The Predictive Value of the Halo Sign in Color Doppler Ultrasonography of the Temporal Arteries for Diagnosing Giant Cell Arteritis

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ABSTRACT. ***Objective***. The diagnosis of giant cell arteritis (GCA) usually requires a temporal artery biopsy. Recently it has been reported that a periluminal dark halo, detected by color Doppler ultrasonography (US) of the temporal arteries, is a characteristic sign of GCA. We evaluated the predictive value of this dark halo sign in diagnosing GCA.

Methods. During a period of 2 years 69 patients suspected of having GCA were examined by US of both temporal arteries. Temporal artery biopsy was performed in 32 of these patients. The diagnosis of GCA was made if a patient had a biopsy showing arteritis, or met all the following criteria: (1) American College of Rheumatology GCA classification criteria were fulfilled; (2) there was a prompt clinical response to treatment with 40–60 mg/day of prednisone; and (3) no other diagnosis related to the patient's symptoms was made during 6 month followup.

Results. Periluminal dark halo was observed in 24 of 69 patients. GCA was diagnosed in 12 of them, giving a positive predictive value (PPV) of only 50%. No halo was detected in 45 cases of which only 2 had GCA, resulting in a high negative predictive value (NPV) of 96%. The sensitivity and specificity of the halo sign for diagnosing GCA were 86% and 78%, respectively.

Conclusion. The PPV of the halo sign in US of the temporal arteries is unsatisfactory for diagnosing GCA. However, the NPV is very high. Thus the lack of a halo can practically serve to rule out a diagnosis of GCA, and precludes the need for a biopsy in most instances. (J Rheumatol 2002;29:1224–6)

Key Indexing Terms:
TEMPORAL ARTERITIS DIAGNOSTIC TESTS ULTRASONOGRAPHY

The diagnosis of giant cell arteritis (GCA) is based mostly on clinical signs and symptoms, but confirmation with a temporal artery biopsy is sought in many cases. However in 10–42% of patients eventually diagnosed as GCA, the arteries in the biopsy specimen do not show signs of inflammation[1-3], the so called biopsy negative GCA. Attempts have been made to improve the yield of the temporal artery biopsy, such as trying to localize areas of narrowing by Doppler ultrasonography (US), to biopsy both sides, or increase the number of sections of the specimen[1,4-6]. However, these methods increased the rate of biopsy-proven GCA only slightly. Further, although temporal artery biopsy is a minor operation, some patients do not agree to this procedure. In such cases the diagnosis is based solely on clinical grounds.

Recently, Schmidt, *et al* reported that color Doppler US of the temporal arteries showed a hypoechoic halo around the lumen of the inflamed arteries[7]. It was thought to represent edema in the vessel wall, and was found to be sensitive and highly specific for GCA. It seemed feasible that such a diagnostic modality would enable the treating physician to make a diagnosis of GCA without performing a temporal artery biopsy. However, the positive predictive value (PPV) and negative predictive value (NPV) of the halo sign were not evaluated, and the promising results have not been confirmed by other investigators. We thus studied this method prospectively in our patients and evaluated its predictive value in diagnosing GCA.

MATERIALS AND METHODS

During a period of 2 years, 69 patients suspected of GCA were referred to the vascular laboratory and underwent color Doppler US of the temporal arteries. Patients were referred from the departments of internal medicine, geriatric medicine, and ophthalmology, and from the outpatient rheumatology clinic. US was performed by an experienced vascular technician, and results were confirmed by one of the investigators (DS). The scanner used was Acuson Sequoia 512 with an L 15-8 MHz multi-frequency linear array transducer, with a foot print size of 26 mm. Both common superficial temporal arteries and the parietal and frontal rami were examined, in both

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longitudinal and transverse planes. Presence of a hypoechoic (dark) periluminal halo was ascertained if it appeared repeatedly in both planes.

Thirty-two patients subsequently underwent temporal artery biopsies. In cases with a positive halo, an effort was made by surgeons to biopsy the documented site of the halo. Biopsies were not performed in 37 cases: in 23 of them other diagnoses were confirmed between time of US and the scheduled biopsy, 10 did not agree to the procedure, and 4 patients were taking anticoagulant therapy. The time interval between the US and biopsy was several hours to 3 days. In 30 cases both sides were biopsied. One sided biopsy was performed in 2 patients. No patient was receiving steroid therapy at the time of US, and in 14 cases steroids were begun 1 to 2 days prior to biopsy.

GCA was diagnosed if a patient had positive biopsy or met all the following criteria: (1) American College of Rheumatology GCA classification criteria[8]; (2) there was prompt clinical response to treatment with 40–60 mg/day of prednisone, together with decreasing erythrocyte sedimentation rate and C-reactive protein levels, and (3) no other diagnosis related to the patient's symptoms was made during a followup period of 6 months.

RESULTS

GCA was diagnosed in 14 patients. Nine were biopsy positive, 4 were biopsy negative, and one refused a biopsy. The final diagnoses in the other 55 patients were polymyalgia rheumatica (PMR, 12 cases), infectious disease (12 cases), malignancy (11 cases), nonarteritic anterior ischemic optic neuropathy (6 cases), nonspecific headaches (5 cases), osteoarthritis (5 cases), fibromyalgia (3 cases), and depression (1 case). The PMR patients were subsequently followed for 1 to 2 years, and none have developed GCA during that period.

A periluminal dark halo was observed in 24 of the 69 patients. It was bilateral in 19, and unilateral in 5 cases. Twelve of these 24 cases were diagnosed as having GCA, while in the other 12 patients GCA diagnosis was not confirmed histologically or clinically. The final diagnoses in these 12 patients with the "false positive" halo sign were PMR (4 cases), infectious diseases (4 cases), malignancy (3 cases), and osteoarthritis (one case). There was no significant difference between the 12 patients with the "true positive" and the 12 with false positive halo sign regarding the location and extent of the involved regions. Table 1 describes the relationship between the presence of a halo and GCA diagnosis. From these data, the sensitivity, specificity, PPV, and NPV of the halo sign for diagnosing GCA were calculated (Table 2).

Giant cells were found in 4 of the 9 biopsy positive arteries. There was no correlation between the presence of a halo and of giant cells in the biopsy specimens. Five of the 14 GCA patients had prominent temporal arteries on palpation. There was no correlation between this finding and the presence of a halo.

Table 1. Relationship between the presence of a hypoechoic periluminal halo in color Doppler ultrasonography of the temporal arteries and giant cell arteritis (GCA) (cases with temporal artery biopsies are in parentheses).

	GCA	No GCA	Total
Halo	12 (7)	12 (9)	24 (16)
No halo	2 (2)	43 (14)	45 (16)
Total	14 (9)	55 (23)	69 (32)

Table 2. Sensitivity, specificity, positive (PPV) and negative predictive values (NPV) of the halo sign for diagnosing giant cell arteritis (GCA), when diagnosis is based either on a temporal artery biopsy or on clinical diagnostic criteria*.

	GCA (per criteria)	GCA (per biopsy)
Sensitivity, %	86	78
Specificity, %	78	61
PPV, %	50	44
NPV, %	96	88

* See Materials and Methods section for GCA diagnostic criteria used in this study.

DISCUSSION

Vascular US can describe morphologic changes in the vessel wall and flow characteristics in the lumen. Both may be abnormal in GCA, but specificity of stenosis or occlusion for the diagnosis GCA was inferior to that of the halo sign[7]. Narrowing of the lumen occurs also in atherosclerosis and arteriosclerosis[2,9,10], thus we considered stenosis and occlusion of the temporal arteries to be phenomena less characteristic of GCA. In this study we specifically looked for a certain morphologic change in the vessel wall, the halo sign, which probably represents inflammation-induced edema and evaluated its predictive value in diagnosing GCA.

Our data show that the NPV of the halo sign for diagnosing GCA is very high, but the PPV is unsatisfactory. This is in contrast with the findings of Schmidt, *et al*[7]. Although they reported only on sensitivity and specificity, it was possible to calculate the PPV and NPV from their data. Both were very high: the calculated PPV was 100% and the NPV was 91%. This group further extended their observations and later reported data from more patients[11]. Again, the PPV and NPV could be calculated from these data, and were 95% and 96%, respectively. Further data on this subject were reported in an abstract form by Salvarani, *et al*. They also studied the halo sign specifically, but only in biopsy-proven GCA patients, and considered it to be positive when the halo thickness was at least 1 mm[12]. This probably accounts for their low sensitivity (40%) and high specificity (93%). However, the PPV and NPV that could be calculated from their data were comparable with our results: the PPV for biopsy-proven GCA was low at 55%, while NPV was high at 88%.

The NPV was consistently high in all 3 studies. The reasons for the differences in the PPV are not clear. Lack of experience with the technique and over diagnosis of the halo sign could be one reason. We did not observe a "learning curve": there was no significant difference in the PPV and

NPV when results from the initial 25 patients were compared with the following 44 patients. Another reason for the different results could be the use of a different scanner, or different settings of the scanner[7,11]. However, the scanner used in our study was considered to have adequate resolution for temporal artery US, according to a recent report[11]. In our opinion, the most likely explanation for the varied results is personal variation in the interpretation of the US regarding the presence of a halo.

Four of the 12 patients with PMR had positive halo signs. It could be debated whether these represent false positive results or missed diagnoses of GCA. Since all 4 patients responded to low dose prednisone (20 mg or less) and did not develop any sign or symptom of GCA during followup of 1 to 2 years, we believe that GCA diagnosis was not missed in these cases.

In conclusion, while results of PPV vary, the NPV of the halo sign for diagnosing GCA is consistently high. Thus, color Doppler US of the temporal arteries cannot replace temporal artery biopsy in diagnosing GCA. However, lack of a halo may practically serve to rule out a diagnosis of GCA: in cases with negative biopsies there are often doubts regarding the possible diagnosis of "biopsy negative GCA". In such cases a previous US with a negative halo sign could help the physician rule out GCA.

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