Involvement of the Femoropopliteal Arteries in Giant Cell Arteritis: Clinical and Color Duplex Sonography

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ABSTRACT. ***Objective.*** To determine the extent and clinical significance of giant cell arteritis (GCA) of the femoropopliteal arteries.

Methods. This was a retrospective clinical color duplex sonography (CDS) study; 60 of 112 consecutive patients with the diagnosis of GCA underwent complete clinical examination of the lower extremities including the vasculature, systolic ankle pressure measurement, and CDS scans of the femoropopliteal arteries within 1 year after diagnosis of GCA. Circumferential, hypoechogenic, homogenous wall thickening was regarded as a hallmark of femoropopliteal GCA.

Results. GCA of femoropopliteal arteries was present in 32 (53.3%) of 60 patients. In general, femoropopliteal GCA developed bilaterally (100%) and 14 patients (23.3%) had significant lower extremity artery obstructions secondary to vasculitis, all leading to symptomatic lower extremity ischemia, with development of critical leg ischemia in 4 patients. Compared with subjects without lower extremity vasculitis, patients with femoropopliteal involvement had a significant time delay until diagnosis (mean 23.9 vs 11.1 weeks; p = 0.03) and a higher frequency of concomitant vasculitis of the arm arteries (74.2% vs 42.9%; p = 0.02).

Conclusion. Femoropopliteal artery involvement appears to be a clinically relevant manifestation of GCA, frequently leading to symptomatic lower extremity ischemia. CDS of the femoropopliteal arteries is a noninvasive diagnostic tool for detection of lower extremity vasculitis in GCA. (J Rheumatol First Release Jan 15 2012; doi:10.3899/jrheum.110566)

Key Indexing Terms:
COLOR DUPLEX SONOGRAPHY FEMOROPOPLITEAL ARTERIES GIANT CELL ARTERITIS
LARGE-VESSEL VASCULITIS PERIPHERAL ARTERIAL DISEASE WALL THICKENING

Giant cell arteritis (GCA) is a primary vasculitis of large and medium size arteries, almost exclusively affecting individuals above 50 years of age[1,2]. Formerly, GCA was recognized as a localized disease predominantly affecting the cranial arteries, in particular the superficial temporal arteries (temporal arteritis) and the arteries supplying the optic nerve. With rapid technical developments and the wide availability of vascular imaging methods, GCA is increasingly recognized as a systemic vascular disease with the potential for serious extracranial vascular complications[3,4,5]. Evidence for extracranial artery involvement comes mainly from vascular imaging studies of the aorta and the subclavian and axillary arteries[6,7,8,9]. Involvement of the lower extremity arteries in GCA has been rarely studied[3,4]. Some case reports and case series provide limited information suggesting that GCA of the lower extremity arteries may cause symptomatic limb ischemia and even loss of the affected extremities[10,11,12,13,14,15,16,17,18]. Different imaging modalities including intraarterial angiography, computed tomography, and magnetic resonance imaging have been applied in individual cases to visualize lower extremity vasculitis in GCA[14,15,17,18]. A study using FDG-positron emission tomography (PET) in patients with GCA or polymyalgia rheumatica detected femoropopliteal inflammation in 64% of patients[7].

Color duplex sonography (CDS) is regarded as a first-line imaging technique in GCA, and circumferential, hypoechogenic, homogenous wall thickening of the extracranial arteries has been shown to be highly specific for diagnosis of GCA[19]. Using CDS, myointimal hyperplasia secondary to vasculitis may also be easily visualized in the lower extremity arteries[8,16,19].

The objective of our clinical and sonographic study was to investigate the extent and clinical significance of vasculitis of the femoropopliteal arteries in patients with diagnosis of GCA.

MATERIALS AND METHODS

Study population. Between January 2002 and July 2010, 112 consecutive patients were diagnosed with GCA at our institution. Sixty (53.6%) of these

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patients underwent a complete diagnostic investigation of the lower extremity arteries within 1 year after diagnosis and were included in this retrospective study. Indication for lower extremity CDS in general was at the discretion of the responsible physician, according to symptoms, abnormal clinical findings, or the search for vasculitic manifestations in patients with a suspicion of GCA.

The diagnostic procedure consisted of a detailed medical history and examination by an experienced vascular specialist, and included systolic ankle pressure measurements and a standardized CDS study of the leg arteries. The severity of leg ischemia was graded according to established guidelines[20]. At the time of diagnosis, all patients also had routine laboratory analyses [blood cell count, C-reactive-protein (CRP), erythrocyte sedimentation rate (ESR)] and a CDS study of the superficial temporal, carotid, and proximal arm arteries. Superficial temporal artery biopsy was performed at the discretion of the physician. Diagnosis of GCA was established by fulfillment of at least 3 of the 5 American College of Rheumatology (ACR) classification criteria for cranial GCA and/or based on the typical sonographic feature of circumferential, hypoechogenic arterial wall thickening of the arm or leg arteries in association with elevation of CRP and/or ESR and good clinical and laboratory response to corticosteroid treatment[19,21].

Color-coded duplex sonography of the femoropopliteal arteries. CDS was performed by an experienced physician using the Logic 9^{TM} ultrasound system (GE Medical Systems, Milwaukee, WI, USA). The carotid, subclavian, axillary, brachial, and femoropopliteal arteries were visualized with 2.5–8 MHz linear transducers and the superficial temporal arteries were evaluated with 4.5–13 MHz linear transducers. Lower extremity CDS scans included the following arterial segments: common femoral artery, deep femoral artery, superficial femoral artery, and popliteal artery. In case of clinical suspicion, the crural arteries were also evaluated. As described, a circumferential, hypoechogenic, homogenous wall thickening with or without a hyperechogenic stripe lining the innermost wall layer was regarded as a typical sign for vasculitis of the lower extremity arteries[16,19]. This specific sonographic feature was differentiated from inhomogeneous, excentric, partly calcified arterial wall changes typically observed in atherosclerosis. Hemodynamically significant stenosis of the lower extremity arteries (> 50% diameter reduction) was characterized by a peak velocity ratio (PVR) ≥ 2.0, defined by the relation of peak systolic velocity (PSV) in the stenosis divided by PSV of the adjacent proximal normal arterial segment[22].

Statistical analysis. Retrospective data collection and analysis was approved by the institutional review board. The SPSS 15.0 software package (SPSS, Chicago, IL, USA) was used for statistical analysis. Clinical, laboratory, and sonographic variables of patients with and without femoropopliteal GCA were compared using Fisher's exact test (categorical variables) and the Mann-Whitney U test (continuous variables). Two-sided p values < 0.05 were considered significant. Results for categorical variables are presented as frequency (percentage), continuous variables are displayed as mean ± standard deviation.

RESULTS

Cohort characteristics. Detailed data on clinical characteristics of the overall cohort are given in Table 1. There were no significant differences between patients with and those without a complete investigation of the lower extremity arteries, except for leg claudication, which was not present in any of the patients without a diagnostic study of the lower extremity vasculature.

The main symptoms leading to diagnosis of GCA in 60 patients who underwent a complete lower extremity study were symptoms of cranial arteritis in 27 (45%) patients, symptomatic extremity ischemia in 19 (31.7%) patients, and systemic inflammatory syndrome including polymyalgia rheumatica and fever of unknown origin in 14 (23.3%) patients.

Thirty-nine (65%) of 60 patients fulfilled the ACR criteria for classification of GCA (Table 1). Of those, 23 patients underwent temporal artery biopsy, and 17 patients had a positive temporal artery biopsy result. Three further patients had histological proof of extracranial GCA. Of the 39 patients fulfilling the ACR criteria, 38 patients had a positive result on CDS study of the cranial or extracranial arteries. Twenty-one patients did not fulfill the ACR criteria. In this subgroup, 5 patients underwent temporal artery biopsy, with a positive test result in only 1 patient. All patients who did not meet the ACR criteria showed sonographic evidence of cranial or extracranial GCA together with laboratory signs and symptoms of systemic inflammation.

The mean time between diagnosis of GCA and the CDS study of lower extremity arteries was 6 weeks (range 0–50 wks), with 42 patients (70%) examined within 2 weeks after diagnosis of GCA.

GCA of femoropopliteal arteries. GCA of the femoropopliteal arteries, as defined by CDS criteria, was observed in more than half of the patients [32 of 60 patients (53.3%); Figure 1]. There was no difference in frequency of femoropopliteal GCA between patients who underwent the lower extremity CDS study within 2 weeks after diagnosis and those who had a CDS study and initiation of corticosteroid treatment later. Within the 42 patients who had a lower extremity CDS study within 2 weeks, 23 (54.8%) had sonographic evidence of femoropopliteal involvement. In the remaining 18 patients, i.e., with a CDS study performed later than 2 weeks after diagnosis, 9 patients (50%) showed femoropopliteal involvement ($p = 0.74$).

Of the 32 patients with sonographic evidence of femoropopliteal GCA, 30 also exhibited typical vascular wall thickening of the superficial temporal arteries, carotid arteries, and/or proximal arm arteries. The remaining 2 patients fulfilled the diagnostic criteria for polymyalgia rheumatica and had markedly increased humoral inflammatory markers. One of these patients also experienced an inflammatory aneurysm of the abdominal aorta, and the other complained of bilateral leg claudication secondary to long-segment stenoses of the popliteal and crural arteries.

In all cases, femoropopliteal GCA developed bilaterally. The typical thickening of the arterial wall was most frequently observed in the superficial femoral artery and popliteal artery. The common femoral artery and deep femoral artery were both less frequently involved (Table 2). GCA of the femoropopliteal arteries resulted in hemodynamically significant stenosis or occlusion in 14 (43.8%) of 32 patients, with luminal obstructions most frequently localized in the superficial femoral artery and the popliteal artery (Table 2). While stenotic lesions of the common femoral artery did not occur, the deep femoral artery exhibited significant luminal obstructions secondary to vasculitis in 5 patients (3 of the 4 patients with critical limb ischemia; Table 2). In 6 patients with clinical suspicion of peripheral artery disease of the lower legs, the

Table 1. Comparison of clinical variables of patients with (Patients+) and without (Patients–) a complete diagnostic investigation of lower extremity arteries.

Variable	All Patients	Patients+	Patients–	p
Patients, no. (%)	112	60 (53.6)	52 (46.4)	
Age, mean ± SD, yrs	69 ± 8.4	67.8 ± 8.5	70.3 ± 8.2	0.12
Female, no. (%)	86 (76.8)	47 (78.3)	39 (75.0)	0.82
Headache, no. (%)	59 (52.7)	34 (56.7)	25 (48.1)	0.45
Jaw claudication, no. (%)	47 (42.0)	23 (38.3)	24 (46.2)	0.45
Impaired vision, no. (%)	41 (36.6)	20 (33.3)	21 (40.4)	0.56
Arm claudication, no. (%)	22 (19.6)	14 (23.3)	8 (15.4)	0.35
Leg claudication, no. (%)	17 (15.2)	17 (28.3)	0	< 0.01
PMR, no. (%)	45 (40.2)	24 (40)	21 (40.4)	1.00
Constitutional symptoms, no. (%)	62 (55.4)	37 (61.7)	25 (49.0)	0.25
Time between symptom onset and diagnosis, mean ± SD, wks	18.2 ± 21.8	17.9 ± 19.8	18.5 ± 24.0	0.89
C-reactive protein at time of diagnosis, mean ± SD, mg/dl*	7.3 ± 5.7	7.1 ± 5.4	7.5 ± 6.1	0.69
ESR at time of diagnosis, mean ± SD, mm/h**	75 ± 34	80 ± 35	70 ± 33	0.11
Temporal artery halo (CDS), no. (%)	58 (51.8)	28 (46.7)	30 (57.7)	0.26
Temporal artery biopsy, no. (%)	56 (50.0)	28 (46.7)	28 (53.8)	0.57
Positive temporal artery biopsy, no. (%)	42 (75.0)	18 (64.3)	23 (85.7)	0.12
≥ 3 ACR criteria fulfilled, no. (%)	7 (68.8)	39 (65.0)	38 (73.1)	0.42
GCA of the carotid arteries (CDS), no. (%)	30 (26.8)	21 (35.6)	9 (17.3)	0.05
GCA of the arm arteries (CDS), no. (%)	58 (51.8)	35 (59.3)	23 (44.2)	0.18

* Reference range < 0.5 mg/dl; ** reference range: men < 20 mm/h; women < 30 mm/h; PMR: polymyalgia rheumatica; ESR: erythrocyte sedimentation rate; CDS: color Doppler sonography; ACR: American College of Rheumatology; GCA: giant cell arteritis.

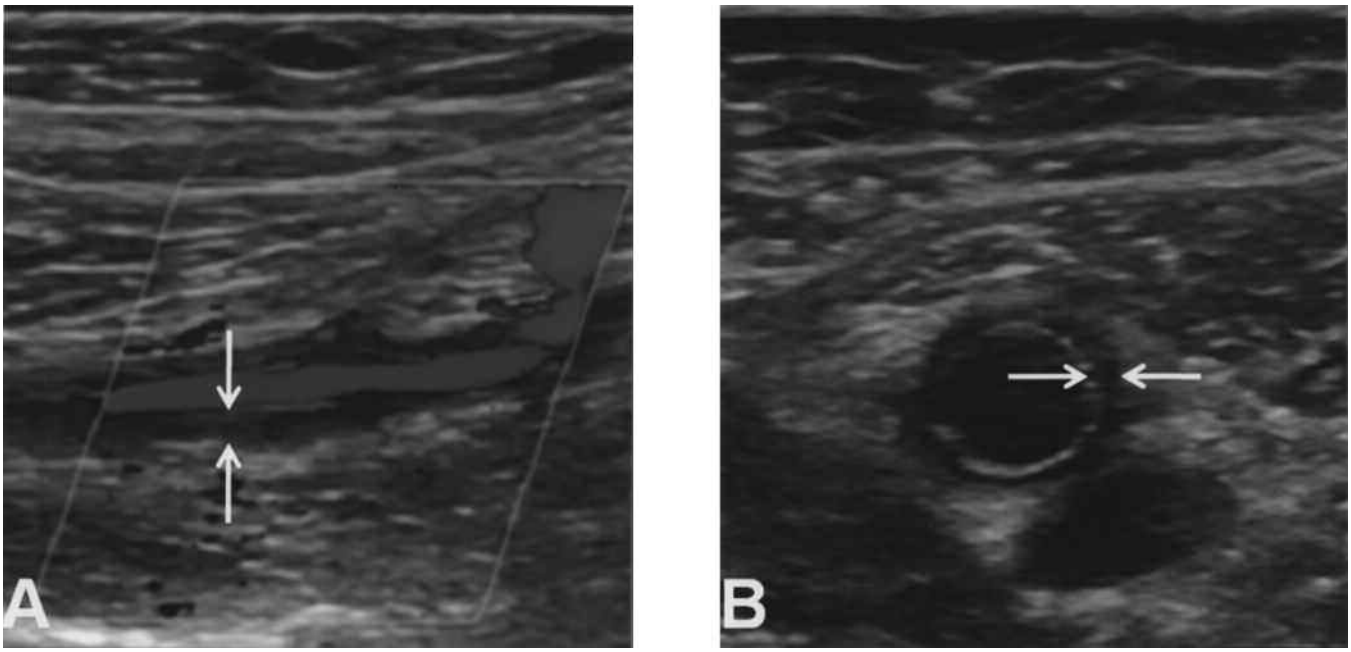

Figure 1. Circumferential hypoechogenic homogenous wall thickening (arrows) of the popliteal artery resulting in long-segment, high-grade stenosis (A). Nonstenotic wall thickening of the superficial femoral artery (arrows) with a hyperechogenic stripe ("beaded tube") lining the innermost arterial layer (B).

crural arteries were also visualized, with detection of bilateral wall thickening leading to stenosis/occlusion in all 6 patients.

All 14 patients with hemodynamically significant vessel obstructions were symptomatic, having either calf and/or foot claudication (10 patients) or critical limb ischemia (4 patients). Leg ischemia was the leading clinical symptom of GCA in 9 patients. Typical features of GCA were frequently present, such as cranial symptoms (10 of 14 patients; 76.9%),

Table 2. Frequency and type of involvement of the different femoropopliteal arterial segments in the 32 patients with giant cell arteritis of the lower extremity arteries.

Vessel	All, n = 32	Stenosis/occlusion Due to Vasculitis, n = 14
Common femoral artery, no. (%)	9 (28.1)	0
Deep femoral artery, no. (%)	9 (28.1)	5 (35.7)
Superficial femoral artery, no. (%)	30 (93.8)	11 (78.6)
Popliteal artery, no. (%)	21 (65.6)	8 (57.1)

polymyalgia rheumatica (6 of 14 patients; 46.2%), arm claudication (3 of 14 patients; 23.1%), or constitutional symptoms (8 of 14 patients; 53.8%). In the subgroup of patients with symptomatic lower extremity vasculitis, concomitant vasculitis of the arm arteries was detected by CDS in 10 of 14 patients, whereas a temporal artery halo was noted in only 5 of 14 patients. Five of the 14 patients underwent temporal artery biopsy, with histological proof of temporal arteritis in 3 patients (60%). Ischemic symptoms were bilateral in 10 of 14 patients and lower extremity ischemia related to GCA was characterized by a rapid progression of symptoms. In patients presenting with critical limb ischemia, the time from onset of claudication to the development of rest pain and/or gangrene was only several weeks (mean 20.3 wks, range 15–28 wks). In 2 patients initially complaining of claudication, unilateral critical limb ischemia had acutely occurred due to spontaneous femoropopliteal artery dissection.

Overall, atherosclerotic plaques of the femoropopliteal arteries were visible in 46 of 60 patients (76.7%). The frequency of atherosclerotic lesions depicted by CDS was not significantly different between patients with and those without femoropopliteal vasculitis, 71.9% and 82.1%, respectively (p = 0.38). Two female patients with GCA presented with short unilateral atherosclerotic occlusion of the superficial femoral artery and another male patient had bilateral atherosclerotic stenoses of the iliac arteries. All 3 patients had longlasting and stable claudication. None of these patients was considered to have femoropopliteal GCA by the CDS criteria.

Spot calcifications resulting in a hyperechogenic stripe lining the innermost layer of the thickened vessel wall were detected in 21 (65.6%) of the 32 patients classified as having femoropopliteal vasculitis (Figure 1). The presence of the hyperechogenic stripe did not differ between patients examined within or later than 2 weeks (65.2% vs 66.7%; p = 1.00).

Followup. The mean followup time was 25.1 ± 20.9 months (range 1–62 mo). One of the 2 patients with acute dissection of superficial femoral artery required unilateral femorocrural bypass surgery for limb salvage. Another patient, who presented with bilateral critical limb ischemia, also required femoropopliteal bypass surgery and minor amputation. GCA of femoropopliteal arteries was confirmed histologically in both cases, despite previous use of corticosteroid treatment (Figure 2). Both patients remained free of symptoms and the bypasses were patent in the long term (after 16 and 60 months, respectively). Two other patients with critical limb ischemia, 1 with acute dissection of the superficial femoral artery, were managed conservatively with high-dose corticosteroids, antiplatelet agents, and intravenous prostanoids. One of these patients showed resolution of rest pain and ulcer healing after 1 month of medical therapy and was then lost to followup. The other patient experienced relief of rest pain, with stable claudication (maximum walking distance 500 meters) after 24 months of followup.

Patients with claudication secondary to vasculitis all were managed conservatively with corticosteroid treatment and antiplatelet agents. Worsening of symptoms did not occur after initiation of corticosteroid treatment. Four patients initially complaining of bilateral claudication were free of symptoms during followup. The remaining patients had either improvement of symptoms or stable claudication (3 patients in each of 2 groups).

Endovascular revascularization procedures were not performed in any patients reported here. In patients with subclinical nonstenotic involvement, new onset of claudication did not occur during followup.

Comparison of patients with and without femoropopliteal GCA. Characteristics of subjects with and without vasculitis of the femoropopliteal arteries are summarized in Table 3. Patients with femoropopliteal GCA less frequently had symptoms of cranial GCA (jaw claudication) and significantly more often exhibited GCA of the arm arteries by the CDS criteria. In this group, we also observed a trend toward a lower percentage of subjects presenting with a halo of the superficial temporal artery. Accordingly, patients with femoropopliteal involvement were less likely to fulfill 3 or more of the ACR criteria for classification of cranial arteritis. Further, the time between symptom onset and diagnosis was significantly longer in the group with femoropopliteal involvement. Of note, there were no significant differences between the 2 groups regarding the inflammatory response (CRP, ESR) and the presence of systemic symptoms and traditional cardiovascular risk factors.

DISCUSSION

To our knowledge, our study describes the largest series of patients with femoropopliteal vasculitis in GCA, including a considerable number of patients with subclinical lower extremity artery involvement. Our data indicate that vasculitis of the lower extremity arteries is a rather frequent and clinically relevant manifestation of GCA. More than 50% of the 60 patients with GCA included in our study presented with a circumferential, hypoechogenic, homogenous wall thickening of femoropopliteal arteries indicative for vasculitis. This sonographic feature has been shown to be highly specific for GCA of the extracranial arteries in a recent case-control study[19] and in an earlier study by Schmidt, *et al*[8]. Notably, we were able

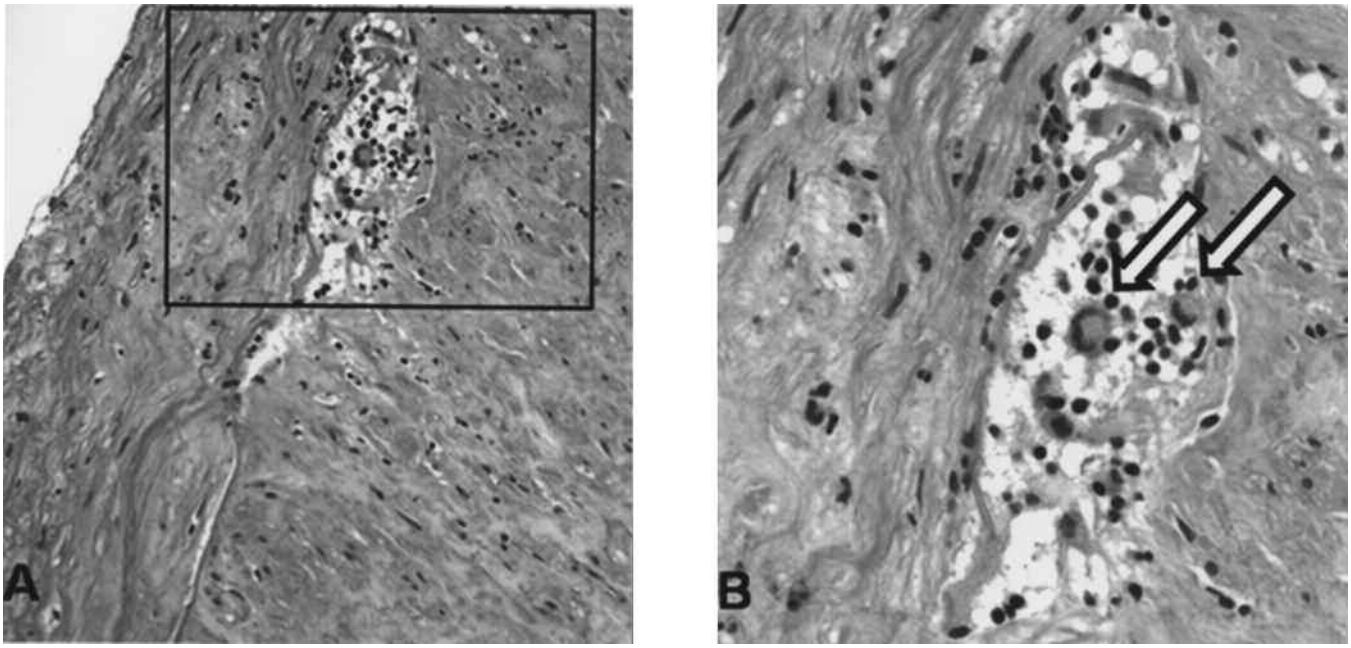

Figure 2. Histological specimen of femoropopliteal vasculitis in a 73-year-old woman with GCA who required bypass surgery for critical limb ischemia due to spontaneous dissection of the left superficial femoral artery (courtesy of Dr. K. Wagner, Department of Pathology, Ludwig-Maximilians-University, Munich). Cross-section shows intimal thickening, disruption of the inner elastic lamina, loose multinucleated giant cells, and scanty mononuclear cell infiltration (A; H&E stain, original magnification ×20). Inset (B) shows multinucleated giant cells (arrows; original magnification ×40).

to confirm the sonographic findings by histology in 2 of our patients with femoropopliteal GCA who required bypass operations for limb-threatening ischemia.

Although there was no histological proof of vasculitis in the remaining patients with lower extremity GCA, the presence of the hypoechogenic circumferential wall thickening in other vascular areas in all but 2 patients underscores the vasculitic nature of the similar sonographic pattern in the lower extremity arteries. Only 1 subject exhibited isolated lower extremity vasculitis, as described occasionally in the literature[23].

Although sonographic diagnosis of extracranial GCA is based on hypoechogenic vessel wall thickening, no clear cutoff value has yet been established, with reference values reported in the literature ranging from 1.0 mm to 1.5 mm[9,24]. Therefore, we defined presence of vasculitic wall thickening exclusively on a qualitative basis, as done previously in studies examining the superficial temporal arteries and also the extracranial arteries[8,19,25]. Another methodological shortcoming of using CDS scanning for the diagnosis of extracranial GCA is the lack of data on interobserver variability. At present, such data are available only for the superficial temporal arteries, indicating an interobserver agreement of 100% for the presence of the temporal artery halo[25]. Considering the much larger diameter of the femoropopliteal arteries, it may be argued that the reproducibility of the hypoechogenic wall thickening is similar. However, this remains to be investigated.

In agreement with published case series, the superficial femoral and popliteal arteries were the most frequently affected vessel segments[14,16,17,18]. The hypoechogenic vessel wall thickening typically was not restricted to one arterial segment, but often diffusely affected the entire femoropopliteal vessel axis. Similar to what is known from sonographic studies of the upper extremity arteries and from studies utilizing 18-FDG-PET imaging, femoropopliteal GCA in our patients always developed bilaterally[7,9]. Thus, bilateral hypoechogenic, homogenous wall thickening of the femoropopliteal arteries may be regarded as a diagnostic hallmark of GCA[4,16,19]. As described, GCA may not be restricted to the femoropopliteal segments of the lower extremities[14,15,16,17,18]. In our study we occasionally observed vasculitis of the crural arteries in 6 patients, although we did not systematically investigate the calf vessels.

Almost every second patient with sonographic evidence of femoropopliteal vasculitis was symptomatic, complaining of either claudication or symptoms of critical limb ischemia. In 9 patients, claudication or critical limb ischemia was the leading clinical symptom. All symptomatic patients showed hemodynamically significant, long and tapered luminal narrowing, and/or occlusions of the femoropopliteal arteries. Severe disease of multiple arterial segments, including the deep femoral artery, with a limited capability of the arterial system to sufficiently collateralize vessel obstructions may explain the development of severe limb-threatening ischemia observed in 4 of our patients. This appears to be different from GCA of the upper extremity arteries, where subclavian and/or axillary artery obstructions are often sufficiently collateral-

Table 3. Comparison of clinical variables of patients with giant cell arteritis (GCA) with and without femoropopliteal artery involvement.

Variable	Femoropopliteal GCA	No Evidence for Femoropopliteal GCA	p
Patients, no. (%)	32 (53.3)	28 (46.7)	
Age, mean ± SD, yrs	66.4 ± 8.2	69.5 ± 8.8	0.31
Female, no. (%)	26 (81.3)	21 (75.0)	0.76
Hypertension, no. (%)	19 (59.4)	21 (75.0)	0.27
Diabetes, no. (%)	4 (12.5)	4 (14.3)	1.00
History of smoking, no. (%)	12 (37.5)	10 (35.7)	1.00
Dyslipidemia, no. (%)	5 (15.6)	8 (28.6)	0.35
Headache, no. (%)	15 (46.9)	19 (67.9)	0.12
Jaw claudication, no. (%)	8 (25)	15 (53.6)	0.03
Impaired vision, no. (%)	8 (25)	12 (42.9)	0.18
Arm claudication, no. (%)	8 (25.0)	6 (21.4)	0.77
Leg claudication, no. (%)	14 (43.8)	3 (10.1)	0.01
PMR, no. (%)	15 (46.9)	9 (32.1)	0.30
Constitutional symptoms, no. (%)	20 (62.5)	17 (60.7)	1.00
Time between symptom onset and diagnosis, mean ± SD, wks	23.9 ± 23.4	11.1 ± 11.9	0.03
Ankle pressures right leg, mean ± SD, mm Hg	126 ± 49	155 ± 30	0.01
Ankle pressures left leg, mean ± SD, mm Hg	130 ± 46	160 ± 35	< 0.01
C-reactive protein at time of diagnosis, mean ± SD, mg/dl*	7.3 ± 5.9	6.8 ± 4.7	0.98
ESR at time of diagnosis, mean ± SD, mm/h**	82 ± 32	78 ± 38	0.62
Temporal artery halo (CDS), no. (%)	11 (34.4)	17 (60.7)	0.07
Temporal artery biopsy, no. (%)	11 (34.4)	17 (60.7)	0.07
Positive temporal artery biopsy, no. (%)	6 (54.5)	12 (70.6)	0.44
≥ 3 ACR criteria fulfilled, no, (%)	17 (53.1)	22 (78.6)	0.06
GCA of carotid arteries (CDS), no. (%)	15 (48.4)	6 (21.4)	0.06
GCA of arm arteries (CDS), no. (%)	23 (74.2)	12 (42.9)	0.02

* Reference range < 0.5 mg/dl; ** reference range < 20 mm/h. PMR: polymyalgia rheumatica; CDS: color Doppler sonography; ACR: American College of Rheumatology; ESR: erythrocyte sedimentation rate.

ized and rarely cause severe symptomatic or even limb-threatening upper extremity ischemia[6,9].

Apparently differently from chronic atherosclerotic disease, ischemic symptoms progressed rapidly, with development of limb-threatening ischemia within only several weeks. As observed in 2 of our patients with symptomatic leg ischemia, spontaneous dissection of the femoropopliteal arteries may lead to acute hemodynamic deterioration and critical limb ischemia. A tendency for spontaneous dissection is known for GCA of the aorta, but to date has not been described for the aortic branches[4]. Unusual rapid development of ischemic lower extremity symptoms in conjunction with additional clinical features suggesting systemic inflammation in patients over age 50 years should raise suspicion for underlying extracranial GCA[4,14,16,17,18]. This is of particular clinical importance, given the observation that patients with critical ischemia of the lower extremities secondary to vasculitis frequently require surgical revascularization. Moreover, major amputation related to lower extremity GCA has been reported[12,13,14,17,18]. It is of clinical importance that revascularization should be performed after induction of remission of the inflammatory process[4]. Of note, endovascular procedures typically are not feasible in these patients due to long-segment stenoses and/or occlusions[4,16].

In contrast to critical ischemia, lower extremity vasculitis presenting with exercise-induced ischemia (claudication) can be managed conservatively in the majority of cases[14,15,16,17,18]. Indeed, complete relief of claudication without revascularization was documented in 4 of our patients and in previous case series[14,18].

Patients with femoropopliteal GCA exhibited the classical cranial form of GCA less often, and thus they had a lower (although nonsignificant) rate of positive temporal artery biopsy results and less frequently met the ACR criteria for cranial arteritis. Different disease patterns of GCA have been described by Brack, *et al*[6] in a comparison between patients with classical cranial GCA and patients with involvement of the proximal arm arteries. These investigators as well as Schmidt, *et al* in a later study found that patients with upper extremity artery involvement exhibited a significantly lower frequency of cranial symptoms[6,9]. Moreover, in our study vasculitis of the proximal arm arteries was associated with femoropopliteal GCA, indicating a distinct disease pattern with widespread extracranial vascular inflammation[4].

Symptomatic ischemia of the upper and lower extremities in the same patient has been reported previously[8,9,10,14,16,17,18]. In the study by Aschwanden and coworkers, 7 of 9 patients with lower extremity involvement also had vasculitis of the arm arteries by the CDS criteria[19]. It has been argued that the ACR criteria may be of limited value in the diagnosis of extracranial GCA[4,6]. The probably low sensitivity of the ACR criteria and the highly specific ultrasound findings in the upper and lower extremity arteries emphasize the central role of CDS in the diagnostic investigation of patients with suspected extracranial GCA[19]. However, because a considerable number of patients in our cohort were diagnosed solely on the basis of extracranial CDS findings, we are not able to provide information on the diagnostic yield from CDS of the extracranial arteries in addition to the established diagnostic criteria.

Our observational study was not intended to estimate the prevalence of femoropopliteal involvement in patients with GCA. Since only half the total cohort of GCA patients underwent a complete sonographic assessment of the lower extremity vasculature, and because the majority of patients were recruited from our Department of Vascular Medicine, where patients are referred for investigation of vascular problems, the rate of femoropopliteal involvement we observed may overestimate the unknown true prevalence of femoropopliteal vasculitis in GCA. On the other hand, CDS studies performed within a year after initiation of corticosteroid treatment of GCA potentially may lead to false-negative results. Although we could not observe different rates of femoropopliteal vasculitis in patients with CDS studies performed within 2 weeks or later after diagnosis of GCA, Schmidt, *et al* reported a complete resolution of the temporal artery halo and a frequent disappearance (30%) of hypoechogenic wall thickening of the arm arteries during corticosteroid treatment[25,26]. In contrast, Aschwanden, *et al* in their study on extracranial involvement in GCA documented that wall thickening remained unchanged in the majority of vessel segments (76 of 84) at 6-month followup. In particular, these observations included wall thickening of the lower extremity arteries[19].

Atherosclerotic plaques of the femoropopliteal arteries were frequently found in our cohort of patients older than age 50 years. A study using high resolution B-mode ultrasound of the carotid arteries reported a frequency of carotid plaques in 82% of patients with biopsy-proven GCA and 87.5% of matched controls[27]. More recently, Aschwanden, *et al* described atherosclerosis in at least one of the vascular segments investigated in 82.1% of their patients[19]. These data are comparable to the frequency of arteriosclerotic plaques detected in the femoropopliteal arteries in our study (76.7%). A hyperechogenic stripe lining the innermost layer of the thickened wall was detected in 2 out of 3 patients with femoropopliteal vasculitis in our study. Whether these spot calcifications result from early atherosclerosis accompanying inflammation of the vessel wall or are secondary to the vasculitic process itself remains unclear[4].

Our study provides evidence that involvement of the lower extremity arteries is a clinically relevant finding in patients with GCA. It is very likely that peripheral artery disease due to GCA currently may be underestimated or even misinterpreted as an aggressive form of atherosclerosis in those who are symptomatic[3,4,14,16,17]. In view of our results, we recommend use of CDS of femoropopliteal arteries in investigations of all patients with proven or suspected GCA and/or polymyalgia rheumatica who have symptoms suggestive of lower extremity ischemia (e.g., calf or foot claudication), and in all patients older than age 50 years with a systemic inflammatory disorder of unknown etiology (e.g., fever of unknown origin)[16,28]. It remains unclear whether patients with widespread arterial inflammation involving the lower extremity arteries may have a different prognosis with regard to treatment response and risk of relapse. Therefore, in patients without symptomatic lower extremity ischemia in whom diagnosis of GCA is already established (e.g., by positive temporal artery biopsy), CDS of the extremity arteries provides no additional diagnostic information. Increased awareness of the presence of different disease patterns of GCA may help to avoid the substantial diagnostic delay observed in our patients with lower extremity vasculitis.

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