Is temporal artery biopsy essential in all cases of suspected giant cell arteritis?

C. Grossman[1], I. Barshack[2], G. Bornstein[1,3], I. Ben-Zvi[1,4]

[1]*Rheumatology Unit,*
[2]*Department of Pathology,*
[3]*Department of Internal Medicine D,*
[4]*Department of Internal Medicine F,*
The Chaim Sheba Medical Center,
Tel-Hashomer, Israel,
affiliated to Sackler Faculty of Medicine,
Tel-Aviv University, Israel.

*Chagai Grossman, MD**
*Iris Barshack, MD**
Gil Bornstein, MD
Ilan Ben-Zvi, MD

**These authors contributed equally to this study and share co-first authorship of this manuscript.*

Please address correspondence to:
Chagai Grossman, MD,
Rheumatology Unit,
The Chaim Sheba Medical Center
Tel Hahsomer,
52621 Israel.
E-mail: chagaigr@gmail.com

Received on January 13, 2015; accepted in revised form on February 17, 2015.

Clin Exp Rheumatol 2015; 33 (Suppl. 89): S84-S89.

Key words: giant cell arteritis, temporal artery biopsy, ACR classification criteria

Competing interests: none declared.

ABSTRACT

Objective. *Temporal artery biopsy (TAB) is performed in cases of suspected giant cell arteritis (GCA), and is the gold-standard for diagnosis of the disease. Current American College of Rheumatology (ACR) classification criteria may aid in the diagnosis of GCA. We aimed to assess whether TAB is essential in all cases of suspected GCA, or whether ACR criteria can replace the need for this procedure in some cases.*

Methods. *Retrospective analysis of 216 patients who underwent TAB in a single hospital between 2000 and 2013. Pre-TAB and post-TAB ACR criteria were calculated. Sensitivity and specificity of ACR criteria for the diagnosis of GCA were assessed.*

Results. *Overall, 55 patients had histological evidence of GCA.Out of 161 patients with negative TAB findings, 34 were diagnosed with GCA, and 127 were not diagnosed with GCA. Sensitivity of TAB for the diagnosis of GCA was 61.7%. Sensitivity and specificity of ACR criteria for diagnosis of GCA before performing TAB were 68.5% and 58%, respectively. Sensitivity and specificity of ACR criteria after performing TAB biopsy were 89.8% and 64.5%, respectively.*

Conclusion. *Temporal artery biopsy should be performed in the majority of patients with suspected GCA, and may be obviated only in patients with a pre-TAB ACR score of ≤1. In all other cases, when GCA is suspected, ACR criteria should not be a substitute to TAB, as they are not highly specific.*

Background

Giant cell arteritis (GCA) is a vasculitis that involves large and medium -sized vessels, with a predilection for the extra cranial branches of the carotid artery in the elderly (1-3). The pathogenesis of GCA is complex. It is based on activation of dendritic cells in the adventitia, as well as co-expression of CD161 by CD4 T cells recruited in the arterial wall, and activation of several cytokines which are responsible for the clinical manifestations of GCA (4). Genes located in MHC region, in particular HLA-DRB1*04, are crucial members of the immune and inflammatory response in GCA (5). Other candidate genes have not been found to play a significant role in the susceptibility or severity of GCA (6, 7). The clinical manifestations of GCA are quite varied and can be classified into four subsets: Symptoms related to cranial arteritis, extra cranial arteritis, systemic manifestations, and polymyalgia rheumatica (PMR) (8-10). The diagnosis of GCA is based on clinical grounds. Temporal artery biopsy (TAB) remains the gold standard for the diagnosis of GCA (11, 12) yet temporal artery biopsy may be normal in as 20–40% of the patients (13-18). The American College of Rheumatology (ACR) 1990 criteria may be used to assist in the diagnosis of GCA (19). These are a set of classification criteria which serve best in distinguishing between GCA and other vasculitidies. According to the ACR 1990 criteria (19) diagnosis of GCA can be made when 3 of 5 of the following criteria are met:

1. Age of onset of 50 years or older.
2. New onset headache.
3. Temporal artery tenderness or decreased pulse.
4. Erythrocyte sedimentation rate (ESR) >50 mm/hour.
5. Positive histology of a TAB

The utility of the ACR criteria for diagnostic purposes in GCA is controversial, but has been suggested in several studies to be of use in the diagnostic work-up of GCA (20-25). The aim of our study was to assess whether performance of TAB may not be necessary in all cases of suspected GCA, based on the utilisation of the ACR criteria.

Patients and methods

We retrospectively reviewed all patients who underwent TAB in the Chaim Sheba Medical Center between the years 2000 and 2013. Patients' clinical and demographic data was extracted from computerised medical records and manual medical files. We included only cases with complete clinical and laboratory information, including initial clinical presentation, ESR, values of complete blood count and chemistry results, as well as information on whether the diagnosis of GCA was determined and therapy initiated. Post-fixation TAB specimen length was recorded.

The research protocol was approved by the local institutional review and complies with the declaration of Helsinki.

GCA diagnosis

Temporal artery biopsies were performed under local anesthesia by general or ophthalmic surgeons. All patients underwent unilateral biopsies. Diagnosis of biopsy proven GCA required the histological findings of interruption of the internal elastic laminate with infiltration of mononuclear cells into the arterial wall (26). Some patients were diagnosed as TAB-negative GCA based on clinical judgment of the treating physician, provided the patient's symptoms and signs improved within 3 days of corticosteroid treatment (40 mg of prednisone or more), and no other better alternative diagnosis could be reached after a thorough evaluation and clinical follow-up.

Clinical and laboratory data

The clinical information collected included the presence of constitutional symptoms, headache, jaw claudication, symptoms compatible with PMR, visual manifestations, cerebrovascular manifestations and an abnormal temporal artery on physical examination. The following laboratory data was collected: haemoglobin, leukocytes and platelets levels, ESR and the presence of elevated liver enzymes. Based on the aforementioned data, each patient's pre-TAB and post-TAB ACR classification criteria score was calculated. Sensitivity of TAB for the diagnosis of GCA was calculated as well.

Table I. Baseline clinical and laboratory findings in 216 patients referred for temporal artery biopsy

Variable	
Males – no. (%)	81 (37.5)
Age (years+SD)	72.2 ± 9.5
Headache – no. (%)	112 (51.8)
Constitutional syndrome – no. (%)	117 (54.1)
Abnormal temporal artery on physical examination – no. (%)	37 (17.1)
Jaw claudication – no. (%)	23 (10.6)
Polymyalgia rheumatica– no. (%)	58 (26.9)
Visual manifestations – no. (%)	47 (21.8)
Cerebrovascular accidents – no. (%)	13 (6)
Elevated liver enzymes no. (%)	40 (18.5)
ESR (mean+SD) mm/1st hour +SD	83 ± 26.9
Haemoglobin (g/Dl) +SD	11.3 ± 1.6
Platelet count– no.+SD	390.9 ± 155.8
Leukocyte count – no. +SD	14 ± 40
Length of temporal artery specimen - cm+SD	1.1 ± 0.58
Temporal artery specimen length ≤1- cm (%)	92 (42.6%)
Mean pre-biopsy ACR score	2.58 ± 0.77
Mean post-biopsy ACR score	2.85 ± 0.97

*ACR: American College of Rheumatology.

Table II. Baseline clinical and laboratory findings in 89 patients diagnosed with giant cell arteritis – comparative analysis between patients with positive and negative temporal artery biopsy.

Variable	Biopsy positive GCA	Biopsy negative GCA	*p*-value
No. (%)	55 (61.8)	34 (38.2)	
Males – no. (%)	19(34.5)	16(47.1)	0.372
Age (years+SD)	72.2 ± 8.2	72.6 ± 9.4	0.835
Headache – no. (%)	36 (65.5)	24 (70.5)	0.542
Constitutional syndrome – no. (%)	36 (65.5)	20 (58.8)	0.652
Abnormal temporal artery on physical examination – no. (%)	14 (25.5)	6 (17.6)	0.444
Jaw claudication – no. (%)	1 4 (25.5)	5 (14.7)	0.292
Polymyalgia rheumatica– no. (%)	14 (25.5)	15 (44.1)	0.102
Visual manifestations – no. (%)	14 (25.5)	9 (26.5)	1
Cerebrovascular accidents – no. (%)	3 (5.5)	0	0.284
Elevated liver enzymes no. (%)	11 (20)	9 (26.5)	0.6
ESR (mean+SD) mm/1st hour +SD	88 ± 18.2	92 ± 20.6	0.34
Haemoglobin (g/Dl) +SD	11.5 ± 1.5	11.2 ± 1.2	0.372
Platelet count– no+SD	418.5 ± 141.7	375.5 ± 164.1	0.173
Leukocyte count – no. +SD	10.8 ± 4.2	13 ± 11.1	0.187
Length of temporal artery specimen – cm+SD	1.17 ± 0.69	1.2 ± 0.63	0.83
Temporal artery specimen length ≤1cm.- no. (%)	24 (43.6)	15 (44.1)	1
Mean pre-biopsy ACR score	2.9 ± 0.78	2.88 ± 0.64	0.86
Mean post-biopsy ACR score	3.9 ± 0.78	2.88 ± 0.64	<0.001

*GCA: Giant cell arteritis.

Statistical analysis

Continuous data was described as mean and standard deviation (mean±SD), and categorical variables as percentages. The clinical characteristics of study subjects were compared with Chi-Square tests for categorical variables and independent *t*-tests or analysis of variance (ANOVA) tests for continuous variables. Sensitivity and specificity of ACR criteria and sensitivity of TAB for the diagnosis of GCA were calculated. We also distinctively assessed sensitivity and specificity of ACR criteria for diagnosis of GCA using a positive TAB as the gold standard test.

Results

During the study period, 216 TAB were performed. The mean age of the patients was 72.2 (±9.5), and 81 (37.5%) were males. The most common presenting symptoms were constitutional syndrome (54.1%), headache (51.8%)

and PMR (26.9%) (Table I). Fifty-five biopsies were compatible with the diagnosis of GCA (25.4%) and 161 were negative (74.6%). Overall, 89 patients were diagnosed with GCA, 34 of which were diagnosed based on clinical grounds alone, despite a negative TAB. Within the group of patients diagnosed with GCA, baseline clinical and laboratory findings were similar in those with negative and positive TAB (Table II). Out of 161 patients with a negative TAB, 127 were not eventually diagnosed with GCA (74.5%). The calculated sensitivity of TAB for the diagnosis of GCA was 61.7%. Before TAB, 105 of 216 (48.6%) of patients met ACR criteria for GCA with a score of 3 or more. Sixty one (58%) of these were eventually diagnosed with GCA. We could not obtain complete information regarding the final diagnosis of all the patients who fulfilled the ACR criteria and were not eventually diagnosed with GCA. However, a relatively high rate of patients had a self-limited disease (Table III). None of the patients who were diagnosed with GCA had a pre-biopsy ACR score of ≤1 (Table IV). Out of 28 patients with pre-biopsy ACR score of 2 who were diagnosed with GCA, 19 (67.8%) had positive TAB, and the biopsy led to fulfillment of the ACR criteria (Table V). It is clearly shown that as more ACR criteria are fulfilled, the frequency of positive TAB is higher. After TAB, 124 patients had an ACR score of ≥3 and 92 patients had an ACR score of ≤2. Of these, 80 (64.5%) and 9 (9.7%) were eventually diagnosed with GCA, respectively (Table VI). The sensitivity and specificity of the ACR criteria for the diagnosis of GCA according to each ACR score individually is presented in Table VII. The overall sensitivity and specificity of the ACR score in the diagnosis of GCA without TAB was 68.5% and 58%, respectively.

Performance of TAB increased the sensitivity and specificity of the ACR criteria for diagnosis of GCA to 89.8% and 64.5%, respectively (Fig. 1). When using a positive TAB as the gold standard test for diagnosis of GCA, the sensitivity of the ACR criteria was 100%, whereas the specificity was 44.3%.

Table III. Final diagnosis of 44 patients with ACR criteria score ≥3 and negative temporal artery biopsy who were not diagnosed with giant cell arteritis.

Diagnosis	Number of patients (%)
Unknown	14 (32)
Self limited disease	13 (30)
Neurological disorder	6 (14)
Polymyalgia Rheumatica	5 (12)
Infectious disease	2 (4)
Rheumatological disorder (other than GCA or PMR)	2 (4)
Opthalmic disorder	2 (4)

*ACR: American College of Rheumatology; GCA: Giant cell arteritis; *PMR: Polymyalgia rheumatica.

Table IV. Pre-temporal artery biopsy ACR criteria score according to diagnosis of GCA.

ACR score	Diagnosed with GCA	Not diagnosed with GCA
0	0	0
1	0	8
2	28	75
3	42	33
4	19	11

*ACR American College of Rheumatology; GCA Giant cell arteritis.

Table V. Pre-temporal artery biopsy ACR criteria score according to biopsy findings and diagnosis of giant cell arteritis.

ACR score	Positive TAB	Negative TAB diagnosed with GCA	Negative TAB not diagnosed with GCA
0	0	0	0
1	0	0	8
2	19	9	75
3	22	20	33
4	14	5	11

*ACR: American College of Rheumatology; GCA: Giant cell arteritis; *TAB: Temporal artery biopsy.

Table VI. Post-Temporal artery biopsy ACR criteria score according to diagnosis of giant cell arteritis.

ACR score	Diagnosed with giant cell arteritis	Not diagnosed with giant cell arteritis
0	0	0
1	0	8
2	9	75
3	39	33
4	27	11
5	14	0

*ACR: American College of Rheumatology; GCA: Giant cell arteritis.

Table VII. Sensitivity and specificity of ACR criteria in diagnosis of giant cell arteritis according to individual ACR score.

ACR score	Sensitivity	Specificity
1	0%	0%
2	10%	10.7%
3	44%	54%
4	30%	71%
5	16%	100%

*ACR: American College of Rheumatology; GCA: Giant cell arteritis.

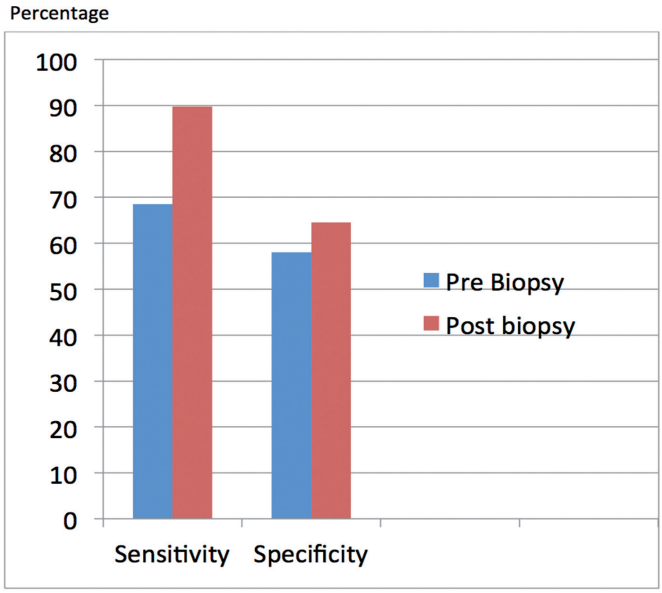

Fig. 1. Pre- and post-temporal artery biopsy sensitivity and specificity of the American College of Rheumatology (ACR) in the diagnosis of giant cell arteritis.

Discussion

The 1990 ACR criteria for the diagnosis of GCA were formed by comparing patients who had established GCA with patients with other vasculitidies. The conclusion was that 3 of 5 criteria must be present in order to classify a patient as having GCA (19). The sensitivity and specificity of these criteria were 93.5% and 91.2%, respectively. However, it must be acknowledged that they serve as classification criteria, and as such, may perform well in distinguishing GCA from other vasculitidies, but their role in the diagnosis of GCA has yet to be validated.

One of the ACR criteria is a positive TAB, which is considered the gold standard for the diagnosis of GCA, that is to say has a specificity of 100%. However, TAB may be normal in as 20-40% of the patients (13-18). Hence, the sensitivity of TAB for the diagnosis of GCA is not optimal. Accordingly, clinical judgment and integration of clinical and laboratory data are essential for the diagnosis of GCA. In our study, only 61.8% of patients diagnosed with GCA had positive TAB, indicating a relatively low yield of TAB. This may be attributed to the relatively short length of temporal artery biopsies in our cohort (Table I), as only 57.4% of the patients who underwent TAB had a temporal artery length ≥1 cm, which has previously been described to be associated with increased diagnostic yield of GCA (13) (27). Clinical and laboratory features of biopsy-proven GCA, as well distinction between biopsy-provent and biopsy-negative GCA, has previously been described by Gonzalez-Gay *et al*. (28). According to their studies, several disease patterns exist in GCA, *e.g*. patients with headache were found to have an abnormal temporal artery on physical examination more commonly than other GCA patients. Moreover, thay showed that several clinical differences exist between patients with biopsy-proven GCA and biopsy-negative GCA. Predictors for positive-proven GCA were abnormal temporal artery on physical examination, a history of constitutional syndrome and visual complications. Accordingly, it appears that patients with negative-biopsy GCA have less severe ischemic complications than those with biopsy-proven GCA. In our study, we found a relatively low rate of headache, abnormal temporal artery on physical examination and jaw claudication, in comparison with Gonzalez-Gay's study population (17).

We may assume that our population represents a subset of GCA patients with a relatively low rate of intra-cranial involvement, as other manifesations of the disease, like PMR and constitutional syndrome, were similar to previous studies (17, 28). Unlike previous studies (17, 29), we found a similar clinical spectrum in patients with biopsy-proven and biopsy-negative GCA (Table II). This may be explained by the relatively low yield of TAB in our study, which as mentiomed earlier is attributed to the short length of TAB specimen in our study. It is possible that some patients who were classified as biopsy-negative GCA would have had a positive TAB if the temporal artery specimen was longer. This may be a possible explanation for the lack of significant difference between these two subsets of GCA – biopsy-positive and biopsy-negative – in our study population. Since the diagnosis of GCA is made primarily on clinical grounds, some believe that TAB is not necessary. The role of TAB in combination with clinical data, including ACR criteria, was assessed in several studies. Lenton *et al*. assessed whether TAB affects clinical decision-making in patients with suspected GCA. They found little evidence that clinical decision-making was affected by the results of TAB in their group of patients (22). Davies and associates demonstrated that the ACR criteria had a sensitivity of 68% for the diagnosis of GCA before undergoing TAB. In their study, which included 111 patients, TAB changed the diagnosis in only 1 case. They concluded that using ACR criteria and restricting biopsy to those cases in which it may change diagnosis, may reduce the number of biopsies without jeopardizing diagnostic accuracy (23). Two additional studies demonstrated that TAB does not affect the management in the majority of patients with suspected GCA. The authors of these studies concluded that TAB has benefit only for patients who have a pre-biopsy ACR criteria score of 2 or 3 (24, 25). On the other hand, Murchison's group study found that 9 of 35 patients with positive biopsies would not have been diagnosed with GCA using ACR criteria alone and additional 16 patients (45.7%) met only 2 ACR criteria and required the positive biopsy to establish ACR diagnosis of GCA. In addition, 11 of 39 patients (28.2%) with negative biopsies met the criteria and would have been diagnosed with GCA. It should be noted that in this study, none of the patients with negative TAB were eventually diagnosed with GCA. Based on these findings, the

authors concluded that the ACR criteria should not be used to determine the presence or absence of GCA, that all patients suspected of GCA should undergo TAB, and that the results of TAB and not the ACR criteria, should be the only indicator for the presence of GCA (20).

In our study, the ACR criteria had a sensitivity of 68.5% for the diagnosis of GCA before performing TAB, which increased to 89.8% after TAB. Twenty eight patients had a pre-TAB ACR score of 2 and were diagnosed with GCA. Nineteen of these patients (67.8%) had a positive biopsy and fulfilled the ACR criteria only after undergoing TAB. This highlights the fact that TAB is essential in patients with a pre-TAB ACR score of 2, given that it may establish the diagnosis in a large proportion of these patients. Only 8 patients in our study had a pre-biopsy ACR score of 0 or 1. None of them were diagnosed with GCA after TAB. Based on this finding, it can be determined that TAB may be obviated in patients with an ACR score of <2. This is in concordance with previous studies mentioned above (23-25). The specificity of the ACR criteria for the diagnosis of GCA before obtaining TAB was 58%. After the performance of TAB, the specificity slightly increased to 64.5%. Among the patients who fulfilled the ACR criteria, the specificity of an ACR score of 3 was 54%, and although the specificity of an ACR score of 4 was higher, it only reached 71%. Based on our findings, we may conclude that the ACR criteria are insufficient in establishing the diagnosis of GCA. Therefore, even in patients with an ACR score of 4, a TAB is crucial for establishing the diagnosis of GCA. Our findings contradict previous studies that determine that TAB should be done only in patients with a pre-biopsy ACR score of 2, in which it might change the diagnosis (23), or only in patients with a pre-biopsy ACR score of 2-3 (24, 25). Our conclusion is similar to the one of Murchison's group (20), which stated that ACR criteria have no role in the diagnostic work-up of GCA, and that TAB is crucial in all patients suspected of having GCA. The difference between their study population and ours is that they analyzed patients seen in the neuro-opthalmology unit and only included patients with evidence of visual loss. Therefore, their conclusion may apply only to patients with visual loss, which may be a sole clinical manifestation of GCA. Accordingly, applying the ACR criteria on this population of patients suspected of GCA would naturally not be adequate, and all these patients should undergo GCA. Our study population is not restricted to patients with visual loss, and represents the broad spectrum of clinical manifestations of patients suspected of GCA. Therefore, our conclusions are more relevant to daily clinical practice where the clinical picture is diverse. Based on the results of this study, we believe that TAB should be performed in the majority of patients suspected of GCA. The ACR criteria only have a limited role in the diagnostic work-up of GCA. An ACR score of 2 or less after performing TAB has a high negative predictive value, and can probably exclude GCA. Therefore, in the minority of patients with a pre TAB ACR score of ≤1, a TAB can safely be omitted, and the diagnosis of GCA can likely be excluded. In all other cases, that is to say a pre-TAB ACR score of 2-4, TAB should not be obviated. In these cases, ACR criteria cannot substitute TAB and cannot serve as diagnostic criteria, in light of their low specificity.

Despite the fact TAB has a significant false negative rate, it still remains the gold standard for the diagnosis of GCA, and is a very low risk procedure.

The ACR criteria may have a certain role in patients with suspected GCA with a negative TAB, as these constitute a relatively large proportion of patients. In this subset of patients, clinical judgment must be employed in order to determine whether the diagnosis of GCA can be established despite a negative TAB, taking in account the relatively low specificity of the ACR criteria for diagnosis. In conclusion, TAB should be performed in the majority of patients with suspected GCA, and may be obviated only in patients with a pre-TAB ACR score of ≤1. In all other cases, when GCA is considered, ACR criteria should not be a substitute to TAB.

References

1. GONZALEZ-GAY MA, VAZQUEZ-RODRIGUEZ TR, LOPEZ-DIAZ MJ *et al*.: Epidemiology of giant cell arteritis and polymyalgia rheumatica. *Arthritis Rheum* 2009; 61: 1454-61.
2. HEALEY LA, WILSKE KR: Manifestations of giant cell arteritis. *Med Clin North Am* 1977; 61: 261-70.
3. NORDBORG E, NORDBORG C, MALMVALL BE, ANDERSSON R, BENGTSSON BA: Giant cell arteritis. *Rheum Dis Clin North Am* 1995; 21: 1013-26.
4. SAMSON M, AUDIA S, MATRIN L, JANIKASHVILI N, BONNOTTE B: Pathogenesis of giant cell arteritis: new insight into the implication of CD161+ T cells. *Clin Exp Rheumatol* 2013; 31 (Suppl. 75): S65-73.
5. CARMONA FD, GONZALEZ-GAY MA, MARTIN J: Genetic component of giant cell arteritis. *Rheumatology* (Oxford) 2014; 53: 6-18.
6. MARQUEZ A, SOLANS R, HERNANDEZ-RODRIGUEZ J *et al*.: Analysis of two autoimmunity genes, IRAK1 and MECP2, in giant cell arteritis. *Clin Exp Rheumatol* 2014; 32 (Suppl. 82): S30-3.
7. SERRANO A, CARMONA FD, CASTANEDA S *et al*.: A case-control study suggests that the CCR6 locus is not involved in the susceptibility to giant cell arteritis. *Clin Exp Rheumatol* 2013; 31 (Suppl. 75): S5-8.
8. NESHER G: The diagnosis and classification of giant cell arteritis. *J Autoimmun* 2014; 48-49: 73-5.
9. MURATORE F, PAZZOLA G, PIPITONE N, BOIARDI L, SALVARANI C: Large-vessel involvement in giant cell arteritis and polymyalgia rheumatica. *Clin Exp Rheumatol* 2014; 32 (Suppl. 82): S106-11.
10. TALARICO R, BOIARDI L, PIPITONE N *et al*.: Isolated aortitis versus giant cell arteritis: are they really two sides of the same coin? *Clin Exp Rheumatol* 2014; 32 (Suppl. 82): S55-8.
11. HALL S, PERSELIN S, LIE TJ, O'BRIEN PC, KURLAND LT, HUNDER GG: The therapeutic impact of temporal artery biopsy. *Lancet* 1983; 2: 1217-20.
12. GONZALEZ-GAY MA, ALONSO MD, AGUERO JJ, BAL M, FERNANDEZ-CAMBLOR B, SANCHEZ-ANDRADE: Giant cell arteritis in Mediterranean countries: comment on the article by Salvarani *et al*. *Arthritis Rheum* 1992; 35: 1249-50.
13. GONZALEZ-GAY MA: The diagnosis and management of patients with giant cell arteritis. *J Rheumatol* 2005; 32: 1186-8.
14. HAUSER WA, FERGUSON RH, HOLLEY KE, KURLAND LT: Temporal arteritis in Rochester, Minnesota, 1951 to 1967. *Mayo Clin Proc* 1971; 46: 597-602.
15. ROTH AM, MILSOW L, KELTNER JL: The ultimate diagnoses of patients undergoing temporal artery biopsies. *Arch Ophthalmol* 1984; 102: 901-3.
16. SALVARANI C, MACCHIONI P, ZIZZI F *et al*.: Epidemiologic and immunogenetic aspects of polymyalgia rheumatica and giant cell arteritis in northern Italy. *Arthritis Rheum* 1991; 34: 351-6.
17. GONZALEZ-GAY MA, GARCIA-PORRUA C, LLORCA J, GONZALEZ-LOUZAO C, RODRIGUEZ-LEDO P: Biopsy-negative giant cell

arteritis: clinical spectrum and predictive factors for positive temporal artery biopsy. *Semin Arthritis Rheum* 2001; 30: 249-56.
18. BREUER GS, NESHER R, NESHER G: Negative temporal artery biopsies: eventual diagnoses and features of patients with biopsy-negative giant cell arteritis compared to patients without arteritis. *Clin Exp Rheumatol* 2008; 26: 1103-6.
19. HUNDER GG, BLOCH DA, MICHEL BA *et al*.: The American College of Rheumatology 1990 criteria for the classification of giant cell arteritis. *Arthritis Rheum* 1990; 33: 1122-8.
20. MURCHISON AP, GILBER ME, BILYK JR *et al*.: Validity of the American College of Rheumatology criteria for the diagnosis of giant cell arteritis. *Am J Ophthalmol* 2012; 154: 722-9.
21. HUNDER GG: The use and misuse of classification and diagnostic criteria for complex diseases. *Ann Intern Med* 1998; 129: 417-8.
22. LENTON J DONNELLY R, NASH JR: Does temporal artery biopsy influence the management of temporal arteritis? *QJM* 2006; 99: 33-6.
23. DAVIES C, FROST B, ESHAN O, MCLAIN AD, SHANDALL A: Temporal artery biopsy...who needs one? *Postgrad Med J* 2006; 82: 476-8.
24. VARMA D, O'NEILL D: Quantification of the role of temporal artery biopsy in diagnosing clinically suspected giant cell arteritis. *Eye* (Lond) 2004; 18: 384-8.
25. QUINN EM, KEARNEY DE, KELLY J, KEOHANE C, REDMOND HP: Temporal artery biopsy is not required in all cases of suspected giant cell arteritis. *Ann Vasc Surg* 2012; 26: 649-54.
26. LIE JT: Illustrated histopathologic classification criteria for selected vasculitis syndromes. American College of Rheumatology Subcommittee on Classification of Vasculitis. *Arthritis Rheum* 1990; 33: 1074-87.
27. TAYLOR-GJEVRE R, VO M, SHUKLA D, RESCH L: Temporal artery biopsy for giant cell arteritis. *J Rheumatol* 2005; 32: 1279-82.
28. GONZALEZ-GAY MA, BARROS S, LOPEZ-DIAZ MJ, GARCIA-PORRUA C, SANCHEZ -ANDRRADE A, LLORCA J: Giant cell arteritis: disease patterns of clinical presentation in a series of 240 patients. *Medicine* (Baltimore) 2005; 84: 269-76.
29. DUHAUT P, PINEDE L, BORNET H *et al*.: Biopsy proven and biopsy negative temporal arteritis: differences in clinical spectrum at the onset of the disease. Groupe de Recherche sur l'Arterite a Cellules Geantes. *Ann Rheum Dis* 1999; 58: 335-41.