The Relationship between the Clinical Assessment, Temporal Artery Biopsy and the Positive Diagnosis of Giant Cell Arteritis

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ABSTRACT

Purpose: The purpose of this study was to examine the relationship between the clinical assessment, histology report and the positive diagnosis of giant cell arteritis.

Methods: In 2011, a retrospective study (2005-2011) of 40 diagnosed temporal artery biopsy patients was conducted at an ophthalmic practice in Sydney, NSW. All patients had been consulted by the same neuro-ophthalmologist prior to the biopsy. Relevant data was extracted from patients' records and entered into a database for statistical analysis. A scoring system was developed for each sign and symptom to facilitate analysis. Patients with incomplete or inaccurate records were excluded from the study.

Results: A total of 40 patients were included in the study. The average age of participants was 78 years (range 55 to 92). At initial presentation, common signs included headache (87%), jaw claudication (45%) and a change in vision (50%). Blood testing revealed raised inflammatory markers of erythrocyte sedimentation rate (ESR) (55%) and C-reactive protein (CRP) (90%) at presentation. A positive final diagnosis of temporal arteritis was made in 72.5% of all patients, despite only 52.5% of cases returning a positive temporal artery biopsy result.

Conclusion: This study has supported the importance of a temporal artery biopsy in combination with a detailed clinical assessment in the diagnosis of giant cell arteritis. In an ophthalmic setting a temporal artery biopsy is a useful tool to assist diagnosis, however with a false-negative risk careful clinical evaluation by the orthoptist and neuro-ophthalmologist will ensure that giant cell arteritis is promptly detected in patients.

Keywords: giant cell arteritis, histology, clinical assessment, positive diagnosis

INTRODUCTION

Giant cell arteritis (GCA) is the most common form of systemic large-vessel vasculitis in adults over the age of 50 years.[1] The condition typically involves inflammation of large and medium-sized arteries, and classic manifestations include headache, jaw claudication, visual symptoms and polymyalgia rheumatica.[2] It is essential that clinicians are able to quickly and confidently establish the diagnosis of GCA to prevent irreversible visual loss, which occurs in 10 to 15% of patients.[2,3]

The prevalence of GCA in North America and Europe is approximately 200 cases per 100,000 population and the incidence is 20-30 per 100,000.[4] The average age of diagnosis is 70 years.[5] Women are more likely to suffer from GCA than men (ratio 2.6:1).[4,6] There is a strong correlation between temporal arteritis and polymyalgia rheumatica, with 50% of GCA patients suffering from both conditions.[7] However, only 30% of polymyalgia rheumatica patients develop GCA. Giant cell arteritis is treated with corticosteroids, which alleviates symptoms usually within 24 to 72 hours and prevents irreversible visual loss.[3] The condition tends to be self-limiting over months to several years, but recurrences are seen in some patients.[8]

Temporal artery biopsy has been the traditionally-accepted method of diagnosing GCA.[9] It has been reported that histological tissue examination has a sensitivity of 24-90% and a specificity of 81-100%.[8] This large variation may be due to only a small segment of the artery removed for biopsy or the characteristic skip lesions of the condition resulting in an unaffected segment being examined. As such, it is accepted that a temporal artery biopsy is a useful tool in diagnosis but it should never be accepted as the solitary indicator of giant cell arteritis.[9] Patients with a typical clinical picture and positive response should be regarded as having GCA despite a negative biopsy result.[10]

The aim of the present investigation was to examine the relationship between the ophthalmologist's diagnosis of giant cell arteritis and the histology report. The overall

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objectives of the investigation were to (i) to examine the relationship between signs, symptoms, pathology and the positive diagnosis of giant cell arteritis, (ii) to compare the diagnosis of giant cell arteritis between the histology report and the ophthalmologist's final diagnosis and (iii) to compare our findings against the literature.

METHOD

A retrospective study was conducted at an ophthalmic practice in Sydney, where clinical staff reviewed medical records to identify all temporal artery biopsy patients between 2005 and 2011. All patients were previously seen by the same neuro-ophthalmologist in the ophthalmic clinic or in a hospital consultation prior to the biopsy. The biopsy was performed as soon as the neuro-ophthalmologist considered a diagnosis of GCA. The procedure was performed at local hospitals under local anesthesia. The site of the biopsy was left to the discretion of the neuro-ophthalmologist and the size was approximately 2 cm in length.

Relevant data was extracted from the identified patient records and entered into a database for statistical analysis. A scoring system was developed for each sign and symptom to facilitate analysis. Patients with incomplete or inaccurate records were excluded from the study.

RESULTS

There were 30 females (75%) and 10 males (25%) in the study. The average age of patients was 78.04 years (SD 8.82), ranging from 55 to 92 (Figure 1). A positive final diagnosis of temporal arteritis was made in 72.5% of all patients; however, only 52.5% of cases returned a positive temporal artery biopsy result (Table 1).

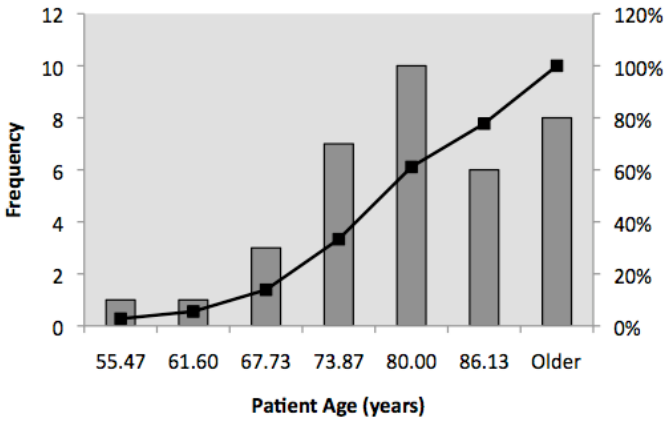

Figure 1. Distribution of patient age.

Table 1. Relationship between patient age and a positive GCA diagnosis

Age (years)	Number of patients	Number with positive GCA diagnosis (%)	
		Biopsy report diagnosis	Doctor's final diagnosis
55-65	2	1(50)	1 (50)
65-75	12	6 (50)	7 (58.3)
75-85	17	10 (55.5)	16 (88.8)
85-95	9	4 (44.4)	5 (55.5)
Total	**40**	**21 (52.5)**	**29 (72.5)**

A total of 15 markers were examined and interpreted by the orthoptist and neuro-ophthalmologist for detection of GCA (Table 2). Each marker was either scored 1 or 0 depending on whether the patient showed evidence of the marker or not. The maximum possible score was 15. For the total sample, there was a group average score of 6.56 (SD 1.7) indicating that on average patients had evidence of six to seven markers for GCA (Table 3). For the group of patients who had a negative biopsy but a positive final diagnosis the average marker score was slightly higher at 6.77 (SD 1.8) (Table 3). There was no apparent difference in evidence of markers between males and females.

Table 2. Checklist of indicators used in the diagnosis of GCA

Change in vision (blurring, loss of, diplopia)	Scalp tenderness
Headache	Loss of appetite
Jaw claudication	Unexplained weight loss
Neck stiffness	Elevated ESR
Night sweats	Elevated CRP
Joint pain	Tender temporal artery
Facial/ear pain	Enlarged temporal artery
	Non-pulsatile temporal artery

Table 3. Average marker score for GCA

	Total group	Group with negative biopsy, final positive diagnosis
Average	6.56	6.77
Standard deviation	1.7	1.8

On initial presentation 87% of patients complained of a headache and 45% reported jaw claudication (Table 4). Visual symptoms such as unilateral or bilaterally blurred vision, episodes of loss of vision, visual distortions and diplopia were reported in 50% of all patients (Table 4). Four patients (10%) presented to the ophthalmic practice with a sudden and total loss of vision in one eye and a positive diagnosis of temporal arteritis was later confirmed from the biopsy (Table 4).

Table 4. Relationship between signs and symptoms and a positive GCA diagnosis

Clinical examination	Number of patients (%)	Number of patients (%)	
		Biopsy report diagnosis	Doctor's final diagnosis
Headache	33 (87)	20 (60)	26 (78.8)
Jaw claudication	18 (45)	12 (66.6)	17 (94.4)
Visual abnormality	20 (50)	10 (50)	15 (75)
Night sweats	7 (17.5)	5 (71.4)	7 (100)
Neck stiffness	10 (24.4)	5 (50)	9 (90)
Scalp tenderness	12 (30)	7 (58.3)	8 (66.7)
Loss of appetite	13(32.5)	5(38.4)	9 (69.2)
Tender temporal artery	19 (47)	9 (47.3)	14 (73.7)
Enlarged temporal artery	15 (37.5)	11 (73.3)	13 (86.7)
High ESR (>35)	22 (55)	10 (45.5)	15 (68.2)
High CRP (>5)	36 (90)	20 (55.6)	25 (69.4)
High ESR and CRP	22 (55)	10 (45.5)	16 (72.7)

Clinical examination conducted by the neuro-ophthalmologist revealed a tender temporal artery in 47% of patients, and it was enlarged and non-pulsatile in approximately 37-40% of all patients. Normal intraocular pressures (range 10-21 mmHg) were noted in 36 patients for the right eye (mean=15, SD 4.6) and 38 patients for the left eye (mean=14, SD 4.1).

Blood testing of inflammatory markers prior to the biopsy revealed that 55% of patients had an erythrocyte sedimentation rate (ESR) level above normal for their age bracket and gender. A positive final diagnosis was made in 68.2% of all patients who presented with a pre-biopsy abnormal ESR level. However, only 45.5% of these patients returned a positive biopsy result. An above normal C-reactive protein (CRP) level was evident in 90% of cases pre-biopsy. Of these, 69.4% of patients with a high CRP had a positive final GCA diagnosis. However, only 55.6% of these patients recorded a positive biopsy result.

Thirty-four of the 40 patients (85%) commenced corticosteroid treatment prior to the biopsy procedure. Due to their signs, symptoms and high inflammatory parameters, three patients were administered intravenous corticosteroid therapy, methyl prednisolone, a more aggressive high-dose intervention than oral intake.

DISCUSSION

It is well known that the single greatest risk factor for developing giant cell arteritis is ageing.[2] A published review of 1,435 of positive-biopsy cases revealed that only two patients were under the age of 50.[11] This suggests that clinicians should primarily consider GCA as a condition of the elderly with only strong clinical evidence warranting suspicion in younger people.[2,3,11] These findings agree with our results, where the number of patients with a final positive diagnosis steadily increased with age (Table 1). In addition, women are more likely to suffer from the condition than men and this is represented in our study with a dominant female population (30 females vs 10 males).

The results of the study have supported the literature and shown that a biopsy alone does not provide sufficient information to determine a diagnosis of giant cell arteritis. The biopsy underestimated the total number of patients with a positive final diagnosis by approximately 20% (Table 1). This underestimation could be attributed to factors including the nature of the disease, where it is characterised by skip lesions or the small size of the biopsied area.[2,5,9]

Headache (87%) and jaw claudication (45%) were two common symptoms reported by patients at initial presentation to the orthoptist (Table 4). It has been reported that a headache is an important sign of GCA but it is not always reliable in the diagnosis of the condition because it can be due to many other diseases.[6] This is supported in our study with 26 of the 33 (78.8%) patients with a reported headache ending with a final positive diagnosis of GCA (Table 4). In comparison jaw claudication is less commonly reported yet it is a relatively specific indicator for GCA, as indicated in our study through 94.4% of patients with this symptom having a final positive diagnosis of the condition (Table 4).[11]

Analysis of the blood inflammatory markers showed that 55% of patients had an ESR level above normal and 90% had an abnormally elevated CRP level prior to the temporal artery biopsy (Table 4). In the literature there is great variation in what is considered to be a normal ESR rate.[6] As such patients may still have GCA even in the presence of a normal/low ESR level so whilst it is a useful inflammatory marker, it should be treated with caution.[6]

The CRP level is thought to be a more useful marker in diagnosing and monitoring GCA, as it is highly sensitive to inflammation and unlike ESR it is not influenced by age or gender.[6] Interestingly in this study, only 69.4% of patients with a high CRP had a final positive diagnosis of GCA (Table 4). This lower sensitivity might be explained by differences in normal CRP levels for different laboratories, which were not recorded in the research database. As a result of this lack of information and to enable some analysis it was decided by the neuro-ophthalmologist to consider a CRP level above 5 as abnormal.

If GCA was suspected at initial presentation the neuro-ophthalmologist immediately commenced patients on a high dose of corticosteroids in an effort to prevent irreversible visual loss. It could be argued that corticosteroid therapy

prior to the biopsy masked the condition and resulted in a false-negative report. However, this is heavily refuted in the literature where it has been reported that the characteristics and inflammatory markers of GCA can be seen in the artery for two to six weeks after initiation of treatment.[1,3,6]

It is likely that the ophthalmologist overruled the negative biopsy result in patients who had a strong presentation of clinical signs and symptoms, pathology and a positive response to corticosteroid intervention (Table 4). This is evident in the marker scores as they show that the overall group vs the overruled negative biopsy group had a similar score for GCA, that is, prior to the biopsy they were equally suspected of having GCA (Table 3). The incidence of false-negative biopsy results in our study agrees with the literature, where it has been reported that a temporal artery biopsy has poor sensitivity. From this we can conclude that it is essential to complete a thorough clinical examination as the detection of GCA can be dependent on this.

Thus, it can be accepted that a temporal artery biopsy is a useful tool in the diagnosis of GCA but it should not be used as the solitary indicator. A positive biopsy result is a clear indicator for GCA but it can produce false-negative results.[1] Careful clinical evaluation must be performed for all patients who are suspected of having GCA. These findings are well-supported in our study; 94% of patients who reported jaw claudication and 86.7% patients with an enlarged temporal artery were later found to have a final positive diagnosis of GCA (Table 4). Other reported symptoms such as a headache, night sweats and neck stiffness were also strongly associated with a final positive diagnosis.

CONCLUSION

Temporal artery biopsy is an important tool to be used in the diagnosis of giant cell arteritis. However, with the risk of a false-negative result (20% of our cases) it is not the solitary indicator for GCA. Orthoptists are crucial members of the clinical assessment team and they have an important role in the detection of GCA. This study reinforces that it is essential for both the orthoptist and ophthalmologist to take a detailed history and conduct a thorough examination including blood testing to reveal indicators for GCA. A failure to do so may result in undetected GCA, leading to an irreversible loss of vision in patients.

ACKNOWLEDGEMENTS

Dr Sara Booth-Mason and the ophthalmic team at Gordon Eye Surgery, Gordon, NSW.

Linda Santamaria, Editor, Australian Orthoptic Journal.

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