Impact of cranial and axillary/subclavian artery involvement by color duplex sonography on response to treatment in giant cell arteritis

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Objective: **Color duplex sonography (CDS) today is broadly used in the diagnostic workup of patients with suspected cranial or extracranial giant cell arteritis (GCA). This study aimed to determine the prognostic impact of the disease pattern assessed by CDS on the treatment response in GCA.**

Methods: **This was a retrospective, longitudinal follow-up study of 43 patients who were diagnosed with GCA at our institution between 2002 and 2010. All patients underwent CDS of the temporal and subclavian/axillary arteries at baseline and were observed for at least 6 months. Vasculitis was sonographically characterized by a circumferential, hypoechogenic wall thickening. According to the CDS findings, patients were categorized into patients with involvement of the subclavian/axillary arteries only (group A1, n = 17), patients with involvement of both the subclavian/axillary arteries and the temporal arteries (group A2, n = 9), and patients with isolated cranial GCA (group B, n = 17). Data on recurrences, corticosteroid doses, and steroid-sparing agents were extracted from the medical records. Treatment response over time was analyzed by Kaplan-Meier curves with log-rank testing.**

Results: **The mean follow-up time was 25.4 months and did not differ between groups ($P = .4$). Patients in group A1 were significantly younger than patients in groups A2 and B ($P < .01$). The interval between symptom onset and diagnosis was significantly longer in groups A1 and A2 compared with group B ($P < .01$). The number of recurrences per month was significantly higher in group A2 compared with group A1 and group B (A1, 0.07; A2, 0.13; B, 0.03; $P < .01$). Whereas there were no significant differences in the mean time until a daily prednisolone dose <10 mg was reached, patients in group A2 more frequently required steroid-sparing agents (A1, 24%; A2, 56%; B, 24%; $P = .04$).**

Conclusions: **Extensive vascular involvement of both the temporal and subclavian/axillary arteries, as depicted by CDS, may be associated with a poor treatment response in GCA. (J Vasc Surg 2015;61:1285-91.)**

Giant cell arteritis (GCA) is the most common form of the primary systemic vasculitides, typically affecting people older than 50 years.[1] Historically, the clinical and scientific focus was mainly on the cranial disease pattern, characterized by involvement of the branches of the external carotid artery and the ophthalmic artery. However, in recent years and facilitated by the increased use of advanced noninvasive imaging technologies, extensive involvement of the extracranial arteries has been shown to be highly prevalent in GCA.[2-10] The thoracic aorta (45%-65%) and the subclavian/axillary arteries (30%-75%) are the arterial segments most frequently affected.[2-10] Whereas involvement of the carotid and subclavian/axillary arteries in GCA is virtually always accompanied by thoracic aortitis, it is not uncommon for extracranial GCA to occur without concomitant involvement of the temporal arteries (up to 50% of cases).[3,8]

Involvement of the extracranial arteries has not been routinely assessed in previous randomized and observational studies evaluating immunosuppressive treatment strategies in GCA.[11-17] Therefore, it is currently unclear whether treatment responses may differ between patients with isolated cranial and extracranial GCA. The present retrospective longitudinal follow-up study aimed to evaluate whether color duplex sonography (CDS) findings of the temporal, carotid, and subclavian/axillary arteries at baseline are associated with the treatment response in GCA.

METHODS

The clinical characteristics of our well-characterized cohort of patients with a first diagnosis of GCA have been published previously.[8] Patients diagnosed with GCA between 2002 and 2010 were eligible for inclusion in the present study when they had regular (monthly) follow-up visits at the Divisions of Vascular Medicine and Rheumatology for at least 6 months after treatment initiation.

All patients underwent a complete CDS study of the bilateral temporal, carotid, subclavian, and axillary arteries at the initial diagnostic workup (LOGIQ 9 ultrasound system; GE Medical Systems, Milwaukee, Wisc). The carotid,

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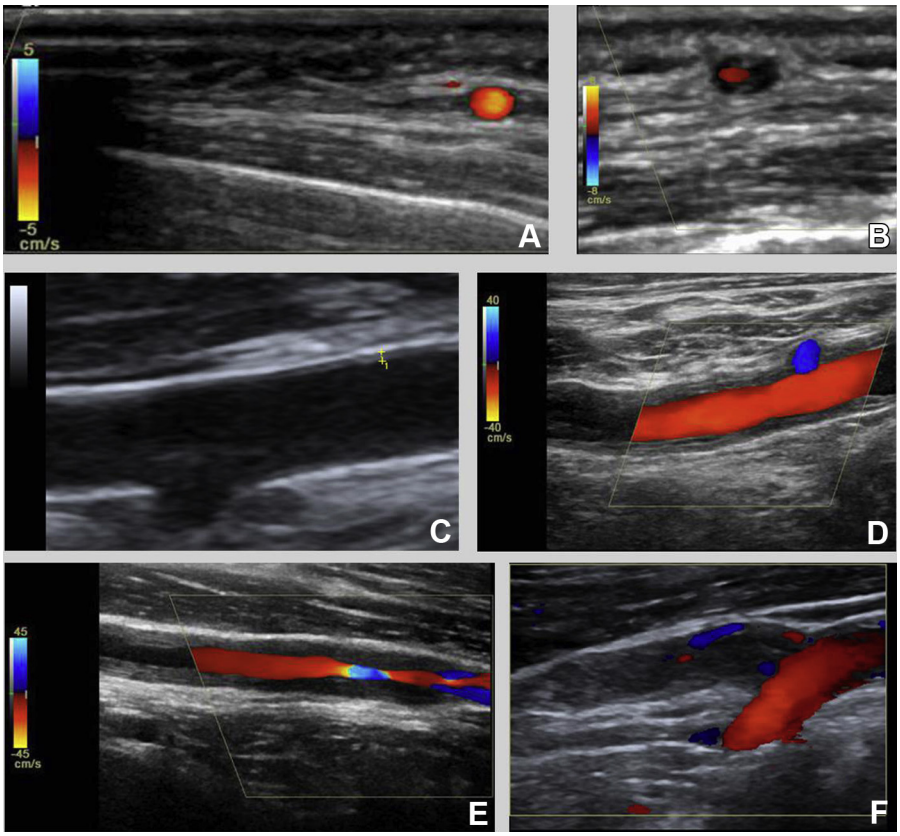

Fig 1. The hypoechogenic, circumferential wall thickening as the sonographic criterion for diagnosis of giant cell arteritis (GCA). **A,** Normal superficial temporal artery with complete color filling of the lumen. **B,** Halo of the superficial temporal artery. **C,** Normal vessel wall of the axillary artery. **D-F,** Hypoechogenic, circumferential wall thickening of the axillary arteries without luminal obstruction **(D)**, with resulting stenosis **(E)**, and with resulting occlusion **(F)**.

subclavian, and axillary arteries were visualized with 2.5- to 8-MHz linear transducers, and the superficial temporal arteries were evaluated with 4.5- to 13-MHz linear transducers. A circumferential, homogeneous, hypoechogenic wall thickening was regarded as a typical sonographic sign of GCA (Fig 1).

The diagnosis of GCA was finally established by a positive finding on temporal artery biopsy, by fulfillment of at least three of the American College of Rheumatology classification criteria for cranial GCA, or in the presence of the above-mentioned typical CDS findings, together with typical clinical signs and a systemic inflammatory response rapidly responsive to corticosteroid treatment.[5,8,18,19] All patients were required to be at least 50 years of age at the time of diagnosis.

At our institution, patients with GCA usually are treated according to criteria outlined by Tatò and Hoffmann in 2008.[20] Related to the retrospective study design, individual corticosteroid doses, steroid tapering, and the use of adjunctive steroid-sparing agents were at the discretion of the treating physician based on her or his judgment of disease activity. A chart review was performed using a standardized reporting form. Data on the clinical course (ie, recurrent cranial, extracranial, or systemic symptoms), inflammatory markers (erythrocyte sedimentation rate, C-reactive protein level), steroid dosage, use of adjunctive immunosuppressive drugs, and adverse events attributable to long-term corticosteroid use were obtained from the medical records. In case of missing information, the patient's general physician was contacted to complete the data.

The study end points included the proportion of patients over time who (1) experienced one or more disease flares, (2) were able to taper the daily prednisolone dose to <10 mg, and (3) required the use of steroid-sparing agents. A vasculitis relapse was defined as the recurrence of clinical signs or symptoms or an otherwise unexplained rise of the inflammatory markers (C-reactive protein level >0.5 mg/dL), with subsequent improvement after increase of the corticosteroid dosage.[15]

Patients with (group A) and without (group B) a positive CDS study of the subclavian and axillary arteries were compared. In a second comparison, the group of patients with sonographic signs of extracranial GCA was further