Involvement of the ophthalmic artery in giant cell arteritis visualized by 3T MRI

Julia Geiger¹, Thomas Ness², Markus Uhl¹, Wolf A. Lagrèze², Peter Vaith³, Mathias Langer¹ and Thorsten A. Bley¹,⁴

Introduction

GCA is the most common form of systemic vasculitis in adults over the age of 50 years. There is considerable overlap with PMR, a related disease [1]. Extracranial artery involvement, especially of the aorta and its branches, is not uncommon [2]. Typically, large- and medium-sized arteries are affected: the eye’s ciliary arteries, being so tiny, are among the small arteries thus affected [3]. Classic symptoms such as headache, jaw claudication and tenderness in the temporal region usually appear prior to the onset of ocular manifestation [4]. Cranial ischaemic complications, in particular visual loss, mainly due to anterior ischaemic optic neuropathy (AION) or central retinal artery occlusion (CRAO), are the most feared ophthalmological sequelae of GCA [5]. The incidence of ocular manifestation is generally estimated at ~30% [5–8]. Visual ischaemic complications are frequently preceded by amaurosis fugax constituting a prodromal signal before permanent loss of vision appears [9]. Another ocular manifestation is diplopia due to ischaemia of the extraocular muscles or brain stem [6]. Ophthalmological examination is mandatory in all cases of suspected GCA. As GCA is a potentially blinding disease, early diagnosis and immediate steroid treatment is essential to prevent irreversible visual loss [10]. High-resolution MRI at 1.5 and 3 T has been established as a valuable new diagnostic tool to non-invasively determine superficial cranial artery involvement in GCA [11]. Here we hypothesize that it is possible to visualize mural inflammation of the ophthalmic artery in patients with GCA using high-resolution MRI.

Methods

Study population

Fifty patients with GCA who had undergone MRI of the superficial cranial arteries were analysed retrospectively with regard to ophthalmic artery involvement. Patients were included whose orbits were entirely within the field of view. Our ultimate patient cohort consisted of 43 patients (30 females, 13 males, range 54–85 years, mean age 71 years) examined over a 4-year period. Thirty-four patients underwent temporal artery biopsy. All patients were diagnosed with GCA by experienced rheumatologists; in 27 cases, diagnosis was validated by temporal artery biopsy. Data on clinical symptoms were retrieved from medical records including ophthalmic evaluation reports. We also recorded elevated CRP and ESR values before glucocorticoid therapy was initiated. We introduced an age- and gender-matched control group consisting of 15 patients (11 females, 4 males, range 57–88 years, mean age 68.5 years) in whom GCA was excluded by imaging findings and temporal artery biopsy. All patients gave written informed consent prior to the MRI examination. The study was approved by our institutional ethics committee and was performed according to the Declaration of Helsinki.

MRI examination

All patients were referred to MRI before undergoing temporal artery biopsy. Fourteen patients were examined on a 1.5T-scanner (Magnetom Sonata, Siemens, Erlangen, Germany) using an eight-channel phased-array head coil. High-resolution MR examination was performed according to a protocol described elsewhere [12]. Post-contrast, fat-saturated, multi-slice T1-weighted spin-echo (SE) sequences were acquired with a sub-millimetre spatial resolution of 200 × 300 μm² (TR 500 ms, TE 22 ms, field of view 120 × 120 mm², acquisition matrix size 384 × 512). Eleven slices covered a distance of 63 mm. Examinations on the 3T-system (TRIO, Siemens, Erlangen, Germany) were performed with the same high spatial resolution (195 × 260 μm²) and 3-mm slice thickness (field of view 200 × 200 mm², acquisition matrix size 260 × 300).
A dedicated 12-channel neurovascular coil was used to assess the cranial, cervical and upper thoracic vasculature.

**Evaluation**

In a consensus reading, two experienced radiologists (T.A.B. and M.U.) evaluated the MR findings. Image quality criteria and the presence of artefacts were rated subjectively. Inflammatory changes such as contrast enhancement of the vessel wall and mural thickening of the ophthalmic arteries were visually evaluated as follows: minus (−): no mural enhancement and thickening; plus (+): mural enhancement and thickening.

No enhancement was judged as physiological, whereas contrast enhancement was considered as arteritic involvement. Evaluation was performed on state-of-the-art radiology work stations (J-Vision; AGFA, Köln, Germany).

**Results**

In all 43 included patients, images were of good diagnostic quality, and the superficial temporal artery (our reference artery) was well depicted. On corresponding slices the ophthalmic artery was identified at its origin in the internal carotid artery, pursuing it along its course through the orbit. In patients with inflammation, we observed contrast enhancement and mural thickening as in the superficial temporal and occipital arteries (Fig. 1A). Out of 43 patients, 20 showed mural inflammatory enhancement of the ophthalmic arteries in post-contrast imaging. Bilateral inflammatory changes (Figs 2, 1D and E) were detected in 14/43 cases, in five patients the left side and in one patient the right side were affected (Fig. 3A). Three patients showed marginal enhancement without relevant mural thickening. We usually observed the inflammatory changes in the section that crosses over the optic nerve, and in the superomedial angle in a few cases. The vessel was barely detectable in normal patients as a thin hypointense structure crossing the optic nerve (Figs 1B and C).

No significant correlation between MRI results and findings on fundoscopy on the one hand and MRI results and patients’ complaints on the other hand was found. On ophthalmological examination typical signs of AION were noted in nine patients and posterior ischaemic optic neuropathy (PION) in one. Four patients revealed CRAO and one had narrowing of the retinal arteries. Two patients had visual symptoms not related to arteritis. Seven patients were positive in MRI and ophthalmoscopy, whereas 13 were MR-positive but their ophthalmic examination was normal. Eight patients were MR-negative but revealed signs typifying arteritis in the ophthalmic examination. However, 15 patients were considered negative in both investigations.

Twenty-six patients in our cohort presented with ocular symptoms (60%). When comparing visual impairment and inflammatory changes in the ophthalmic artery, we had anticipated seeing a correlation, and in fact 11 patients were symptomatic and MR-positive. Yet, nine had no arteritis-related visual symptoms, whereas MRI revealed signs of inflammation. Fifteen MRI-negative patients had visual symptoms. Eight were MRI-negative and clinically asymptomatic. Summarizing the various visual symptoms, we observed visual reduction or loss in 21 cases, mainly in one eye. Two complained of diplopia, and one of visual reduction in the right eye (Fig. 3B). Two other patients presented with amaurosis fugax and three with eye pain, in one of them in conjunction with visual reduction.

Diagnosis was validated by temporal artery biopsy in 27 patients. Biopsy was negative in seven patients, and no biopsy was performed in nine. The mean level of CRP was increased to 13.49 mg/dl (range 0.3–30.3 mg/dl) in patients with MRI signs of ophthalmic artery involvement and to 8.43 mg/dl (range 0.3–30.7 mg/dl) in the others. The ESR was elevated in those with ophthalmic artery involvement with a mean of 79 ± 35 mm in the first hour and 73 ± 32 mm in the other group. The MRI examination was performed in 11 patients prior to initiation of glucocorticoid treatment, ranging from 0 to 14 days (average 2.1 days; 1.9 days in patients with MRI signs of ophthalmic artery involvement and 2.6 days in patients without). Detailed laboratory, histological and MRI findings as well as the results of the ophthalmic examination, clinical symptoms and the duration of glucocorticoid therapy are illustrated in Table 1.

No signs of ophthalmic artery involvement were detected in patients of the control group in whom GCA had been excluded. None of them had visual symptoms.

**Fig. 1.** (A) High-resolution MRI of the superficial cranial arteries and the ophthalmic arteries in a 73-year-old female patient (Patient 41) with no visual symptoms. The superficial temporal artery and the occipital artery reveal strong bilateral mural contrast enhancement (white arrows), while the ophthalmic arteries (open arrows) do not depict inflammatory changes. (B and C) Show the ophthalmic arteries at a higher magnification. (D and E) A second MRI with the same settings was performed 3 months later, which shows strong contrast enhancement of both ophthalmic arteries (white arrows). In spite of continuous corticoid therapy, the patient had developed a relapse with elevated laboratory findings.
of the right ophthalmic artery. This patient did not present with visual impairment, and oculomotor examination was normal.

**Discussion**

High-resolution MRI has been shown to detect inflammatory changes in superficial cranial arteries [11–13]. In a retrospective study, first we analysed inflammatory involvement of the ophthalmic arteries in GCA patients using post-enhanced T1-weighted images. Secondly, we correlated our MRI findings with documented clinical symptoms and ophthalmic diagnoses. Inflammatory changes in the ophthalmic arteries were detected in 20 out of 43 patients (46%) with clinically obvious or histologically proven GCA. The ophthalmic artery is the first branch of the internal carotid artery that arises after penetrating the dura. Entering the orbit, the ophthalmic artery lies inferolateral to the optic nerve before crossing over it in most people (83%). Its course and the branching patterns in the sequence of origin vary greatly. In the most common sequence, the first branches form the central retinal artery and the medial and lateral posterior ciliary arteries. These are the ophthalmic artery’s most important branches supplying the retina and optic nerve [14].

There has been ophthalmic artery involvement in up to 76% of the patients who died during the active phase of GCA, according to autopsy reports. The posterior ciliary arteries were affected in 75%, whereas the proximal central retinal artery was inflamed in 60%. The parts of the distal central retinal artery where it lies within the optic nerve were affected less often [15]. Crompton and co-workers [16] made similar observations when they hypothesized that the more severely affected arteries are those lying in the optic nerve’s dural sheath (the latter being an extension of the dura). Their findings of the arteries in the orbit correlate with the involvement pattern of the internal carotid and vertebral arteries. They assumed that there is a correlation between the amount of elastic tissue in the arterial walls and the inflammation’s severity [15].

Vision loss, the most severe and feared ocular complication of GCA, is reported in 15% of the patients, even in contemporary series [5]. It results in ischaemic vessel occlusion and leads to AION, the most frequent disease affecting the optic nerve in the elderly. AION is classified in its arteritic and non-arteritic forms [17]; the latter is more frequent, and is usually caused by an embolic occlusion [18]. Funduscopy reveals an oedematous optic nerve head in both cases, whereas flame-shaped bleedings in the retinal nerve fibre layers occur more frequently in the non-arteritic form. GCA leads to an occlusion in the posterior short ciliary arteries in the majority of cases. Rarely, central retinal, cilioretinal or ophthalmic artery occlusions may lead to a central artery or branch artery occlusion [19]. There have been recent reports of an association between the degree of intimal hyperplasia dependent on neovascularization [20], consecutive luminal narrowing and the risk of ophthalmic complications [21]. In contrast, there are very few reports of visual loss due to infarctions of the occipital cortex because of involvement of the supplying arteries [22], and was not present in our study.

Complete blindness may be the presenting manifestation of ocular involvement, but most patients have premonitory symptoms such as amaurosis fugax or diplopia [23]. GCA must be considered an ophthalmic emergency in such cases. Hence, early diagnosis and immediate corticoid treatment is mandatory to prevent permanent vision loss of one or both eyes or to achieve visual improvement in eyes with impending visual loss [24]. There is seldom recovery in visual acuity and visual field after complete visual loss despite of high-dose steroid treatment. Visual deterioration, however, occurs within the first week in 27% of patients [25].

The differences observed in our study between the funduscopy and MRI results, as well as the contradictory visual symptoms and MRI findings, may have to do with the size of the arteries. The mural thickness of the ophthalmic arteries resembles that of the superficial cranial arteries and can therefore be detected with an inplane spatial resolution of $195 \times 260 \ \mu m^2$ of the MRI protocol. The tiny posterior ciliary arteries, which are mainly responsible for vessel occlusion leading to visual reduction, cannot be detected with the proposed imaging protocol. These arteries were presumably not affected in asymptomatic patients. The mural enhancement of the larger ophthalmic arteries that we observed did not seem severe enough to cause clinical symptoms, and occlusion of the ophthalmic artery generally is not the cause for AION.
Also, there was poor correlation between patients’ complaints and ophthalmoscopic results leading to nine false negative cases. In these patients, symptoms including eye pain were presumably not detectable as a morphological correlation on funduscopy. Other authors discuss an involvement of the orbit in patients with atypical visual symptoms as an uncommon presentation of GCA [26, 27]. However, no inflammatory signal changes in the ophthalmic arteries were detected in 20 out of 43 patients (46%) with clinically proven and/or biopsy proven GCA. In these patients, symptoms including eye pain were presumably not detectable as a morphological correlation on funduscopy.

In summary, MRI findings suggest a frequent involvement of the ophthalmic arteries in the course of GCA inflammation. This is the first report of successful depiction of ophthalmic artery involvement in GCA utilizing high-resolution MRI. Mural changes in the ophthalmic arteries were detected in 20 out of 43 patients (46%) with clinically proven and/or biopsy proven GCA. Histological proof of ophthalmic artery involvement is not feasible. However, the imaging criteria for assessing mural inflammation of the ophthalmic arteries are the same as those applied for assessing the superficial temporal arteries, which have been histologically validated in various studies.

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References
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