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Concise report

Atherosclerosis as a potential pitfall in the diagnosis of giant cell arteritis

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Abstract

Objectives. To explore whether the increase in the intima-media thickness (IMT) in arteriosclerotic disease correlates with the increase in the IMT in temporal arteries (TAs) and if that could mimic the US GCA halo sign.

Methods. Consecutive patients ⩾50 years old with high vascular risk and without signs or symptoms of GCA were included. The carotid US IMT measurements were obtained using a standardized software radiofrequency-tracking technology. Colour Doppler US and grey-scale measurements of the IMT in the branches of both TAs were performed by a second sonographer using a 22 MHz probe.

Results. Forty patients were studied (28 men) with a mean age of 70.6 years. The carotid IMT exhibited significant correlation with the TA IMT. A carotid IMT >0.9 mm was associated with a temporal IMT >0.3 mm. Only one patient had an IMT >0.34 mm in two branches.

Conclusions. Atherosclerotic disease with a carotid IMT >0.9 mm increases the TA IMT and might mimic the halo sign. As atherosclerosis is common in this age group, we propose a cut-off of TA IMT >0.34 mm in at least two branches to minimize false positives in a GCA diagnosis.

Key words: giant cell arteritis, arteriosclerosis, vasculitis, ultrasound, imaging

CLINICAL SCIENCE

Rheumatology key messages

- Atherosclerotic disease might lead to an erroneous diagnosis of GCA with ultrasound.
- A carotid intima-media thickness >0.9 mm can be associated with a false halo sign in temporal arteries.
- An intima-media thickness cut-off >0.34 mm in at least two temporal arteries achieves good diagnostic accuracy.

Introduction

GCA is the most common form of vasculitis in the elderly [1–3]. Temporal artery (TA) biopsy is considered the gold standard for diagnosis. However, although it has a specificity value that is accepted as 100%, it has low sensitivity. The percentage of false negatives in GCA ranges from 9 to 62% [4–7].

False-negative biopsies highlight the need for alternative diagnostic approaches. GCA is characterized by inflammatory infiltration of the artery wall. This inflammation is visualized by US as a hypoechoic (dark) thickening of the vessel wall that is well delineated towards the luminal side, resulting in the so-called halo sign. In the last decade, the US halo sign has become an important diagnostic tool and today four meta-analyses support the diagnosis of GCA using US [2, 8–10].

False-positive halos have been described in malignant and infectious diseases [11]. However, there could be other causes for false-positive halos in the US diagnosis of GCA. The arteriosclerotic process, which is frequently observed at the age of GCA presentation, produces calcified plaques that are easily visible, with a characteristic hyperechoic appearance, also produce a hypoechoic increase of the intima-media thickness (IMT) in the arterial wall [12–14] that can be similar to the halo sign in carotid arteries. Whether this situation can occur in vessels as TA branches has not been defined. This study aimed to determine whether the homogeneous hypoechoic wall IMT thickening caused by atherosclerosis can also appear in the TA and produce a halo sign–like image that might be confused with a true halo sign of GCA.

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Methods

Patients

Forty consecutive patients ⩾50 years of age with high or very high vascular risk (see supplementary material available on *Rheumatology* Online), according to the European guidelines on cardiovascular disease prevention [15], who attended our cardiovascular high-risk outpatient clinic were included in the study. The exclusion criteria were as follows: signs or symptoms of GCA past or present and an ESR ⩾40 mm/h.

Data collection and procedures

The medical history, clinical examination, laboratory data and US were performed at the time of each subject's inclusion in the study (May 2015–May 2016). The study was approved by the ethics board of the Hospital Universitario La Paz (HULP PI-1824). All subjects provided informed written consent.

US of the carotid arteries

The US examinations of the carotid arteries were performed by L.M.B. using an Mylab Seven system (Esaote, Genova, Italy) with a 4–13 MHz probe. The system employed a dedicated software radiofrequency-tracking technology to obtain IMT (QIMT®) [16]. Each patient was placed in the supine position with his/her head slightly bent in the opposite direction of the examination site. The common carotid artery (CCA), carotid bulb and proximal portions of the internal and external carotid arteries on both sides were scanned for plaques using transverse and longitudinal views. A carotid plaque was defined as a focal structure that encroaches into the arterial lumen of at least 0.5 mm or 50% of the surrounding IMT value or that demonstrates a thickness >1.5 mm measured from the media-adventitia interface to the intima-lumen interface [17].

The IMT was measured at the distal wall of the left and right CCA, 10 mm proximal to the carotid bifurcation over the proximal 15 mm long segment [17]. The mean (S.D.) of the IMT values from six cardiac cycles were continuously calculated by the software. When the S.D. was <20 μm, the sonographer froze the image and collected the mean IMT value. These measures were performed from three different angles of approach on both CCAs (anterior, intermediate and lateral) [15]. For analysis, the maximum IMT was defined as the thickest mean IMT value recorded in either the right or left CCA.

Ultrasonography of the temporal superficial artery

A second sonographer (E.d.M.) used a Mylab Twice (Esaote, Genova, Italy) device with a 10–22 MHz probe. Colour Doppler frequency was set at 12.5 MHz with a colour gain of 51 and a pulse repetition frequency (PRF) of 2 kHz. He performed colour Doppler US and grey scale; the highest, well-defined value measurement of the IMT of the TA and its branches in longitudinal and transverse views on both sides, as completely as possible, was chosen. The OMERACT definition of the halo sign—'homogeneous, hypoechoic wall thickening, well delineated towards the luminal side, visible both in longitudinal and transverse planes, most commonly concentric in transverse scans'—was applied [18]. In addition to this definition, an IMT >0.3 mm was regarded as a potential halo sign.

This sonographer was blinded to the clinical, laboratory and carotid US data. The 5 s videos of the parietal and frontal branches of every examination were stored for reliability. Two trained ultrasonographers performed an interreader exercise several months after the examination.

Table 1 Influence of carotid IMT on TA IMT measurements

	Branches of TA, parietal and frontal		
Carotid IMT, mm	*n*	Halo/IMT, mm, mean (S.D.)	Min–max, mm
⩽0.7	12	0.247 (0.043)	0.16–0.29
>0.7 and ⩽0.9	46	0.254 (0.037)	0.18–0.33
>0.9 and ⩽1	42	0.269 (0.034)	0.18–0.36
>1 and ⩽1.2	50	0.282 (0.052)	0.17–0.45
>1.2	10	0.284 (0.067)	0.19–0.40

Min–max: minimum and maximum measurements.

Statistical analysis

SPSS software (version 20.0; IBM, Armonk, NY, USA) was used for statistical analysis. The quantitative variables are provided as the mean with S.D. and range. Upon univariate analysis, the Student's *t*-test for independent samples was used to compare continuous variables and the chi-squared test was used to compare categorical variables. Spearman's correlation coefficients between the sonographic findings were calculated. For interreader reliability purposes, Cronbach's α was used on the recorded videos.

Results

Forty patients were studied [28 men (70%)], with a mean age of 70.6 years (S.D. 6.9). Three patients were active smokers and 27 were ex-smokers. Arterial hypertension was present in 39 (97.5%) patients, dyslipidaemia in 34 (85%) and diabetes in 19 (47.5%). The mean ESR was 13.6 mm/h (S.D. 11.0). Eighty carotid arteries and 160 TA branches were studied. Atherosclerotic plaques were observed in 50 carotid arteries. The carotid IMT ranged from 0.528 to 1.480 mm.

The increase in the carotid IMT is associated with an increase in the IMT of the TA (Table 1), with a weak Spearman correlation (parietal branches 0.282, $P = 0.012$; frontal branches 0.228, $P = 0.048$). We did not achieve any statistical significance between the size of the plaque and the temporal IMT.

Table 2 shows that with an IMT cut-off >0.34 mm, four patients (10%) could mimic the halo sign. When at least two affected branches were required to make the US

TABLE 2 Influence of arteriosclerosis on TA IMT values

Patient	Carotid IMT, mm	Right		Left		Number of branches with halo	
		TA frontal, mm	TA parietal, mm	TA frontal, mm	TA parietal, mm	Cut-off IMT >0.3 mm	Cut-off IMT >0.34 mm
4	1.185	0.37	0.31	0.31	0.31	4	1
5	0.948	0.26	0.31	0.31	0.27	2	0
6	1.135	0.18	0.31	0.24	0.25	1	0
7	1.164	0.31	0.28	0.28	0.28	1	0
9	1.243	0.37	0.4	0.45	0.35	4	4
10	1.196	0.28	0.28	0.34	0.28	1	0
11	1.21	0.31	0.31	0.25	0.28	2	0
12	1.165	0.29	0.28	0.28	0.31	1	0
14	1.37	0.29	0.22	0.31	0.31	2	0
16	1.0331.033	0.25	0.28	0.23	0.34	1	
17	1.027	0.28	0.32	0.37	0.34	3	1
18	0.9890.989	0.25	0.31	0.28	0.28	1	0
19	1.017	0.19	0.28	0.25	0.31	1	0
25	0.8020.310.25	0.29	0.27	0.31	0.25	1	0
30	1.200	0.31	0.29	0.21	0.24	1	0
32	0.9780.978	0.31	0.3	0.36	0.25	3	1
35	0.766	0.23	0.28	0.33	0.29	1	0
37	1.048	0.34	0.33	0.27	0.31	3	0

Carotid measurements are expressed as the higher mean values in the carotid arteries.

diagnosis, only one patient (2.5%) produced a false-positive halo sign.

The reliability analysis for TA measures showed an inter-reader Cronbach's α of 0.845 (95% CI 0.758, 0.901; $P < 0.0001$) and 0.820 (95% CI 0.719, 0.884; $P < 0.0001$) for the parietal and frontal branches, respectively.

Discussion

Using modern high-resolution probes >20 MHz, one can visualize and measure the IMT of the TAs. IMT measurement may be more correct for evaluating vasculitic wall oedema than morphologic criteria with colour Doppler US. One can avoid the bias of colour gain, PRF or other potential Doppler artefacts. Moreover, the US appearance of atherosclerotic IMT in the carotid and other medium vessels such as the femoral arteries may be hypoechoic [12–14]. However, to date, there is no information as to whether the IMT of TA vessels is increased in patients with atherosclerosis.

To the best of our knowledge, this study is the first to report that atherosclerosis is a potential cause of false-positive halo sign and that a weak but significant correlation exists between the IMT of carotid arteries and the IMT of TA superficial branches. A carotid IMT >0.9 correlates with an increase in TA IMT. These findings raise the question of what should be the cut-off for accurately diagnosing and assessing GCA. Previous studies have suggested cut-off values for the halo sign between 0.3 and 1 mm [2, 9, 10, 19].

A recent study evaluating the IMT in 40 GCA patients compared with controls suggested a cut-off of 0.42 mm for the common superficial TA, 0.34 mm for the frontal branch and 0.29 mm for the parietal branch [20]. Our proposal is similar to this study; in our analysis, a good cut-off is an IMT in the TA branches >0.34 mm with at least two branches affected in the same patient. This cut-off excluded 97.5% of the arteriosclerotic patients in our study. To improve specificity, the proposal of at least two branches is also reported by other authors [9, 10]. Only in patients without arteriosclerotic disease should a cut-off of 0.3 mm be accepted as indicative of GCA.

Our study has several limitations. It is important to mention the absence of direct comparison with a GCA control group to confirm that the cut-off of 0.34 mm is appropriate. The subjects included may have a higher cardiovascular risk than the overall patients typically tested for suspected GCA. However, our objective was to explore whether arteriosclerotic disease could influence the presence of a false halo sign, thus we selected patients with a high probability of presenting an arteriosclerotic increase of carotid IMT. In real-world clinical practice that includes patients with a high pre-test probability of GCA, the percentage of mistakes would be expected to be less. Another limitation is that the proportion of males is higher than the usual distribution in GCA, and we do not know whether this finding could have increased the IMT values. Finally, another limitation was that we did not perform axillary examination since our objective was the IMT in medium-size vessels. We thought that in large vessels the increase in IMT would be present.

In conclusion, our study demonstrated that atherosclerotic disease might lead to an erroneous GCA diagnosis based on a false-positive halo sign. Evidence regarding

the appropriate cut-off in the diagnosis of GCA should be established. Measurements >0.34 mm in at least two TA branches may improve the diagnostic accuracy.

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Supplementary data

Supplementary data are available at *Rheumatology* Online.

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