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Research

Giant Cell Arteritis Diagnosis by Biopsy or Ultrasound: Are we Classifying a Homogeneous Population?

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ABSTRACT

Giant cell arteritis (GCA) is a granulomatous vasculitis with autoimmune origin that is defined by the presence of mononuclear cell infiltrates and the formation of giant cells. It appears in elderly patients and involves the aorta and its branches, particularly the superficial temporal artery. In these patients, rapid diagnosis and immediate initiation of treatment are essential to prevent vascular complications, particularly visual loss and ischemic stroke.

Keywords: Cell arteritis ; Biopsy; Giant cells

INTRODUCTION

The diagnosis of CGA is based fundamentally on the criteria of the American College of Rheumatology (ACR) published in 1990 [1], according to findings of the anamnesis, physical examination and laboratory tests (age of onset greater than or equal to 50 years, headache of recent onset, hypersensitivity of the temporal artery or decrease of the pulse and increase of the ESR to 50 mm/h or higher), and on the temporal artery biopsy [2]. However, there are some discrepancies regarding its diagnostic strength, pointing out in some studies possible weaknesses of the biopsy: it is effective when its result is positive, since it is accepted that its specificity and its positive predictive value are 100%, but its sensitivity is low. The number of false negatives in the temporal artery biopsy varies according to the literature between 9 and 44% [3], although according to diverse sources these rates can still be higher [4]. The causes of this variability of the biopsy in the negative cases are fundamentally three: the patchy and symmetric condition of the lesions, the surgical technique and the pathologist's interpretation. Experts recommend samples larger than 1 cm and choosing the clinically most symptomatic artery to improve sensitivity. This low sensitivity of the biopsy justifies the search for new diagnostic methods, and this is where imaging techniques arise, especially colour Doppler ultrasound (CDUS).

In recent years, CDUS has proved validity in the diagnosis of GCA in multiple articles, including three meta-analysis [5-7] that collected 23 studies with 2,036 patients. These results are obtained by detecting three echographic signs: hypoechoic halo, stenosis and vascular occlusion. The hypoechoic halo is the most specific sign and confirms the edema of the vascular wall of vasculitis. In the systematic literature review and meta-analysis informing the EULAR recommendations imaging in diagnosis of large vessel vasculitis about the value of the 'halo' sign in the diagnosis of cranial GCA yielding a pooled sensitivity of 77% (95% CI 62% to 87%) and a specificity of 96% (95% CI 85% to 99%) [8].

In the latest EULAR recommendations of 2018 for the use of imaging in GCA, CDUS is recognized as the first diagnostic tool to be performed in centers with experience due to its low invasiveness, its higher cost-effectiveness and its lower rate of false negatives compared to the temporal artery biopsy [9]. Furthermore, CDUS is included with the same value as temporal artery biopsy in the draft classification criteria for GCA exposed at the American College Rheumatology annual meeting in Chicago 2018 [10].

In summary, nowadays ultrasound is the test of choice in some hospitals as opposed to the biopsy that is still performed in others and both models are accepted as valid; however, questions are still raised whether they diagnose the same type of pathology or represent different subtypes of the same autoimmune disease. The aim of the present study is to analyse whether there is homogeneity in the clinical characteristics, therapeutic needs and evolutional data depending on whether the patients are

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diagnosed based on the anatomopathological result of the biopsy or on the ultrasound diagnosis.

MATERIALS AND METHODS

This is an observational and retrospective study in which between January 2013 and December 2017 patients were included from a hospital in which the diagnosis was based on the biopsy and patients from another hospital where the same was confirmed by experts in ultrasound. The A cohort included 63 patients with an anatomopathological diagnosis, and the B cohort 138 patients diagnosed by ultrasound. Demographic parameters like age of onset or sex, analytical like ESR or CRP, clinical, and evolutionary parameters like relapses and number of relapses were collected from the medical records, as well as dose of cortisone at month 12 and 24. In the same way complications such as infections, osteoporotic fractures or exitus were collected.

Ultrasound examination were done with a Mylab Twice Esaote with a 22 MHz frequency for grey scale and 12.5 MHz for color Doppler with a color gain of 60 and a PRF of 2 KHz were used. For axillary arteries a 13 MHz frequency for grey scales and 7.2 MHz for color Doppler with a PRF of 3.5 KHz and a color gain of 61. Examination was done by two expert sonographers with good previous accuracy reported [11]. Biopsy was informed by the pathology department. The study protocol was approved by the hospital ethics board. Quantitative demographic and analytical data are described using the mean and standard deviation, while Chi^2 was used in the analytical study to compare qualitative variables and Student's t for quantitative variables. The SPSS program version 20.0 was used. Statistical analyses were also conducted among hospitals to assess possible therapeutic differences.

RESULTS

201 patients were included, 63 diagnosed by biopsy and 138 by using colour doppler ultrasound. The following table shows the means of the demographic (age of onset and sex) and analytical data in the baseline (ESR in mm/h, CRP in mg/dl) compared in patients diagnosed by biopsy and by ultrasound, where no differences were found (Table 1). As clinical parameters of giant cell arteritis we analysed recent onset headache, jaw claudication, symptoms of rheumatic polymyalgia, visual disturbances (especially acute ischemic optic neuropathy or AION) and the most relevant neurologic symptoms (especially acute stroke or transient ischemic attack or TIA). Between the clinical parameters, only small significant differences in ischemic pathology probably due to test selection differences were found, although no differences were found between evolutionary data including dose of steroids at month 12 and 24 in mg/day and also no significant differences were found either when comparing rate of complications like bone fractures, serious infections (defined as those that require hospital admission or put the patient´s life at risk) or rate of exitus.

Table 1: Differences in clinical and laboratory parameters between hospitals according to diagnostic tests performed.

Different parameters	Diagnosis biopsy (n=63)	Diagnosis ultrasound (n=138)	p
Age of onset	78,3 (± 6,6)	77,6 (± 7,7)	0,492
Sex	47/63 (71.2%)	87/131 (66.4%)	0,311
ESR in mm/h	84,8 (± 31,4)	69 (± 27,2)	0,142
CRP in mg/dl	26,9 ± 64	53,4 ± 59,4	0,096
Relapses	30/62 (48,4%)	67/136 (49,3%)	0,909
Number of relapses	0,9 ± 1,1	1,1 ± 2,5	0,373
Headache	44/63 (69,8%)	82/136 (60,3%)	0,210
Jaclaudication*	20/63 (31,7%)	15/136 (11%)	0,001
Polymyalgia rheumatica	24/63 (38,1%)	48/136 (35,3%)	0,752
Visual disturbances	20/63 / 31,8%)	32/136 (23,5%)	0.22
AION	14/63 (22,2%)	17/136 /12,5%)	0,079
ACVA/TIA*	15/63 (23,9%)	13/136 (9,6%)	0,036
Jaw claudication*	20/63 (31,7%)	15/136 (11%)	0,001
Steroids month 12 (mg/day)	7,3 (± 4,6)	7,9 (± 4,3)	0,432
Steroids month 24 (mg/day)	5,7 (± 5,7)	4,7 (± 4,5)	0,330
Fractures	4/63 (6,3%)	17/136 (12,5%)	0,189
Serious infections	9/63 (14,3%)	32/136 (23,5%)	0,134
Exitus	8/63 (12,7%)	15/136 (11%)	0,732

Lastly, no significant differences were found in the comparison of treatments between hospitals, showing a similar disease management in both hospitals regarding concomitant use of methotrexate and cumulative doses of steroids.

DISCUSSION

In the last years there was a debate in the scientific community about the relevance of performing the diagnosis of GCA based on the ultrasound of temporal arteries or the diagnosis should necessarily be based on biopsy. Time has changed the acceptance of the value of ultrasound, from a residual value in the diagnosis of GCA in the first decade of this century, until the present when has been accepted as the technique of choice, in well- trained units, in the EULAR recommendations in the follow-up and diagnosis of large vessel vasculitis published in 2018 [9]. Finally, at the last annual meeting of the American College of Rheumatology (Chicago 2018) the draft of the new diagnostic classification criteria of this disease [10] has been presented in which the sign of the halo in ultrasound has the same value as the positive biopsy of the temporal artery.

These changes are probably important in clinical practice and in the care of our patients, but new questions arise in the scientific community. One of them is if the patients who are diagnosed by biopsy or ultrasound [11,12] represent the same subtype of disease or we are qualifying patients with different clinical profiles including classic cranial arteritis and extracranial GCA, otherwise known as large-vessel GCA [13,14] in terms of their clinical characteristics, severity and therapeutic needs.

Our results showed as there were no significant differences in the demographic characteristics of the patients in both groups. We also explored different outcomes as corticosteroid used at 12 and 24 months, relapses and exitus, without appreciating any

significant difference. Only ischemic pathology as acute cerebrovascular stroke/transient ischemic attack and jaw claudication showed significant increase in patients diagnosed by biopsy, if this represent a bias of selection of the diagnostic test or a relevant difference needs more studies. We don't have yet other studies that compare both diagnostic procedures, new studies should be done in this aspect.

As limitations of the study we can highlight the fact that it is a retrospective study without the characteristics of a clinical trial and the possible differences in the management of the disease when collecting data from different hospitals, although there seem to be no significant differences when analysing both centers separately.

CONCLUSION

The diagnostic suspicion of GCA confirmed by biopsy or ultrasound in expert hands seem to classify similar patients with homogeneous characteristics. Relevant outcomes such as subsequent evolution, the dose of corticosteroids required or the rate of relapse, death or other complications do not show significant differences.

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