Concise Report

Do temporal artery duplex ultrasound findings correlate with ophthalmic complications in giant cell arteritis?

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Objective. Ophthalmic complications are common in acute GCA. Do temporal artery ultrasound and clinical parameters correlate with the occurrence and severity of ophthalmic complications?

Methods. The results of temporal artery ultrasound examinations are compared with the occurrence of anterior ischaemic optic neuropathy (AION), central retinal artery occlusion (CRAO), branch retinal artery occlusion (BRAO), diplopia and amaurosis fugax in 222 consecutive patients with newly diagnosed, active GCA.

Results. Temporal artery ultrasound displayed vasculitic wall swelling (halo), stenoses and/or acute occlusions in 84% (58% in 67 large-vessel GCA patients and 95% in 155 patients without proximal arm vasculitis). Ophthalmic complications occurred in 64 (29%), AION in 30 (14%), CRAO in 7 (3%), BRAO in 2 (1%), amaurosis fugax in 16 (7%) and diplopia in 9 patients (4%). Ophthalmic complications were insignificantly more common if temporal artery ultrasound was positive (31 vs 17%; \(P = 0.11\)) as a greater number of patients without arm vasculitis showed eye involvemnt (34 vs 18%; \(P = 0.02\)). The number of pathological temporal artery segments, presence of stenoses or bilateral findings did not correlate with ophthalmic complications. Age \(\geq 72\) yrs at diagnosis correlated with a higher incidence of ophthalmic complications.

Conclusion. Ophthalmic complications occurred less frequently if proximal arm vasculitis was present. Findings of temporal artery ultrasound did not correlate with eye complications.

Key words: GCA, Ultrasonography, Histology, Anterior ischaemic optic neuropathy, Amaurosis fugax, Diplopia, Central retinal artery occlusion, Branch retinal artery occlusion.

Introduction

Ophthalmic complications are common in the acute phase of GCA. A meta-analysis of studies between 1966 and 2002 described a prevalence of 37% [1]. Cohorts that have been analysed thereafter, arrive at prevalences of 17 and 32% [2, 3].

The most common entities are anterior ischaemic optic neuropathy (AION), central retinal artery occlusion (CRAO), branch retinal artery occlusion (BRAO), diplopia and amaurosis fugax. Vasculitic occlusive disease of the posterior ciliary arteries, which are branches of the ophthalmic artery, causes AION. These arteries supply the optic nerve. In CRAO, the central retinal arteries are affected, which are also branches of the ophthalmic artery. In BRAO, arterial branches that supply the inner layer of the retina are affected. Occlusion leads to sectoral pattern of retinal opacification. Diplopia is most commonly caused by abducens nerve palsy. Amaurosis fugax is a transient monocular vision loss.

Duplex ultrasound of the temporal arteries depicts characteristic hypoechoic (dark) wall swelling (halo), stenoses and acute occlusions in acute GCA [4]. A meta-analysis of studies on temporal artery ultrasound described a sensitivity of 87% and a specificity of 96% for the clinical diagnosis of temporal arteritis [5]. Furthermore, ultrasound of proximal arm arteries, in particular axillary arteries, is a valuable diagnostic tool to reveal large-vessel GCA that may occur with or without temporal arteritis [6, 7].

It has been recently shown that histological features correlate with the presence of ophthalmic complications [8, 9]. Nevertheless, this issue remains controversial since other studies had not confirmed such a relationship [10, 11]. Temporal artery ultrasound results are at hand before biopsy results. Does the extent of temporal artery duplex ultrasound findings also correlate with presence and extent of ophthalmic complications? In this case, the results of the ultrasound examination might influence therapy of acute GCA. In addition, we looked for clinical parameters that might correlate with ophthalmic complications.

Methods

Patients

This study describes 222 consecutive patients who had been newly diagnosed with GCA in a specialized rheumatological ultrasound clinic between January 1994 and February 2008. The patients had to fulfil all of the following criteria to assure that only patients with the definite diagnosis of GCA were included in this analysis:

- Newly diagnosed GCA.
- No corticosteroid treatment, or corticosteroid treatment for \(\leq 10\) days at the time of the ultrasound examination.
- More than three positive ACR classification criteria for temporal arteritis [12].
- Good response to a prednisolone dose of \(\geq 40\) mg/day within 1 week as determined by the treating rheumatologist.

If patients fulfilled less than three ACR classification criteria for temporal arteritis, ultrasound had to delineate homogeneous circumferential wall swelling of the proximal arm arteries with a diameter \(\geq 1.5\) mm [6]. Furthermore, patients could fulfill less than three ACR criteria together with positive histology. In these two
patient groups and in biopsy-negative patients fulfilling three or four ACR classification criteria, the diagnosis had to be confirmed by two rheumatologists. Patients had to show good response to corticosteroid treatment and diagnosis had to remain unchanged for at least 6 months similar to previously published studies [13]. Histology was regarded positive if vasculitis with a predominance of mononuclear cell infiltration, granulomatous inflammation and/or giant cells was present [12].

Routine diagnostic work-up included the examination by an ophthalmologist. If temporal artery biopsy was performed, ultrasound was always done before biopsy. Biopsy was regarded as positive if infiltrates, granulomas or giant cells were present. Ethical approval for this study was obtained from the local ethical committee of Medical Centre for Rheumatology, Berlin-Buch.

Ultrasound examination

Temporal artery ultrasound was performed by a rheumatologist who is also an experienced sonographer (W.A.S.). This included the examination of the following eight segments in two planes with colour Doppler ultrasound: common superficial temporal artery, parietal, proximal and distal (>2 cm distal from the bifurcation) frontal ramus on the both sides. Pulsed wave Doppler mode was applied in areas with persistent colour signal in the diastole with or without aliasing. Stenosis was considered to be present if blood flow velocity was more than twice the rate recorded in the area before the stenosis, perhaps with wave forms demonstrating turbulence [4]. Ultrasound was performed with linear probes (5–10, 8–14 and 6–18 MHz) of ATL Ultramark 9 HDI (Advanced Technology Laboratories, Bothell, WA, USA), Esaote Technos MPX or Esaote MyLab 70 (Esaote SPA, Genua, Italy). Ultrasound of proximal arm arteries was performed with the same equipment.

Statistical analysis

We applied the SPSS V.14 statistical package (SPSS Inc., Chicago, IL, USA) for statistical analysis. The t-test, the Mann Whitney U-test, the Fisher’s exact test or the chi-square test were used to compare results. Cut-offs for age and ESR were decided whether patients were above or below the median.

Results

Of the 222 patients, 71% was female. The mean age was 71 yrs (1 s.d. ± 8 yrs, from 50 to 93 yrs). PMR occurred in 45% of the patients, 64% had headaches and 46% had jaw claudication. Mean ESR was 78 mm/h (1 s.d., 21 mm/h, from 8 to 130 mm/h). Histology was performed in 114 patients and was positive in 86 patients (75%). Ultrasound was performed in 118 patients prior to corticosteroid treatment, 57 patients had received the first corticosteroid dose within <24 h, 44 patients within 2–4 days, 1 patient within 6 days and 2 patients within 9 days. Ultrasound findings were independent from the duration of corticosteroid therapy in these patients.

Eighty-four patients fulfilled three, 71 fulfilled four and 37 fulfilled five ACR classification criteria for temporal arteritis. Twenty-seven patients with large-vessel GCA fulfilled two criteria (age ≥50 yrs and ESR ≥50 mm/h), and one patient with large-vessel GCA fulfilled only one criterion (age ≥50 yrs, ESR 38 mm/h). Two more patients without proximal arm vasculitis fulfilled only two criteria. All patients met the aforementioned inclusion criteria [13].

Ophthalmic complications occurred in 64 patients (29%), AION in 30 (14%), CRAO in 7 (3%), BRAO in 2 (1%), amaurosis fugax in 16 (7%), and diplopia due to abducens paresis in 9 patients (4%). These were significantly more common in patients without proximal arm vasculitis (52 patients; 34%) compared with those with large-vessel GCA (12 patients; 18%; P = 0.02). AION occurred in 18 and 3%, diplopia in 5% and 1% and amaurosis fugax in 5% and 13%, respectively. CRAO and BRAO occurred only in patients without proximal arm vasculitis.

Temporal artery ultrasound was positive in 186 of the 222 patients (84%), in 58% of 67 large-vessel GCA patients and in 95% of 155 patients without proximal arm vasculitis. Halos, stenoses and occlusions of temporal arteries occurred in 73, 55 and 21% (all patients), in 82, 67 and 37% (patients without proximal arm vasculitis) and in 51, 27 and 15% (large-vessel GCA patients), respectively.

Of the 28 patients with large-vessel GCA and negative temporal artery ultrasound, 5 (18%) had eye involvement, 4 (4%) had AION, 3 (11%) had amaurosis fugax and 1 (4%) had diplopia. In four patients with large-vessel GCA and negative findings of temporal artery ultrasound temporal artery histology was positive. Three of these four patients did not exhibit eye involvement, one had amaurosis fugax. One of eight patients without proximal arm vasculitis and negative ultrasound findings had diplopia, the other seven patients did not exhibit any ophthalmic complications.

Ophthalmic complications were insignificantly more common with positive temporal artery ultrasound findings (31 vs 17%; P = 0.11) due to a greater number of patients without proximal arm vasculitis. Table 1 shows that none of the ultrasound findings correlated with the occurrence and/or severity of ophthalmic complications. Table 2 shows that age at diagnosis, but no other features correlated with eye involvement.

In conclusion, occurrence and severity of ophthalmic complications in active GCA do not correlate with findings of temporal artery ultrasound. The individual patient with newly diagnosed GCA needs treatment irrespective of ultrasound findings in case of established diagnosis.

Table 1. Temporal artery ultrasound findings in relation to ophthalmic complications in 222 patients with acute, newly diagnosed GCA

<table>
<thead>
<tr>
<th>Ultrasound findings of temporal arteries</th>
<th>All patients</th>
<th>No eye complications</th>
<th>Eye complications</th>
<th>AION</th>
<th>CRAO</th>
<th>BRAO</th>
<th>Diplopia</th>
<th>Amaurosis fugax</th>
</tr>
</thead>
<tbody>
<tr>
<td>N</td>
<td>222</td>
<td>158</td>
<td>64</td>
<td>30</td>
<td>7</td>
<td>2</td>
<td>9</td>
<td>16</td>
</tr>
<tr>
<td>Positive finding, n (%)</td>
<td>186 (84%)</td>
<td>128 (81)</td>
<td>58 (91)</td>
<td>29 (97)</td>
<td>7 (100)</td>
<td>2 (100)</td>
<td>7 (78)</td>
<td>16 (100)</td>
</tr>
<tr>
<td>1 segment involved, n (%)</td>
<td>28 (13%)</td>
<td>18 (11)</td>
<td>10 (16)</td>
<td>4 (13)</td>
<td>1 (14)</td>
<td>0</td>
<td>3 (33)</td>
<td>1 (6)</td>
</tr>
<tr>
<td>2 segments involved, n (%)</td>
<td>33 (15%)</td>
<td>28 (16)</td>
<td>7 (11)</td>
<td>2 (7)</td>
<td>1 (14)</td>
<td>0</td>
<td>2 (22)</td>
<td>2 (13)</td>
</tr>
<tr>
<td>3 segments involved, n (%)</td>
<td>23 (10)</td>
<td>15 (9)</td>
<td>8 (13)</td>
<td>3 (10)</td>
<td>1 (14)</td>
<td>0</td>
<td>3 (33)</td>
<td>1 (6)</td>
</tr>
<tr>
<td>4 segments involved, n (%)</td>
<td>16 (7)</td>
<td>11 (7)</td>
<td>5 (8)</td>
<td>4 (13)</td>
<td>0</td>
<td>1 (50)</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>5 segments involved, n (%)</td>
<td>12 (5)</td>
<td>8 (5)</td>
<td>4 (6)</td>
<td>3 (10)</td>
<td>0</td>
<td>1 (11)</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>6 segments involved, n (%)</td>
<td>23 (10)</td>
<td>17 (11)</td>
<td>6 (9)</td>
<td>2 (7)</td>
<td>3 (43)</td>
<td>0</td>
<td>1 (6)</td>
<td></td>
</tr>
<tr>
<td>7 segments involved, n (%)</td>
<td>13 (6)</td>
<td>8 (5)</td>
<td>5 (8)</td>
<td>2 (7)</td>
<td>1 (7)</td>
<td>0</td>
<td>2 (22)</td>
<td>2 (13)</td>
</tr>
<tr>
<td>8 segments involved, n (%)</td>
<td>38 (17)</td>
<td>25 (16)</td>
<td>13 (20)</td>
<td>9 (30)</td>
<td>0</td>
<td>1 (50)</td>
<td>1 (11)</td>
<td>2 (13)</td>
</tr>
<tr>
<td>Unilateral, n (%)</td>
<td>43 (19)</td>
<td>30 (19)</td>
<td>13 (20)</td>
<td>5 (17)</td>
<td>2 (29)</td>
<td>0</td>
<td>0</td>
<td>6 (38)</td>
</tr>
<tr>
<td>Bilateral, n (%)</td>
<td>132 (59)</td>
<td>93 (56)</td>
<td>45 (70)</td>
<td>24 (80)</td>
<td>1 (14)</td>
<td>2 (100)</td>
<td>7 (78)</td>
<td>7 (44)</td>
</tr>
<tr>
<td>Halo present, n (%)</td>
<td>161 (73)</td>
<td>113 (72)</td>
<td>48 (75)</td>
<td>26 (87)</td>
<td>5 (71)</td>
<td>2 (100)</td>
<td>7 (78)</td>
<td>8 (50)</td>
</tr>
<tr>
<td>Stenosis present, n (%)</td>
<td>122 (55)</td>
<td>84 (53)</td>
<td>38 (59)</td>
<td>21 (70)</td>
<td>5 (71)</td>
<td>2 (100)</td>
<td>1 (11)</td>
<td>9 (56)</td>
</tr>
<tr>
<td>Occlusion present, n (%)</td>
<td>47 (21)</td>
<td>30 (19)</td>
<td>17 (27)</td>
<td>13 (43)</td>
<td>2 (29)</td>
<td>0</td>
<td>1 (11)</td>
<td>1 (6)</td>
</tr>
</tbody>
</table>
Discussion

Ophthalmic complications in acute, newly diagnosed GCA occur less frequently in large-vessel GCA as we have reported earlier [6]. There are no further features of temporal artery ultrasound that correlated with the occurrence and severity of ophthalmic complications.

This is an open, mono-centric study. We are limiting temporal artery biopsies to ambivalent cases since having published our experience with the first 101 patients with acute GCA and 650 controls. Sensitivity and specificity of duplex ultrasound with respect to the clinical diagnosis was 88 and 96%, respectively. Sensitivity was 72% and specificity was 99.5% for the presence of a halo [14]. Results of temporal and proximal arm artery ultrasound influenced the clinical diagnosis which might have generated a selection bias. Therefore, this study does not provide exact data on sensitivities of temporal artery ultrasound. We did not only rely on ACR classification criteria that have a sensitivity of 94% and a specificity of 91% for distinguishing temporal arteritis from other vasculitides, to be sure to only include patients with the established diagnosis of GCA [12].

Recently published studies showed that the occurrence of neuro-ophthalmic complications correlated with the degree of intimal hyperplasia [8, 9]. Furthermore, permanent visual loss correlated with presence and number of giant cells and plasmacytes, neoangiogenesis and the degree of arterial occlusion [9]. Nevertheless, in clinical routine, the results of histology arrive too late for influencing therapeutic decisions like initiation of aspirin treatment [15].

Ultrasound displays oedematous wall swelling, whereas histology describes cell infiltrates and granulomas. Biopsy may miss the area of pathology because of the segmental appearance of GCA. The temporal arteries or the vasculature of the eye may be spared even in acute disease.

Other studies described male sex, absence of systemic symptoms and ESR >70 mm/h as risk factors for ophthalmic complications [16, 17]. In our study, only age ≥72 yrs at diagnosis correlated with a higher incidence of ophthalmic complications.

We conclude that, unlike for histology, there is no correlation between temporal artery ultrasound and the occurrence and severity of ophthalmic complications in newly diagnosed, active GCA. Nevertheless, less patients with proximal arm vasculitis (large-vessel GCA) exhibit ophthalmic complications.

### References