Vertebrobasilar Ischemia and Structural Abnormalities of the Vertebral Arteries in Active Temporal Arteritis and Polymyalgia Rheumatica — An Ultrasonographic Case-Control Study

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ABSTRACT. ***Objective.*** Temporal arteritis (TA) affects large arteries, including the vertebral arteries in up to 15% of cases. High resolution ultrasonography (US) is widely used for noninvasive imaging of the extracranial vertebral arteries. We assessed the prevalence of vertebrobasilar ischemia and structural abnormalities of the extracranial vertebral arteries by US in patients with TA and polymyalgia rheumatica (PMR) and in healthy controls.

Methods. This prospective study included clinical and US data from 93 patients with TA and 34 with PMR. A comparison was made with US findings in a population based, age matched group of 203 elderly subjects.

Results. Vertebrobasilar ischemia in 4 patients with TA was less frequent (4.3%) than neuroophthalmological complications (27.9%). In all 4 patients vertebrobasilar ischemia was associated with proximal vertebral artery occlusive disease. The rate of stenosis (> 50%) and occlusions of the vertebral arteries was significantly higher in the TA patients (12.9%) than in the PMR patients (2.9%) and controls (3%). Concentric hypoechogenic mural thickening of the proximal segments V0/V1 of the vertebral artery was found in only one PMR patient and 2 TA patients.

Conclusion. Vertebrobasilar ischemia is an uncommon complication of TA. Color duplex sonography can help to detect temporal arteritis of the vertebral arteries. Hypoechogenic mural thickening in TA can be indistinguishable from wall hematoma caused by vertebral artery dissection and atherothrombotic occlusive disease. (J Rheumatol 2005;32:2356–60)

Key Indexing Terms:
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Large artery involvement is an uncommon complication of temporal arteritis (TA), affecting up to 15% of patients with TA[1]. In addition to aortitis and coronaritis related complications, vertebrobasilar stroke represents a life-threatening condition in patients with TA[2,3]. Pathological studies found that involvement of the vertebral arteries is as common as that of the ophthalmic, posterior ciliary arteries and the superficial temporal artery, reaching 75%–100%. Due to its affinity to elastic fibers, TA of the vertebral arteries is usually confined to the extradural parts of the vertebral arteries[4]. The spectrum of clinical signs and symptoms in vertebral TA includes occipital and nuchal pain, vertebrobasilar transient ischemic attack, and stroke.

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Involvement of the vertebral arteries can be detected noninvasively with high resolution color duplex sonography (CDS), and is characterized sonographically by hypoechogenic mural thickening[5]. CDS examination has the potential to identify TA patients with vertebral artery involvement accurately and thus to identify individuals with increased risks for complications.

We assessed the prevalence and severity of vertebrobasilar ischemia and of structural abnormalities of the extracranial vertebral arteries in patients with TA and polymyalgia rheumatica (PMR) using CDS, and compared findings with a healthy elderly general population.

MATERIALS AND METHODS

Over a period of 74 months, 127 subsequent patients were included in the study. All patients were studied in active phases of the disease. They had received a diagnosis of either TA (n = 93) or PMR (n = 34) and were treated in the departments of rheumatology, ophthalmology, or neurology of the Central Hospital in Augsburg, Germany. Diagnoses of TA and PMR were made according to standard criteria[6,7]. Diagnostic biopsies could not be done in 12 of the 93 TA and 18 of the 34 PMR patients due to anticoagulation (n = 3), severe internal carotid artery stenosis with collateral flow (n = 4), or other reasons (n = 23). Diagnoses in these cases were thus based on the exclusion of other disease, the effect of adequate doses of steroids, and

followup examinations. TA was confirmed histologically in 55 biopsy specimens (72.4%) of the TA patients and in none of the PMR patients. In the other cases the diagnoses were confirmed by the exclusion of other disease, the effect of adequate doses of steroids, and followup examinations. Additionally, in patients with large artery disease, typical angiographic findings were used for confirmation of the diagnosis.

TA was confirmed histologically in 60 biopsy specimens (64.5%) of the TA patients and in none of the PMR patients. Eighty-five TA and 32 PMR patients had received steroids before ultrasonographic (US) examination (median 2, range 1–24 days).

All cases received CDS of the V0, V1, and V2 segments of the extracranial vertebral arteries. In most patients the V2 segment of the vertebral artery could be visualized up to the C3/4 level. A linear array high resolution 7.5 MHz transducer (Siemens L40 5.1–9 MHz) and Siemens Sonoline Elegra ultrasound system were used. Standard parameters for the B-mode were emission frequency 6 MHz, dynamic range 50 dB, gain 70 dB. For the Doppler sonography, a wall filter of 50 Hz and a pulse-repetition frequency of 3989 Hz were used. The arteries were examined as extensively as possible in transverse and longitudinal sections. Absent flow in a clearly visible vertebral artery was considered to be an occlusion of the artery; segmental increases of blood flow velocity with wave forms showing turbulence were classified as stenosis if they were not attributable to other abnormalities like kinking of the artery. The degree of stenosis was calculated according to hemodynamic principles used in the classification of occlusive carotid artery disease regarding typical pre-, intra-, and poststenotic abnormalities. Distal vertebral artery occlusion of the V3/V4 segment was assumed if the Doppler signal in a normal wide V1/V2 segment of the artery showed a typical high resistance pattern with an absent end-diastolic flow[8]. Concentric hypoechogenic mural thickening of the vertebral arteries was classified as "halo" according to Schmidt, *et al*[9] and as described[10].

As controls, 206 participants of the MEMO Study (Memory and morbidity in Augsburg elderly) were used[11,12]. MEMO is a followup project of the 1989-90 WHO MONICA Survey, Augsburg, Germany (Monitoring Trends and Determinants in Cardiovascular Disease)[13] and examines cognitive function and cardiovascular risk factors for neurodegenerative diseases in an elderly general population. The study was restricted to participants of the second MONICA survey, who were age 65 years and older on October 1, 1997, and lived in the city of Augsburg. The overall response rate among those eligible was 60.6%, yielding a total of 385 participants. In addition to an interview on medical histories and risk factors, all participants received a standardized neurologic examination by a physician and diagnostic investigations based on brain magnetic resonance imaging (MRI), high resolution vertebral artery duplex sonography, and electroencephalography (EEG). For the latter 2 examinations participants were allocated at random to receive either the sonography or an EEG; 206 MEMO participants received duplex sonography. Results of 203 of those were available for analyses. All sonography examinations of the controls in the MEMO Study were performed using an Acuson 128 ultrasound system and a high resolution 7.5 MHz linear array transducer. All US examinations in cases and controls were done by the same investigator (KP). For statistical analysis Fisher's exact test was used. Significance was assumed at p values < 0.05.

RESULTS

Demographic and clinical characteristics in cases and controls are summarized in Table 1. Except for the higher proportion of women in the TA group ($p < 0.01$) and the PMR group ($p = 0.0015$), there were no significant differences between the groups.

A wide spectrum of clinical findings was observed in the TA cases. They included typical cranial TA in 78 cases (with neuroophthalmological complications in 26 of all TA patients), large artery involvement in TA in 10 (including 4 cases with vertebrobasilar ischemia with occlusive disease

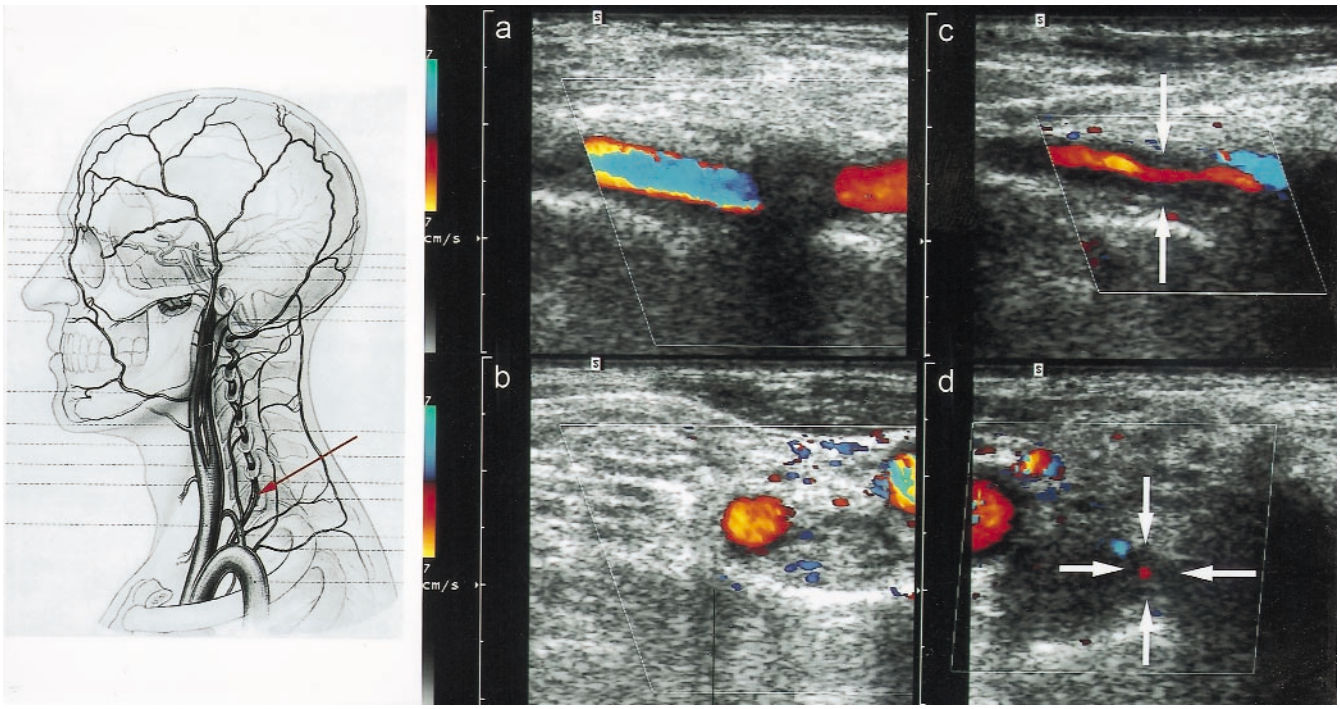

Figure 1. Color duplex sonography of the vertebral arteries in a 79-year-old patient with biopsy proven TA and mild vertebrobasilar stroke (Patient 2, Table 2). MRI angiography showed occlusion of the right vertebral artery: longitudinal and transverse sections of the V1 and V2 segments of the right vertebral artery (C, D). Severe hypoechogenic concentric mural thickening of the V1 and V2 segments of the right vertebral artery (arrows). Left vertebral artery (A, B): normal findings.

Table 1. Demographic and clinical characteristics in 93 patients with temporal arteritis (TA), 34 patients with polymyalgia rheumatica (PMR), and 203 controls.

	TA, n = 93	PMR, n = 34	Controls, n = 203
Age, yrs, median (range)	74 (52–90)	75 (61–86)	73 (65–83)
Women, %	68.8	76.5	47.3
Body mass index > 30, %	15.1	20.6	24.4
History of arterial hypertension, %	49.5	52.9	47.4
History of diabetes mellitus, %	10.8	20.6	10.7
Coronary heart disease, %	6.5	11.8	8.9
Current smoker, %	7.5	2.9	9.9

of the extradural vertebral arteries, and involvement of the aorta in 2 and the axillary and subclavian artery in 4 cases), occult or silent TA in 5, and PMR in 34 patients. Eighty-one patients reported occipital or nuchal pain and/or occipital scalp tenderness. Definitive vertebrobasilar ischemic symptoms were seen in 4 of the 93 patients with TA. In 3 patients with vertebrobasilar ischemic symptoms a typical syndrome of cranial arteritis, in one patient typical silent TA, preceded the manifestation of vertebrobasilar ischemia. The data for these patients are given in Table 2.

US findings in the 3 groups are summarized in Table 3. The rate of > 50% stenosis and occlusions of the vertebral arteries was significantly higher (p = 0.0008) in the TA (12.9%) than in the PMR (2.9%) and the control group (3%). The prevalence of concentric hypoechogenic mural thickening of the vertebral arteries without stenosis was very low in the PMR (2.9%) and TA (2.2%) groups. In all cases the V0/V1 segment was involved, in 2 cases bilaterally. In 2 patients a unilateral hypoechogenic 50%–60% stenosis of the V0/V1 segment could be observed.

The 4 reported patients with vertebrobasilar symptoms had occlusions and stenoses of the extradural parts of the vertebral arteries, which were bilateral in 2 cases (Figure 1). Intracranial CDS in all 4 cases revealed no intracranial occlusive vertebrobasilar occlusive disease, but typical collateral flow patterns. All proximal occlusions and stenoses in the patients with and without vertebrobasilar ischemia were hypoechogenic and concentric. In 4 patients, distal unilateral occlusions could not be visualized directly as they were located in the V3/V4 segments. In these cases the echogenicity of the occlusions could not be determined.

DISCUSSION

Vertebrobasilar ischemia in patients with TA in our study was much less frequent than neuroophthalmological complications, and was in all cases associated with proximal vertebral artery occlusive disease. The rate of > 50% stenosis and occlusions of the vertebral arteries was significantly higher in the TA group than in the PMR and control groups.

Cerebral ischemia is an uncommon complication in TA,

Table 2. Demographic, clinical, and paraclinical data from 4 patients with biopsy proven temporal arteritis presenting with vertebrobasilar ischemia.

Patient	Age/Sex	Clinical Manifestation	Beginning of the Disease Before Diagnosis, mo	CRP/ESR	Vertebral Artery CDS Findings	Superficial Temporal Artery CDS Findings	Cranial MRI/CT Findings	Vascular Risk Factors
1	69 F	TIA with diplopia, dysarthria, ataxia, central R facial and L arm paresis	6	7.0/49	90% bilateral stenosis V0, V1, V2 segments	Halo/stenosis bilateral	Normal	Arterial hypertension, smoking, HLP, PAD
2	79 M	Mild stroke with dysarthria, L side numbness of the face and ptosis, and transient diplopia	3	14.6/ND	Occlusion R V0, V1, V2 segments; L normal	Halo R	Normal	None
3	80 F	TIA with repeated bilateral cortical blindness	3	4.6/80	Occlusion R V0, V1, V2 segments; 70–80% stenosis L V2 segment	Halo bilateral	Normal	Arterial hypertension
4	90 F	TIA with diplopia and ataxia	2	14.8/ND	R 60% stenosis V2, L normal	Halo/occlusion bilateral	Bilateral unspecific white matter lesions	None

CRP: C-reactive protein (mg %), ESR: erythrocyte sedimentation rate (mm/h), ND: not done, HLP: hyperlipoproteinemia, PAD: peripheral arterial occlusive disease, R: right, L: left, TIA: transient ischemic attack, CDS: color duplex sonography.

Table 3. Color duplex sonography (CDS) of the vertebral arteries: structural abnormalities in 93 patients with temporal arteritis (TA), 34 patients with polymyalgia rheumatica (PMR), and 203 controls.

CDS Result	TA, n = 93 (%)	PMR, n = 34 (%)	Controls, n = 203 (%)
Normal	79/93 (84.9)	32/34 (94.1)	197/203 (97.0)
> 50% stenosis	12/93 (12.9)	1/34 (2.9)	6/203 (3.0)
Halo	2/93 (2.2)	1/34 (2.9)	0

and has been found in a retrospective study in up to 7% of patients with active TA, in one-third of them affecting the posterior circulation[14]. The rate of vertebrobasilar ischemia (4.3%) in our study was very similar. Vertebrobasilar stroke with high, life-threatening, severity has been reported in several single cases[2,3]. Involvement of the intradural parts of the vertebral arteries and the basilary artery by TA or thrombus extension was found in some of them, but was not observed in our study. Interestingly, vertebrobasilar symptoms can complicate the clinical syndrome of occult TA, but also of typical cranial arteritis. In this respect establishing the right diagnosis may be much more difficult in occult TA. For the clinician this means that in all patients with vertebrobasilar ischemia and clinical and laboratory signs of a systemic inflammatory syndrome not explained otherwise, TA should be considered as a possible and treatable cause of the disease. In patients with an established diagnosis of TA, symptoms of vertebrobasilar ischemia like vertigo, dysarthria, and gait disturbances can be misinterpreted as the consequences of drug side effects or other preexisting diseases. In these cases appropriate imaging of the brain and the vertebrobasilar circulation should be done, including US of the extracranial vertebral arteries.

In vivo the involvement of the vertebral arteries in patients with TA has been demonstrated in single case studies mainly by neuroimaging findings indicating vertebral artery occlusive disease[2,3]. Other studies using ^{18}F-fluorodeoxyglucose positron emission tomography (FDG-PET) have shown an increased vascular uptake of FDG in the thoracic and leg vessels in TA and PMR patients responding to steroid treatment[15]. However, no data for vertebral and carotid arteries are available due to the limited spatial resolution of this technique.

High resolution color duplex sonography is helpful in the diagnosis of TA of the temporal and occipital arteries[9,10]. Involvement of the extracranial arteries as measured by high resolution CDS has not been studied systematically, except in one study examining 33 patients with active TA[5]. In this study, characteristic inflammatory mural thickening of arteries other than the superficial temporal artery was found in 30% of cases. In one patient, with no symptoms of vertebrobasilar ischemia, the vertebral artery was found to be affected by TA on one side. On followup these abnormalities persisted[5]. In a recent case[16] with active, biopsy proven TA of the vertebral arteries an initial misdiagnosis of a dissecting aneurysm was made because of a hypoechogenic thickening of the vessel wall of the V1 segment of vertebral artery. In this context wall hematoma of the dissecting aneurysm and hypoechogenic atherothrombotic occlusion are important differential diagnoses that can mimic TA. As TA of the vertebral arteries is mainly confined to the extradural parts of the arteries[4], the CDS abnormalities considered to represent distal vertebral artery occlusion can be assumed to be TA related. As the distal parts of the V2 segment above the C3/4 level and the V3 segment are not directly visualized by CDS, the echogenicity of these lesions could not be studied. Unlike in the carotid arteries, the detection of structural vertebral artery abnormalities is compromised by its more complicated anatomy and partial inaccessibility to CDS, which decreases the accuracy in detecting small arterial wall abnormalities. This may be one explanation for the difference in the frequency of vertebral artery involvement in TA in ultrasound and pathological studies. The other, more important point is the selection of very severe TA cases with fatal complications in pathological studies.

To our knowledge the prevalence of vertebral artery occlusive disease has not been investigated by CDS in a population based study. The proportion of CDS abnormalities in the control group thus cannot be compared with results from other studies.

Our study has several strengths and limitations. Among the strengths is the large number of TA cases who were diagnosed following standardized criteria and in the same clinical setting. Thus, misclassification through application of different diagnostic criteria was minimized. All CDS examinations in cases and controls were done by the same investigator, reducing inter-examiner variability of US results. We had the rare opportunity to compare results among cases with findings in an unaffected sample of the general population, the so-called source population, that gave rise to the cases. This comparison yielded the background proportion of vertebral artery abnormalities in the source population of the same age as the cases.

We conclude that vertebrobasilar ischemia in patients with TA is much less frequent (4.3%) than neuroophthalmological complications (27.9%) and is associated with proximal vertebral artery occlusive disease. But the rate of structural vertebral artery abnormalities as measured by CDS is still significantly higher in TA patients than in PMR patients and a healthy control population of the same age. Hypoechogenic concentric vertebral artery mural thicken-

ing, the so-called halo, is a rare finding in TA and PMR and can mimic wall hematoma of a dissecting aneurysm of the vertebral artery.

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