to surrounding structures are not insignificant, only to discover after the histology report is obtained that no artery was obtained, is a highly undesirable situation. We therefore suggest that TAB should be performed or supervised by individuals undertaking this procedure frequently, perhaps by a team designated to providing this service, in order to prevent an unacceptably high rate of non-arterial biopsy occurring.

In our study, length of TAB was not significantly associated with a positive histology result. This is in contrast with Breuer *et al.*'s findings that TAB in the biopsy-positive patients was significantly longer than in biopsy-negative cases.[9] They reported that 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 greater than 20 mm, and therefore recommended that a biopsy of greater than 5 mm is obtained. Mahr *et al.* also identified 5 mm as the TAB length change point for diagnostic sensitivity and Ypsilantis *et al.* identified the postfixation specimen cut-off length with highest positive predictive value for a positive biopsy to be 7 mm.[8,10] The literature therefore supports the widely held belief that longer artery yields greater diagnostic sensitivity, with some recommending a minimum artery length of 12.5 mm to allow for artery contraction following harvesting and tissue fixation.[11,12] Furthermore, a longer specimen may be required if the artery looks and feels normal.[13]

The majority of individuals suspected of GCA are commenced on steroid therapy prior to surgery, which may influence histological findings, resulting in 'false-negative' biopsies. However, studies have shown that the rates of achieving a positive TAB are not reduced immediately after starting steroid therapy than before.[14] They are, however, less in week two of steroid treatment compared with week one.[15] Recent guidelines by the British Society for Rheumatology and British Health Professionals in Rheumatology for the management of GCA recommend that high-dose glucocorticosteroid therapy should be initiated immediately when clinical suspicion of GCA is raised.[16] They also suggest starting doses for different presentations, such as evolving or established eye involvement and a reducing regimen.

The percentage of positive biopsies was 29% in our cohort. Similarly, Kermani *et al.*'s study involving 1106 patients found that TAB findings were consistent with GCA in 22% of patients.[7] Mahr *et al.*'s[10] study included 1520 patients who had undergone TAB and found only 15% had histological evidence of GCA.

A high proportion of histologically negative individuals (61%) in our study were nevertheless diagnosed and managed as GCA on clinical grounds. Mari and Monteagudo noted that typical symptoms of the disease are those who best predict the successful outcome of the TAB in patients suspected to have GCA.[17] With such a low percentage of positive biopsies and high proportion of patients with negative biopsies in our study being treated as GCA on the basis of clinical and laboratory findings alone, this surely renders the practical relevance of TAB questionable. Colour duplex ultrasonography is a newer, non-invasive, method to diagnose GCA, which may reduce the chances of a false-negative biopsy due to skip lesions.[18] Other new imaging techniques such as positron emission tomography[19,20] and three tesla-magnetic resonance imaging[21,22] which are being used more frequently in the diagnosis and monitoring of disease activity in GCA, will mean that the role of TAB is likely to diminish in the future.

Limitations

Despite this report being limited by the fact that the data are observational, our positive biopsy rate is comparable to other published reports. We also found similar clinical and biochemical criteria associated with positive histology as previously published reports.

Conclusion

From this pilot study, it would be reasonable to reduce the number of TAB performed, provided there is sufficient clinical suspicion of GCA to commence treatment. A raised ESR and higher age may be more useful diagnostic adjuncts to the clinical diagnosis of GCA.

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