Concise Report

Prognosis of large-vessel giant cell arteritis

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Objective. The prognosis of large-vessel GCA (LV-GCA) has not yet been investigated. How does it compare to GCA without arm vasculitis (GCA controls)?

Methods. Charts of 53 LV-GCA patients and 53 GCA controls were reviewed following a predetermined protocol. Telephone interviews of patients or their primary care physicians were conducted. Forty LV-GCA patients underwent follow-up duplex ultrasound examinations of proximal arm arteries.

Results. The mean observation time was 50 (s.d. ± 31) months. None of the LV-GCA patients developed ischaemic arm complications. In 30%, proximal arm artery wall swelling disappeared completely. It decreased in 53%. In 8% it remained unchanged, in 5% it increased and in 5% arteries occluded with collateral flow. After the start of treatment, anterior ischaemic optic neuropathy developed neither in LV-GCA patients nor in GCA controls, amaurosis fugax occurred in 4 and 6%, arterial hypertension in 53 and 66%, strokes in 9 and 9%, myocardial infarction in 2 and 2%, diabetes mellitus in 30 and 25%, osteoporosis in 38 and 23%, and osteoporotic fractures in 15 and 4%, respectively. Mean corticosteroid dose was 3.7 mg/day. Mean duration of therapy was 42 months. All differences were insignificant. Four LV-GCA patients developed vasculitic popliteal artery stenoses.

Conclusions. The prognosis of LV-GCA is benign with regard to ischaemic complications. Proximal artery wall swelling decreases in most cases. Its course is similar to GCA without proximal arm arteritis.

Key words: Giant cell arteritis, Ultrasonography, Colour Doppler ultrasonography, Follow-up studies.

Introduction

Giant cell arteritis (GCA) is a primary vasculitis that frequently involves the temporal arteries and the vasculature of the eye. Furthermore, it has been recently shown that a greater number of GCA patients exhibit extracranial vasculitis due to increased use and higher quality of imaging techniques like MRI, magnetic resonance angiography, CT, PET and duplex ultrasonography [1–9].

The proximal arteries of the upper extremities and, in particular, the axillary arteries are most commonly involved. This entity has been called ‘large-vessel GCA’ (LV-GCA; [10, 11]). The term ‘GCA’ has been more commonly used within the last years than the term ‘temporal arteritis’ because of the more generalized nature of the disease [12].

The patients may complain of intermittent arm claudication, paraesthesia and RP. These symptoms are absent particularly in case of non-stenotic vasculitic artery wall swelling. Furthermore, aortitis has been increasingly recognized in GCA with a higher incidence of aortic aneurysm or aortic dissection than in an age-matched population [13, 14]. Vasculitis of other vessels like carotid, femoral and popliteal arteries is less common [10].

In a recently published study, we could show that patients with LV-GCA as compared with those without proximal arm artery vasculitis were younger. A greater number of LV-GCA patients were females. Headaches, jaw claudication and anterior ischaemic optic neuropathy (AION) occurred less frequently. The median time until diagnosis was longer. ESR and the presence of PMR was similar in both the groups [15]. An earlier retrospective study describing LV-GCA patients with more severe arterial changes arrived at similar results [11].

No data have been published so far on the course of LV-GCA. The aim of this study is to investigate the prognosis of the disease in LV-GCA as compared with GCA without proximal arm involvement. How do the sonographically visible changes of the artery wall develop at follow-up?

Patients and methods

Between August and October 2007 we collected the follow-up data of all 53 patients who had been newly diagnosed in our institution with LV-GCA, i.e. with vasculitis of the proximal arm arteries between 1997 and 2006 (LV-GCA patients) [15]. Furthermore, we collected the follow-up data of the same number of patients in whom we had diagnosed GCA but had excluded proximal arm vasculitis by duplex ultrasound in the same time interval (GCA controls). The control group consists of patients who have been selected from the original group of 123 patients. Age, sex and time between onset of symptoms and diagnosis of GCA were identical in the original group and in the group that has been investigated in this study. The presence of arm vasculitis did not influence the initial corticosteroid dose. All patients received 70 mg of prednisolone orally within the first week with weekly dose reduction of 10 mg in the first 5 weeks. Only patients with eye involvement received doses of 250–1000 mg methylprednisolone intravenously for the first 3 days.

The charts were reviewed following a pre-determined protocol. If the data were missing, then we performed telephone interviews of their primary care physicians in 21 cases (9 LV-GCA patients and 12 GCA controls) or of the patients themselves in 12 cases (four LV-GCA patients and eight GCA controls).

Primary outcome parameters were development of eye complications (amaurosis fugax and AION) and mean corticosteroid dose. Secondary outcome parameters were arterial hypertension, peripheral arterial occlusive disease, stroke, myocardial infarction, aortic aneurysm, malignancy, osteoporosis, osteoporotic fractures and duration of corticosteroid therapy.

Forty LV-GCA patients and 20 GCA controls were followed with duplex ultrasound examinations of the proximal arm arteries by the same sonographer who had performed the first examination (W.A.S.) to determine the course of vasculitic wall changes. We regarded lesions as stenotic if the artery lumen was >50% of the original lumen together with characteristic Doppler curves...
showing turbulences and increased systolic and diastolic blood flow velocities. Arteries were defined as occluded if ultrasound was unable to delineate colour in the former artery lumen, which showed a hypoechoic or mid-echoic appearance. Ethical approval for this study was obtained from the local ethical committee of the Medical Centre for Rheumatology, Berlin-Buch.

Statistical analysis
We applied the SPSS V.14 (Chicago, IL, USA) statistical package for statistical analysis. The t-test, the Mann–Whitney U-test, the two-sided Fisher’s exact test or the χ² test were used to compare results. Logistic regression analysis was performed to compare LV-GCA patients and GCA controls. Results were adjusted to sex, age and time of follow-up, which differed between groups. The statistical power analysis considering a significance level of 5% and a power level of 90% arrived at a sample size of 46 and 43 patients per group for the development of eye complications and the mean corticosteroid dose, respectively, in case of a relative difference of 30% for eye complications or prednisolone doses of 2 mg vs 4 mg.

Results
All 53 LV-GCA could be followed. Follow-up duplex ultrasound examinations were performed in 40 LV-GCA patients.

At baseline 83% of the 53 LV-GCA patients and 64% of the 53 GCA controls were females, respectively (P < 0.01). The mean age was 66 and 72 yrs (P < 0.01) and the median time until diagnosis was 8 and 2 months, respectively (P < 0.01). PMR occurred in 45 and 47%, headaches in 38 and 74% (P < 0.001) and jaw claudication in 24 and 47% (P = 0.025), respectively. Mean ESR was 76 and 73 mm/h, respectively.

The mean time of follow-up was 50 months from diagnosis (1 ± s.d. 31 months), 40 months (1 ± 25 months) for the LV-GCA patients and 59 months (1 ± 33 months; P = 0.001) for the GCA controls. The mean interval between baseline and follow-up ultrasound examination of the proximal arm arteries was 39 months (1 ± s.d. 22 months) for the LV-GCA group and 41 months (1 ± 24 months) for the GCA controls.

Six LV-GCA patients had died. One patient each had died of intestinal perforation, myocardial insufficiency, cervix cancer, cerebral aneurysm bleeding and dementia. In one patient, the cause of death remained unclear.

During follow-up none of the LV-GCA patients developed complications in terms of arm ischaemia. None of them complained of clinically significant arm claudication at follow-up in contrast to 11 patients (21%) who had relevant symptoms at the time of diagnosis.

In 12 (30%) of the 40 LV-GCA patients in whom follow-up ultrasound examinations were performed, complete resolution of vascular wall swelling occurred in the proximal arm arteries, in 21 patients (53%) the wall thickness or the degree of stenosis improved, in 3 patients (8%) the severity of wall pathology remained unchanged, in 2 patients (5%) it worsened and in 2 patients (5%) with previously stenotic proximal arm arteries, these became occluded with development of collateral vascularization.

None of the 20 GCA controls who had follow-up ultrasound examinations developed proximal arm vasculitis.

Table 1 provides information on the prevalence of occlusions, stenoses, non-stenotic wall swelling or normal findings at baseline and at follow-up. Seventeen patients (43%) improved in terms of presence or absence of these findings. In 20 patients (50%), baseline findings were still present although some of them had a lesser degree of stenosis or non-stenotic wall swelling compared with baseline, and in three patients (8%) new stenoses or occlusions occurred.

The occluded vascular segments remained occluded in the two patients who presented with arterial occlusions at diagnosis.

Wall changes improved in other vascular segments. Collateral perfusion increased with time. Both patients finally did not complain of arm claudication.

One patient with vasculitic subclavian and axillary artery stenosis exhibited necrosis of two fingers of the left hand at diagnosis. Angioplasty with consecutive stenting of the subclavian and axillary arteries let to rapid improvement of symptoms. The necroses healed. The arteries remained stenotic but to a lesser degree. Neither necroses nor arm claudication occurred during the follow-up.

Two more patients with stenoses were treated invasively because of arm claudication. One patient received a stent that led from the proximal left subclavian artery to the proximal brachial artery. The stent occluded at its end. A second stent was implanted, which became stenotic at follow-up, but the patient did not complain of arm claudication any more. The other patient underwent bilateral angioplasty that remained open at follow-up.

Seven of the 53 LV-GCA had also non-stenotic homogeneous common carotid artery wall swelling. The thickness of the wall swelling remained the same in two of these patients and decreased in the others.

Unlike in vasculitis of the temporal arteries the sonographically detectable wall swelling of the proximal arm arteries disappeared or changed its appearance only slowly with time. The vasculitic wall swelling became brighter at follow-up examinations as has been previously described [16].

Table 2 shows the clinical data during follow-up for LV-GCA patients and GCA controls.

Although LV-GCA patients were significantly younger at baseline, significantly more patients were females and follow-up was significantly shorter in LV-GCA patients, the rate of complications was not significant between the groups. Differences remained insignificant even after performing logistic regression analysis and adjusting data for age, sex and duration of follow-up.

There was a trend to a higher prevalence of peripheral arterial occlusive disease in LV-GCA patients, which can be explained by vasculitic stenoses of the popliteal arteries in four of these nine LV-GCA patients that were detected with duplex ultrasound. The other five LV-GCA patients exhibited arteriosclerotic stenoses or occlusions of iliac, femoral and/or popliteal arteries.

AION occurred neither in LV-GCA patients nor in GCA controls after start of treatment, and only few patients of both groups experienced amaurosis fugax. Arterial hypertension was common, but strokes and myocardial infarctions were rare in both groups. Osteoporosis, defined by a T-score of < −2.5, was common. Surprisingly, no aortic aneurysms occurred. Steroid dose and mean duration of therapy did not differ significantly within both groups, both with and without logistic regression analysis.

The presence of headache, jaw claudication or PMR at outset did not correlate with any of the outcome parameters listed in Table 2 or with the extent of improvement of arm vasculitis at follow-up.
Table 2. Features at follow-up of 53 LV-GCA patients and 53 GCA controls

<table>
<thead>
<tr>
<th></th>
<th>All patients</th>
<th>GCA with proximal arm artery involvement</th>
<th>GCA without proximal arm artery involvement</th>
<th>P-value</th>
<th>Adjusted P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>N</td>
<td>106</td>
<td>53</td>
<td>53</td>
<td></td>
<td></td>
</tr>
<tr>
<td>AION</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Amaurosis fugax (%)</td>
<td>5</td>
<td>4</td>
<td>6</td>
<td>1.0</td>
<td>0.44</td>
</tr>
<tr>
<td>Arterial hypertension (%)</td>
<td>27</td>
<td>30</td>
<td>25</td>
<td>0.52</td>
<td>0.09</td>
</tr>
<tr>
<td>Diabetes mellitus (%)</td>
<td>10</td>
<td>17</td>
<td>4</td>
<td>0.048</td>
<td>0.07</td>
</tr>
<tr>
<td>Peripheral arterial occlusive disease (%)</td>
<td>9</td>
<td>9</td>
<td>9</td>
<td>1.0</td>
<td>0.50</td>
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<tr>
<td>Stroke (%)</td>
<td>2</td>
<td>2</td>
<td>2</td>
<td>1.0</td>
<td>0.46</td>
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<td>Myocardial infarction (%)</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Aortic aneurysm (%)</td>
<td>2</td>
<td>4</td>
<td>0</td>
<td>1.0</td>
<td>1.0</td>
</tr>
<tr>
<td>Osteoporosis (%)</td>
<td>30</td>
<td>38</td>
<td>23</td>
<td>0.09</td>
<td>0.11</td>
</tr>
<tr>
<td>Osteoporoctic fractures (%)</td>
<td>9</td>
<td>15</td>
<td>4</td>
<td>0.09</td>
<td>0.06</td>
</tr>
<tr>
<td>Steroid medication stopped (%)</td>
<td>34</td>
<td>28</td>
<td>40</td>
<td>0.10</td>
<td>0.24</td>
</tr>
<tr>
<td>Mean steroid dose (patients on steroids) (mg/day)</td>
<td>5.4</td>
<td>5.7</td>
<td>5.1</td>
<td>0.56</td>
<td>0.90</td>
</tr>
<tr>
<td>Mean steroid dose (all patients) (mg/day)</td>
<td>3.7</td>
<td>4.4</td>
<td>3.2</td>
<td>0.19</td>
<td>0.57</td>
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<tr>
<td>Mean duration of steroid therapy (months)</td>
<td>42</td>
<td>36</td>
<td>48</td>
<td>0.03</td>
<td>0.42</td>
</tr>
</tbody>
</table>

The last column shows the P-value that is adjusted for sex, age and duration of follow-up.

Discussion

The course of LV-GCA is benign with regard to ischaemic complications. There have been no necrotic arm lesions, and no events of AION. In this regard, LV-GCA differs considerably from Takayasu’s arteritis where ischaemic complications commonly occur [17]. The course of the disease is similar in LV-GCA as compared with GCA without arm involvement. No data have yet been published that compare both the entities.

Unlike temporal artery vasculitis, proximal arm artery wall thickening remains for a much longer time. In contrast, temporal artery wall swelling resolved after a mean of 16 days after start of corticosteroid treatment [18]. The echogenicity increases slightly and wall thickening remains for a much longer time. In contrast, temporal artery wall swelling resolved after a mean of 16 days after start of corticosteroid treatment [18]. The echogenicity increases slightly and thickening remains for a much longer time. In contrast, temporal artery wall swelling resolved after a mean of 16 days after start of corticosteroid treatment [18].

Aneurysms of the thoracic aorta have been described to develop in LV-GCA. Unlike temporal artery vasculitis, proximal arm artery wall thickening remains for a much longer time. In contrast, temporal artery wall swelling resolved after a mean of 16 days after start of corticosteroid treatment [18]. The echogenicity increases slightly and thickening remains for a much longer time. In contrast, temporal artery wall swelling resolved after a mean of 16 days after start of corticosteroid treatment [18].

In conclusion, LV-GCA does not lead to severe ischaemic complications in its course. Wall swelling of proximal arm arteries decreases in most patients. Its course does not differ from GCA without proximal upper extremity arteritis.

Rheumatology key messages

- Severe ischaemic complications are uncommon in the course of LV-GCA.
- Vasculitic proximal arm artery wall changes decrease in most patients.
- The course of the disease is similar to cranial GCA.

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References