Concise report

Effects of early corticosteroid treatment on magnetic resonance imaging and ultrasonography findings in giant cell arteritis

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Abstract

Objective. To compare the impact of initial corticosteroid treatment on high-resolution MRI and colour-coded duplex sonography (CCDS) findings in patients with GCA (temporal).

Methods. Sensitivity and specificity of CCDS and high-resolution contrast-enhanced MRI studies of 59 patients with suspected GCA were retrospectively analysed. Patients were grouped according to the duration of steroid treatment before imaging: 0–1 day, 2–4 days and >4 days. In 41 patients, imaging results were compared with findings of temporal artery biopsy (TAB).

Results. Sixty-one per cent (36/59) of patients were diagnosed with GCA. TAB findings were positive in 59% (24/41). The compared results of TAB sensitivity of CCDS and MRI under steroid treatment of 0–1 day were 92% and 90%, 2–4 days 80% and 78% and >4 days 50% and 80%, respectively. The compared results of the final clinical diagnosis sensitivity of CCDS and MRI under steroid treatment of 0–1 day was 88% and 85%, 2–4 days 50% and 64% and >4 days 50% and 56%, respectively.

Conclusion. Sensitivity of a first-time CCDS or an MRI for detection of GCA rapidly decreases under corticosteroid treatment. Therefore imaging of patients with suspected GCA should be performed as soon as possible, preferably within the first days of treatment.

Key words: GCA, CSs, MRI, ultrasonography.

Introduction

CSs are the mainstay of treatment in GCA [1]. Treatment should be initiated as early as possible to avoid ischaemic complications. If visual loss occurs before commencing treatment, it may be irreversible. CCDS and high-resolution contrast-enhanced MRI are useful adjunctive methods in the challenging diagnosis of GCA, as they can detect mural inflammatory changes in the temporal arteries [2–5]. A characteristic halo on CCDS and bright mural enhancement of the temporal artery on MRI are typical findings in patients with GCA [6–8]. Both imaging methods have been shown to have comparable sensitivity and specificity in a retrospective analysis [9]. The characteristic mural inflammatory changes seen by both imaging modalities vanish under steroid treatment [10,11] (Fig. 1). However, little is known about the effect of CS treatment on the diagnostic performance of CCDS or MRI regarding the successful detection of characteristic inflammatory changes. Specifically, it is unclear how the time lag between initial CS treatment and CCDS or MRI affects sensitivity and specificity to detect GCA. The purpose of this study was to compare the impact of initial CS treatment on high-resolution MRI and CCDS findings in patients with GCA.
Patients and methods

A total of 130 patients with suspected GCA underwent high-resolution MRI in the Department of Radiology and 159 patients underwent CCDS in the Department of Neurology at our University Medical Centre between May 2003 and February 2007. Patients who underwent both examinations within 10 days and had received steroid treatment for <2 weeks were included in this retrospective study. The final study population consisted of 59 patients (32 women, 27 men; mean age 71 years). The clinical diagnosis of GCA was established by experienced rheumatologists and the ACR 1990 GCA criteria were used for classification [12]. The rheumatologist’s final clinical diagnosis was assigned if the diagnosis of GCA was confirmed in the follow-up period of ≥6 months. Typical criteria for assigning the final clinical diagnosis GCA included clinical and serological findings at presentation and in follow-up visits such as vanishing headaches and decrease in ESR and CRP values under steroid treatment. In four cases, the final clinical diagnosis of GCA was made despite a negative temporal artery biopsy (TAB) result that may have occurred because of skip lesions.

Thirty-six of the 59 patients of this study were diagnosed with GCA and had received CSs for 2.6±2.4 days before CCDS and 3.2±3.2 days before MRI. In 24 of these patients, the results for TAB were positive. In 23 patients, the initial tentative diagnosis of GCA could not be verified, and they were used as control subjects in the statistical analysis. These patients received steroids 2.3±2.9 days before CCDS and 2.8±4.0 days before MRI. The study was approved by the local ethics review committee (Ethik-Kommission der Albert-Ludwigs-Universität Freiburg) and was conducted in accordance with the Declaration of Helsinki.

CCDS was performed in all patients by one of the two neurologists well experienced in CCDS for assessment of GCA (M.R., A.H.). A small, high-frequency linear hockey stick probe was used (Entos; Philips, Bothell, WA; 5–10 MHz; axial and lateral resolution of 0.6 and 0.8 mm at 1-cm depth, attached to an HDI 5000 processor). System settings were balanced to optimize flow signal display with a pulse repetition frequency of 350–1000 Hz, and the colour signal focus was strictly placed at the depth of the insonated vessel. The main stem and the frontal and parietal branches of the superficial temporal artery were depicted in the axial and longitudinal planes. US criteria for a positive diagnosis included a dark, concentric halo surrounding a residual colour flow signal that appeared in at least one vessel segment of the main stem or the branches of the superficial temporal artery.

MRI examinations were performed using a 1.5 T scanner in 21 patients and a 3 T scanner in 38 patients (Magnetom Sonata or Trio; Siemens Medical Solution, Erlangen, Germany) equipped with a dedicated 8-element phase array head coil. The contrast enhanced, fat-saturated, T1-weighted, spin-echo sequence was obtained with a submillimetre spatial resolution of 195×260 μm. The acquisition parameters (1.5 T scanner) were as follows: repetition time (TR) 535 ms, echo time (TE) 22 ms, band width 65 Hz/pixel, field of view (FOV)
Corticosteroid effects on CCDS and MR imaging in GCA

Table 1: MRI and CCDS vs clinical diagnosis and TAB under steroid treatment

<table>
<thead>
<tr>
<th>Steroids before examination</th>
<th>n</th>
<th>TP</th>
<th>TN</th>
<th>FP</th>
<th>FN</th>
<th>Sensitivity, % (95% CI)</th>
<th>Specificity, % (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Reference value clinical diagnosis</td>
<td></td>
<td></td>
<td></td>
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<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0–1 day before CCDS</td>
<td>28</td>
<td>14</td>
<td>11</td>
<td>1</td>
<td>2</td>
<td>87.5 (61.7, 98.5)</td>
<td>91.7 (61.5, 99.8)</td>
</tr>
<tr>
<td>0–1 day before MRI</td>
<td>24</td>
<td>11</td>
<td>11</td>
<td>0</td>
<td>2</td>
<td>84.6 (54.5, 98.1)</td>
<td>100.0</td>
</tr>
<tr>
<td>2–4 days before CCDS</td>
<td>16</td>
<td>5</td>
<td>6</td>
<td>0</td>
<td>5</td>
<td>50.0 (18.7, 81.3)</td>
<td>100.0</td>
</tr>
<tr>
<td>2–4 days before MRI</td>
<td>22</td>
<td>9</td>
<td>6</td>
<td>2</td>
<td>5</td>
<td>64.3 (35.1, 87.2)</td>
<td>75.0 (34.9, 96.8)</td>
</tr>
<tr>
<td>&gt;4 days before CCDS</td>
<td>15</td>
<td>5</td>
<td>4</td>
<td>1</td>
<td>5</td>
<td>50.0 (18.7, 81.3)</td>
<td>80.0 (28.4, 99.5)</td>
</tr>
<tr>
<td>&gt;4 days before MRI</td>
<td>13</td>
<td>5</td>
<td>4</td>
<td>0</td>
<td>4</td>
<td>55.6 (21.2, 86.3)</td>
<td>100.0</td>
</tr>
<tr>
<td>Reference value TAB</td>
<td></td>
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<tr>
<td>0–1 day before CCDS</td>
<td>20</td>
<td>12</td>
<td>4</td>
<td>3</td>
<td>1</td>
<td>92.3 (64.0, 99.8)</td>
<td>57.1 (18.4, 90.1)</td>
</tr>
<tr>
<td>0–1 day before MRI</td>
<td>16</td>
<td>9</td>
<td>4</td>
<td>2</td>
<td>1</td>
<td>90.0 (55.5, 99.8)</td>
<td>66.7 (22.3, 95.7)</td>
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<tr>
<td>2–4 days before CCDS</td>
<td>11</td>
<td>4</td>
<td>5</td>
<td>1</td>
<td>1</td>
<td>80.0 (28.4, 99.5)</td>
<td>83.3 (35.9, 99.6)</td>
</tr>
<tr>
<td>2–4 days before MRI</td>
<td>16</td>
<td>7</td>
<td>5</td>
<td>2</td>
<td>2</td>
<td>77.8 (40.0, 97.2)</td>
<td>71.4 (29.0, 96.3)</td>
</tr>
<tr>
<td>&gt;4 days before CCDS</td>
<td>10</td>
<td>3</td>
<td>1</td>
<td>3</td>
<td>3</td>
<td>50.0 (11.8, 88.2)</td>
<td>25.0 (0.6, 80.6)</td>
</tr>
<tr>
<td>&gt;4 days before MRI</td>
<td>9</td>
<td>4</td>
<td>3</td>
<td>1</td>
<td>1</td>
<td>80.0 (28.4, 99.5)</td>
<td>75.0 (19.4, 99.4)</td>
</tr>
</tbody>
</table>

n: number of patients; TP: true-positive cases; TN: true-negative cases; FP: false-positive cases; FN: false-negative cases. The values for sensitivity and specificity are reported for the various subgroups (previous steroid treatment of 0–1 day, 0–4 days and >4 days).

200 × 200 mm², matrix 1024 × 768 pixel, acquisition time 6 min 55 s, one acquisition, slice thickness 3 mm. Using the 3 T scanner, the band width was slightly increased (76 Hz/pixel) and the TR was reduced to 500 ms. In addition, half Fourier encoding (half Fourier factor = 6/8) was used to decrease the total scan time to 4 min 52 s. Three consecutive acquisitions (10 gapless slices, slice thickness 3 mm) covered a volume of >90 mm³.

Statistical analysis

Sensitivity and specificity were calculated for each imaging modality grouped according to the following duration of steroid treatment: 0–1 day, 2–4 days and >4 days. Specificity between groups was compared with Fisher’s exact test. Areas under the curve (AUCs) were compared non-parametrically according to DeLong et al. [13]. P-values < 0.05, two-tailed, were considered significant. Statistical analysis was performed using SAS 9.2 (SAS Institute, Cary, NC, USA).

Results

Sensitivity of CCDS and MRI was 88% and 85%, respectively, in patients scanned within the first day of CS treatment. In comparison, sensitivity of both methods in patients scanned within 2–4 days of CS treatment was 64% (MRI) and 50% (CCDS) (P_{MRI} = 0.385 and P_{CCDS} = 0.069, compared with patients scanned within the first day), and 56% (MRI) and 50% (CCDS) when scanned >4 days after initiation of steroid treatment (P_{MRI} = 0.178 and P_{CCDS} = 0.069, compared with patients scanned within the first day). Specificity was high in all subgroups (Table 1).

The AUC for MRI and CCDS was 0.923 (95% CI 0.821, 1.000) and 0.896 (95% CI 0.779, 1.000) for patients scanned within 0–1 days of treatment, 0.6964 (95% CI 0.490, 0.903) and 0.750 (95% CI 0.587, 0.913) for patients scanned within 2–4 days of treatment and 0.778 (95% CI 0.606, 0.950) and 0.650 (95% CI 0.395, 0.905) for patients scanned within >4 days of treatment, respectively. The differences among the subgroups and the imaging procedures did not reach the level of significance with P-values ranging from 0.054 to 0.155.

When the accepted diagnostic gold-standard TAB was used as reference, the sensitivity of MRI (90%) and CCDS (92%) was high when scanned within the first day after initiation of CS treatment. In comparison, the sensitivity of both methods decreased in patients scanned within 2–4 days of CS treatment to 77.8% (MRI) and 80% (CCDS) (P_{MRT} = 0.582 and P_{CCDS} = 0.490, compared with patients scanned within the first day), and to 80% (MRI) and 50% (CCDS) when scanned >4 days after initiation of steroid treatment (P_{MRT} = 1.000 and P_{CCDS} = 0.071, compared with patients scanned within the first day).

When compared with results from TAB, the AUC for MRI and CCDS was 0.783 (95% CI 0.555, 1.000) and 0.747 (95% CI 0.535, 0.959) for patients scanned within the first 0–1 days of steroid treatment, 0.746 (95% CI 0.515, 0.977) and 0.817 (95% CI 0.561, 1.000) for patients scanned within 2–4 days of steroid treatment and 0.775 (95% CI 0.461, 1.000) and 0.375 (95% CI 0.046, 0.704) for patients scanned within >4 days of steroid treatment. The differences among the subgroups and the imaging procedures did not reach the level of significance, with P-values ranging from 0.062 to 0.967.

Discussion

This study demonstrates that the diagnostic accuracy of CCDS and MRI in GCA starts decreasing within the first days of steroid treatment. As compared with the final clinical diagnosis, reduced accuracy is mainly because of a
decreasing sensitivity, whereas the specificity remains high.

Immediate initiation of CS treatment is mandatory in GCA to avoid irreversible ischaemic complications such as visual loss [1]. A previous study showed that after months under steroid treatment, the inflammatory changes detected by MRI vanished [10]. A retrospective study compared the sensitivity of high-resolution MRI performed ≤10 days and >10 days after onset of steroid treatment. Greater sensitivity was found in the group that was studied within the first 10 days of treatment (85.7% vs 33.3%) [2]. CCDS mostly detects the inflammatory vessel wall oedema. This oedema seems to be rapidly responding to CS treatment whereas other inflammatory changes on biopsy could be safely detected up to several days after initiation of corticoid treatment. Schmidt et al. showed in a previous US study that the halo disappears after a mean of 16 days, but not before 7 days of treatment [5]. Karahaliou et al. confirmed the disappearance of the halo after a mean of 22 days in their study [14]. In contrast, in treated large-vessel GCA, more echogenic residual US changes remain detectable in the majority of patients for months, even after normalization of systemic inflammatory parameters [15,16]. Such changes might be missed in the smaller temporal artery, where image resolution is lower, or can be indiscernible from atherosclerotic changes commonly occurring in the temporal arteries.

This study analysed the effects of CSs on MRI and CCDS findings in the initial days of treatment and revealed decreasing accuracy early after onset of treatment. Our results indicate that for first-time diagnostic imaging in GCA (without having an untreated reference situation), the sensitive period of detecting unequivocal changes of inflammation is even shorter, potentially as short as 1 day. Therefore, CCDS or MRI examination of patients with suspected GCA should be performed as soon as possible, preferably within the first day after onset of steroid treatment.

PET scanning is increasingly used in similar clinical scenarios. As with MRI and CCDS, positive PET findings decrease under the course of steroid treatment [17]. PET scanning is not routinely performed for detection of GCA in our clinical routine and was not part of this retrospective study.

The diagnostic gold standard for GCA is TAB. CS therapy substantially alters histological findings of inflammatory mural appearance over time but does not significantly decrease the diagnostic value. In contrast to TAB, CCDS and MRI are non-invasive diagnostic methods that can be performed safely and repeatedly. However, in terms of feasibility, TAB seems to be a superior investigation despite being invasive—treatment can be started and the biopsy can be arranged, for example, within the first week. The high sensitivity of MRI and CCDS to steroid treatment brings into question the potential of both methods to detect relapses under steroid treatment. For CCDS, only one report of two patients with recurring halo is available, but there are no data given on the course of steroid treatment in these patients [18]. The authors can report anecdotal cases in which relapses were detected. However, scientific studies evaluating the value of high-resolution MRI or CCDS for the detection of relapsing disease are yet to be performed.

The retrospective character of this study is a limitation. No intra-individual follow-up has been performed. It would be desirable to assess inflammatory changes in the same patients before initiation of CS treatment and repeatedly within the first days of treatment. Furthermore, TAB data were present only in 69% of present patients. The lower specificity of both CCDS and MRI in the subgroup of patients undergoing TAB might be explained by a selection bias of enforcing a diagnosis in patients with negative imaging findings, but strong clinical suspicion. In contrast, compared with the final clinical diagnosis in the whole patient group, the specificity of high-resolution MRI and CCDS was high.

In summary, our results indicate that the sensitivity of CCDS and MRI for detection of GCA decreases rapidly under CS treatment. Unequivocal detection of inflammatory mural changes by a first-time CCDS or an MRI examination decreases substantially within the first days of CS treatment. Therefore, in clinical practice, CCDS and MRI studies in patients with suspected GCA should be performed as soon as possible, preferentially within the first day of treatment. Non-invasive imaging must not delay onset of CS treatment.

Rheumatology key messages

- Mural inflammatory MRI and CCDS findings decrease rapidly within the first days of CS treatment of GCA.
- Non-invasive imaging should be performed before or immediately after onset of CS treatment in GCA patients.

Disclosure statement: The authors have declared no conflicts of interest.

References


