Visual Complications in Patients with Biopsy-proven Giant Cell Arteritis: A Population-based Study

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ABSTRACT. ***Objective.*** To study the clinical and laboratory characteristics of patients with biopsy-proven giant cell arteritis (GCA) with visual complications, and to evaluate the incidence rate of visual complications in GCA compared to the background population.

Methods. Data from 840 patients with GCA in the county of Skåne, Sweden, diagnosed between 1997 and 2010, were used for this analysis. Cases with visual complications were identified from a diagnosis registry and confirmed by a review of medical records. The rate of visual complications in patients with GCA was compared with an age- and sex-matched reference population.

Results. There were 85 patients (10%) who developed ≥ 1 visual complication after the onset of GCA. Of the patients, 18 (21%) developed unilateral or bilateral complete visual loss. The mean age at diagnosis was 78 years (± 7.3); 69% were women. Compared with patients without visual complications, those with visual complication had lower C-reactive protein levels at diagnosis and were less likely to have headache, fever, and palpable abnormal temporal artery. The use of β-adrenergic inhibitors was associated with visual complications. The incidence of visual complications among patients with GCA was 20.9/1000 person-years of followup compared to 6.9/1000 person-years in the reference population, resulting in a rate ratio of 3.0 (95% CI 2.3–3.8).

Conclusion. Ten percent of patients with GCA developed visual complications, a rate substantially higher than that of the general population. Patients with GCA who had visual complications had lower inflammatory responses and were more likely to have been treated with β-adrenergic inhibitors compared with patients without visual complications. (First Release June 1 2016; J Rheumatol 2016;43:1559–65; doi:10.3899/jrheum.151033)

Key Indexing Terms:

GIANT CELL ARTERITIS | VISUAL COMPLICATIONS | INFLAMMATION
CLINICAL CHARACTERISTICS | β-BLOCKERS | RATE RATIO

Giant cell (temporal) arteritis (GCA) is the most common type of primary systemic vasculitis affecting people aged more than 50 years[1]. The incidence of GCA increases with age to reach a peak incidence from 70–80 years[2,3]. The disease often presents with some or all of the following symptoms: headache, jaw claudication, polymyalgia rheumatica (PMR), fever, fatigue, weight loss, and a high erythrocyte sedimentation rate (ESR)[4,5]. Visual complications are the most feared complication of GCA, with devastating consequences if not promptly treated with high-dose glucocorticoids. The rate of visual complications in GCA has been reported from 12% to 15% in previous studies[6,7,8]. This complication is the result of ischemia of the optic nerve secondary to arteritis of the branches of the ophthalmic or posterior ciliary arteries, and less commonly by occlusion of retinal arterioles[5]. Frequent clinical manifestations include permanent or transient loss of vision, diplopia, and amaurosis fugax[9,10]. Delays in diagnosis and treatment are also associated with increased risk of irreversible visual loss among patients with GCA[11]. Studies have shown an association between lower levels of acute-phase reactants and occurrence of visual complications in GCA[6,12,13,14]. It has also been suggested that a variant in the vascular endothelial growth factor gene[15] and genetic variants associated with high interferon-γ expression[16] may predispose patients with GCA to severe ischemic complications. Additional previously reported risk factors for visual complications are presence of giant cells[17] or intimal hyperplasia in the

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temporal artery biopsy (TAB)[18], thrombocytosis at the time of diagnosis[14], and jaw claudication[19,20].

Our population-based study aimed to (1) compare demographic, clinical, and laboratory characteristics of patients with biopsy-proven GCA who developed visual complication with those who did not, (2) study factors associated with visual complications among patients with biopsy-proven GCA, and (3) estimate the incidence of visual complication in patients with biopsy-proven GCA and to compare that with the corresponding rate in the background population.

MATERIALS AND METHODS

Study area and population. The study area was Skåne, the southernmost administrative county of Sweden, with a total population of about 1.25 million on December 31, 2011 (13.2% of the total population of Sweden), living in an area of about 11,034.5 km^2 (2.7% of the total area of Sweden). The county of Skåne includes urban and rural areas with many people employed in agriculture, but also a large research and education sector.

Patients. Patients were identified from a population-based cohort of patients with biopsy-proven GCA diagnosed between 1997 and 2010 who lived in the county of Skåne at the date of GCA diagnosis. Case identification, diagnosis, and demographic features have been previously reported[3]. In short, all patients in the GCA cohort were diagnosed by TAB and were identified from the database of the Department of Pathology at these hospitals within the county of Skåne: Skåne University Hospital in Lund and Malmö, Helsingborg Hospital, and Kristianstad Hospital. There were 840 patients (626 women) with a median age at diagnosis of 75.9 years [interquartile range (IQR) 69.9–81.2].

The Skåne Healthcare Register (SHR). The SHR is a central computerized dataset that registers all healthcare provided in Skåne by using the patient's unique personal identification number, which is automatically assigned to all residents and provides information on date of birth and sex. Every healthcare consultation generates data entries by a healthcare provider and these data are then transferred to the SHR central database. All diagnoses and related healthcare problems are classified according to the Swedish translation of the International Classification of Diseases, 10th ed (ICD-10) system. The use of the SHR database in the identification of visual complications has been described in detail[21].

Case identification and ascertainment of visual complications. By linking the GCA cohort to the database at the SHR, all patients assigned with at least 1 ICD-10 code indicating any of the selected set of visual complications as shown in Table 1 were identified. Visual complications were defined as any signs or symptoms of ophthalmological manifestations occurring after the onset of GCA. However, only cases with visual complications ascertained by ophthalmological examinations were included in our analyses. All case records were reviewed for case ascertainment of visual complications and collection of clinical and laboratory data. Cases with missing or incomplete records and cases with known visual manifestations diagnosed before the onset of GCA, or that were unrelated to GCA, were not included in our study.

Table 1. Ophthalmological complications associated with GCA that were examined in this study.

Visual Complications	ICD-10 Codes
Central retinal artery disorders	H34.0–34.2
Optic nerve pathologies, including optic nerve atrophy and optic disc atrophy	H47.0–47.2
Blindness, diplopia, visual field defect, subjective visual symptoms	H53–H54
Amaurosis fugax	G45.3

GCA: giant cell arteritis; ICD-10: International Classification of Diseases, 10th ed.

Nested case-control study. A nested case-control study was performed within the GCA cohort of 840 patients. Patients found to have visual complications after the onset of GCA were included as cases. For each case, 1 control was randomly selected from patients without visual complication from the same cohort and was matched for calendar year of birth (± 5 yrs), sex, and year of diagnosis.

Data collection. Data from medical records were collected from the time of diagnosis including demographics, both clinical and laboratory characteristics from time of diagnosis, and selected medications and comorbidities prior to GCA diagnosis. All histopathology reports were reviewed and data were collected regarding presence or absence of granulomatous inflammation, giant cells, or concomitant arteriosclerosis. Data on treatment given at the time of the diagnosis of GCA, including oral or intravenous (IV) glucocorticoids, were also collected. The diagnosis delay (time in days from the onset of GCA symptoms to the date of TAB performance) was registered for cases and controls. Concomitant medications at time of the diagnosis of GCA were studied. The following medications were selected: β-adrenergic receptor inhibitors, angiotensin-converting enzyme (ACE) inhibitors, angiotensin II receptor blocker (ARB), anticoagulants (warfarin or low molecular weight heparin), platelet aggregation inhibitors (acetylsalicylic acid, clopidogrel, or dipyridamole), lipid-lowering agents (statins), and nonsteroidal antiinflammatory drugs. Data on the use of the adjunctive immunosuppressive agents [e.g., methotrexate (MTX) and azathioprine] during the first year after GCA diagnosis were also collected. Treatment delay was defined as time in days from the onset of disease to commencement of treatment with glucocorticoids.

The rate and rate-ratio of visual complications. For each patient with biopsy-proved GCA, 4 reference subjects were randomly sampled from the background population. Reference subjects were matched for age, sex, area of residence, and index year. The index year was based on the end of December the year before the diagnosis year for the GCA case. Reference subjects assigned any of the ICD codes for GCA were excluded. All reference subjects were required to have at least 1 clinic visit during the study period with an ICD-10 diagnosis (any) by any physician in the SHR. The person-time was defined as the number of days each person was followed from the date of GCA diagnosis (or index date for reference subject) to the end of followup, as previously described[21]. The followup time was calculated from the date of GCA diagnosis or index date for reference until the earliest of the following: (1) date of occurrence of the visual complication, (2) death, (3) the date when the case or reference subject moved outside the study area, or (4) December 31, 2011.

The rate of visual complications was calculated by dividing the number of patients who developed at least 1 visual complication after the onset of GCA (or the index date for the reference subjects) by the sum of the person-time during the followup. The rate ratio was calculated by dividing the rate for patients with GCA by that of the reference population.

Statistical analysis. Statistical analysis was performed using the Statistical Package for the Social Sciences, SPSS version 22.0 for Windows (IBM SPSS Statistics). Data are presented as means and SD for normally distributed variables, and as median and IQR for not normally distributed variables. For continuous variables, the differences between groups were compared using the nonparametric Mann-Whitney U test or the Student t test, as appropriate. The chi-square test was used for categorical variables. A p value of < 0.05 was considered significant. Potential predictors of visual complications were examined in conditional logistic regression models. Multivariate analyses included variables with p value of < 0.15 in the univariate analysis. For rate ratios, the 95% CI were calculated assuming a Poisson distribution of the observed cases.

The Regional Ethical Review Board for southern Sweden approved the study protocol.

RESULTS

The case-control study. The search in the SHR database identified 100 of 840 patients within the GCA cohort who had been assigned at least 1 of the ICD-10 codes for visual complications. Some patients were excluded upon detailed medical records review: 8 with ophthalmological diagnoses that predated the diagnosis of GCA and were attributed to nonvasculitic preexisting comorbidity according to the ophthalmologist's judgment, and 7 that had either incomplete medical records or incorrectly assigned ICD codes. All diagnoses of visual complications were confirmed by review of medical records. The remaining 85 patients (10% of patients) were thus considered to have developed visual complications confirmed and classified by ophthalmological examination after the GCA diagnosis was established. There were 59 women (69%). Of the patients, 72 had unilateral visual complications and 13 had bilateral visual complications. Eighteen of the 85 patients who had visual complications (21%) developed complete visual loss (16 in 1 eye, 2 in both eyes). A list of all visual manifestations in the 85 cases with GCA is shown in Table 2. The ICD-10 codes for ophthalmological diagnoses assigned among reference subjects in our study are shown in Supplementary Table 1 (available from the authors on request).

The median time from onset of visual manifestation to date of diagnosis of GCA was 3 days (IQR 1–14). The mean age at diagnosis of GCA was 78 years (± 7.3). Table 3 summarizes the demographic, clinical, and laboratory characteristics of cases with visual complications and the controls selected from the GCA cohort as described above. One hundred sixty-three patients (98%, 81 cases and 82 controls) fulfilled ≥ 3 of the 1990 American College of Rheumatology classification criteria for GCA[22]. Compared with controls, patients with visual complications were less likely to have headaches, fever, and a palpable tender temporal artery (Table 3). Symptoms of PMR at the onset of GCA were more prevalent among controls while a previous diagnosis of PMR and the presence of jaw claudication were more prevalent among cases, though these differences were not statistically significant.

The use of β-adrenergic receptor inhibitors was associated with the development of visual complication (37% in cases vs 18% in controls, p = 0.009). There were no significant differences in the frequency of use of other medications (Table 3).

Table 2. Visual manifestations in the 85 cases with GCA and verified ophthalmologic complications.

Visual Manifestations	No. Patients, n = 85
Bilateral permanent blindness	2
Unilateral permanent blindness	16
Transient or permanent visual field defects	5
Transient unilateral or bilateral visual loss	23
Other transient visual symptoms	39

GCA: giant cell arteritis.

Patients with visual complications had significantly lower C-reactive protein (CRP) levels at diagnosis compared with those without visual complications (mean 83 mg/l vs 116 mg/l, p = 0.002). Those with a CRP level within the highest tertile (≥ 108 mg/l) had a reduced risk of visual complications compared with those in the lowest tertile (≤ 60 mg/l, OR 0.31, 95% CI 0.13–0.76).

No such association was found between the level of ESR and occurrence of visual complications. In our study, the risk of visual complications was not significantly different among those with an ESR of 70–100 mm/h (n = 66, OR 1.26, 95% CI 0.64–2.49) or those with ESR > 100 mm/h (n = 30, OR 0.71, 95% CI 0.29–1.72) compared with those with ESR < 70 mm/h (n = 67). All other laboratory results studied are shown in Table 3. Further, there were no significant differences in histopathology features of cases versus controls (Table 3).

The results of the conditional logistic regression analyses are shown in Table 4. In the univariate analysis, the absence of headache or abnormal temporal artery at clinical examination and the use of β-adrenergic inhibitors were significantly associated with a higher risk of visual complications. However, in the multivariate analysis, only the use of β-adrenergic inhibitors was an independent predictor of visual complications (Table 4).

The median initial oral glucocorticoid dose was 60 mg per day (IQR 50–60) for cases compared with 40 mg (IQR 40–50) for controls (p < 0.001). Among the cases, 24% received IV glucocorticoids at the time of diagnosis of GCA compared with 5% of controls (p < 0.001). During the first year following the diagnosis of GCA, the use of adjunctive immunosuppressive therapy (MTX or azathioprine) was more prevalent among cases (17% vs 1.2% controls, p = 0.001).

At the time of diagnosis, 63 cases (74%) were hospitalized (for any reason) compared with 32 controls (40%, p < 0.001). However, there were no differences in the duration of the inpatient stay at first hospitalization following the diagnosis of GCA between cases and controls (mean time of 7.2 days for both, p = 0.95).

Incidence rate of visual complications. Linking of the cohort to the SHR resulted in the identification of 100 (70 women) of 840 patients (12%) with an assigned ICD-10 code for at least 1 visual complication after the diagnosis of GCA. Among the reference background population, visual complications occurred among 146 persons (110 women). The incidence rate among patients with biopsy-proven GCA was 20.9 per 1000 person-years (95% CI 17.0–25.4) compared with 6.9 per 1000 person-years (95% CI 5.8–8.2) among the reference population. The rate ratio was 3.0 (95% CI 2.3–3.8, p < 0.001). Sex-specific incidence rates and rate ratios are shown in Table 5.

Table 3. Comparisons between patients with biopsy-proven GCA with and without visual complications. Values are n (%) unless otherwise specified.

Characteristics	GCA with Visual Complications, n = 85	GCA with no Visual Complications, n = 82	p
Age at diagnosis, yrs, mean (SD)	78.0 (± 7.3)	77.9 (± 6.6)	NA
Female/male	59/26	57/25	NA
Headache	63 (74)	73 (89)	0.01
Jaw claudication	36 (42)	27 (33)	0.20
Fever*	13 (23)	24 (40)	0.04
Temporal artery tenderness	28 (33)	42 (51)	0.01
PMR symptoms at GCA onset	53 (62)	62 (76)	0.06
Diagnosis of PMR prior to onset of GCA	21 (25)	11 (13)	0.06
Diagnosis delay, days, median (IQR)	24 (9–45)	24 (11–35)	0.94
Treatment delay, days, median (IQR)	24 (9–45)	24 (11–35)	0.94
Comorbidities			
Hypertension	43 (51)	37 (45)	0.48
Diabetes mellitus	12 (14)	13 (16)	0.75
Hyperlipidemia	8 (9)	6 (7)	0.62
Ischemic heart diseases	14 (17)	19 (23)	0.27
Cerebrovascular accident	8 (9)	4 (5)	0.37
Thromboembolic disease	15 (18)	10 (12)	0.32
Histopathology findings			
Granuloma	13 (15)	17 (21)	0.36
Giant cells	49 (58)	47 (58)	0.96
Atherosclerosis	11 (13)	7 (9)	0.35
Drugs at GCA onset			
ACE/ARB	21 (25)	12 (15)	0.10
Anticoagulants	6 (7)	2 (2)	0.27
Platelet inhibitors	21 (25)	27 (33)	0.26
Statins	15 (18)	11 (13)	0.45
NSAID	3 (4)	3 (4)	1.00
β-adrenergic inhibitors	31 (37)	15 (18)	0.009
Laboratory data at time of GCA diagnosis			
Hemoglobin, g/dl, mean (SD)	11.8 (± 1.5)	11.6 (± 1.7)	0.56
White blood cell count × 10^9/l, median (IQR)	9.2 (7.5–11)	10 (8–11)	0.39
Platelets × 10^9/l, mean (SD)	413 (± 143)	385 (± 151)	0.32
Albumin, g/l, median (IQR)	33 (29–35)	29 (26–34)	0.03
ESR, mm/h, mean (SD)	73 (± 25)	77 (± 29)	0.38
CRP, mg/l, mean (SD)	83 (± 52)	116 (± 74)	0.002

* Data available for 57 cases and 60 controls. GCA: giant cell arteritis; PMR: polymyalgia rheumatica; IQR: interquartile range; ACE/ARB: angiotensin-converting enzyme inhibitor/angiotensin II receptor blockers; NSAID: nonsteroidal antiinflammatory drugs; ESR: erythrocyte sedimentation rate; CRP: C-reactive protein; NA: not applicable.

Table 4. Conditional regression analysis showing predictors of visual complication in patients with biopsy-proven GCA.

Predictors	Univariate Analysis			Multivariate Analysis		
	OR	95% CI	p	OR	95% CI	p
Headache	**0.33**	**0.13–0.84**	**0.02**	0.36	0.09–1.47	0.15
Fever	0.50	0.20–1.23	0.13	0.48	0.13–1.69	0.25
Abnormal temporal artery*	**0.42**	**0.20–0.85**	**0.01**	1.19	0.28–4.98	0.80
PMR symptoms at diagnosis	0.47	0.21–1.04	0.06	0.32	0.05–1.91	0.21
PMR diagnosis before GCA	2.11	0.95–4.66	0.06	0.96	0.19–4.68	0.96
ACE/ARB	1.88	0.84–4.23	0.12	2.52	0.60–10.4	0.20
β-adrenergic inhibitors	**2.77**	**1.29–5.95**	**0.009**	**6.98**	**1.29–37.8**	**0.02**

* On clinical examination. Significant data are in bold face. GCA: giant cell arteritis; PMR: polymyalgia rheumatica; ACE/ARB: angiotensin-converting enzyme inhibitor/angiotensin II receptor blockers.

Table 5. Rate and rate ratios of ophthalmological complications in GCA compared with reference background population.

Participants	Cases			References			Rate Ratio	95% CI	p
	n	Person-yrs	Rate	n	Person-yrs	Rate			
All	100	4772	20.9	146	20,931	6.9	3.0	2.3–3.8	< 0.001
Men	30	1137	26.3	36	4987	7.2	3.6	2.1–6.0	< 0.001
Women	70	3635	19.2	110	15,944	6.9	2.8	2.0–3.7	< 0.001

GCA: giant cell arteritis.

DISCUSSION

In our population-based study from southern Sweden, 10% of patients with biopsy-proven GCA diagnosed during a period of 14 years developed visual complication after the onset of GCA. Our study shows that patients with biopsy-proven GCA with visual complications have lower inflammatory responses and are more likely to have been treated with β-adrenergic inhibitors compared with patients with GCA without visual problems. Our study also demonstrates a 3-fold higher rate of visual complications among patients with GCA compared with sex- and age-matched reference subjects from the background population in southern Sweden.

Visual complications occurred in 10% of patients with GCA in our study, a rate lower than the 16%–30% reported in other studies using other populations[7,12,13,23]. This discrepancy may be explained by the differences in the study design and in the case mix of included patients. In line with our results, a recently published study suggested a declining incidence of visual symptoms over the past 5 decades[20]. A high degree of physician's awareness with prompt initiation of adequate therapy in newly diagnosed patients with GCA according to current recommendations[24,25] may explain this decline in visual complications of GCA.

In our study, patients with visual complications had less-extensive signs of inflammation measured by CRP and systemic inflammatory manifestations such as fever than those without visual complications. Previous studies have also found an inverse relation between the presence of fever and the development of ischemic complications[26], and that lower inflammatory response occurred in patients with GCA with visual complications compared with patients without visual problems[10,13,14,27].

A high CRP may influence the decision to start treatment even if the clinical manifestations are not fully characteristic of GCA. Further, patients with severe inflammatory symptoms may seek medical care earlier than those with less severe symptoms. A protective effect of fever and elevated inflammatory cytokines against ischemia has been proposed as a reason for these findings[28,29]. Another possible explanation for the negative association between high inflammatory markers and visual complications is that some inflammatory cytokines such as interleukin 6 may exert an antiplatelet or anticoagulant effect, or act by decreasing intimal hyperplasia of the inflamed arteries or preserving endothelial function[23,30,31,32]. We did not find any association between the level of ESR and the occurrence of visual complications in our study. However, an ESR level between 70 mm/h and 100 mm/h was the best predictor of ischemic complications and visual loss in a study enrolling 273 patients with biopsy-proven GCA[33], a finding that was not replicated in our present study. Differences in study design and definitions of visual complications may explain the differences between these studies.

We found that patients with visual complications less frequently presented with headache or temporal artery tenderness than patients without visual problems. These findings are in accordance with previous studies[13,23]. Together with less-prominent inflammatory response, we may expect a higher risk for diagnosis delay or delay in initiating treatment with glucocorticoids among patients with visual complications. However, in our current study, no such differences were evident. This assessment is limited by the difficulties in precisely defining and quantifying the degree of delay in diagnosis because it is difficult to know the time of disease onset.

A novel finding in our study is the negative association between the use of β-adrenergic inhibitors at the time of GCA diagnosis and the development of visual complications. The involvement of β-adrenergic inhibitors in the development of stroke has been demonstrated. In a large single-center study enrolling more than 44,000 patients, the use of non-selective β-adrenergic inhibitors was associated with an increased risk of postoperative stroke as compared with lower risk among patients who were receiving highly selective β1 blockers[34]. It has been suggested that the β-adrenergic inhibitors may impair cerebral vasodilation and increase systemic vascular resistance, resulting in cerebral hypoxia, as has been shown by a number of animal studies[35,36,37,38]. The involvement of β-adrenergic inhibitors and other antihypertensive drugs in this context should be further studied. If confirmed, these findings may have implications for the early management of GCA. We also found a trend toward an association between visual complications and the use of drugs that inhibit the angiotensin system, which did not reach significance in the multivariate analysis.

These associations may also be because of a relation with the indication for treatment, rather than a specific effect of

the drugs. Indeed, the literature suggests that traditional cardiovascular risk factors may also predispose to an increased risk of severe ischemic complication in GCA. In this regard, a population-based study showed that patients with biopsy-proven GCA who had hypertension (HTN) had a significantly increased risk of developing severe ischemic complications[39]. However, in our present study, we did not find any significant association between other prevalent cardiovascular comorbidities or diabetes mellitus and the occurrence of visual complications in GCA. This is in agreement with several other studies[13,40]. Differences in study designs and sample size may explain the different outcomes. Not only was the use of β-adrenergic inhibitors more common among those with visual complications, but there was also a trend toward an association with ACE inhibitor/ARB treatment. Therefore we cannot exclude that these findings reflect an underlying association between severe HTN and visual complications in GCA. Although there was no major difference in the prevalence of HTN overall in our study, patients with severe HTN, who would be more likely to receive current treatment with β-adrenergic inhibitors or ACE inhibitors/ARB at any time, could be predisposed to visual complications. This should be further studied in other populations and other study settings.

In accordance with a previous report[41], our study did not find a significant association between the use of anticoagulation and platelet aggregation inhibitors and visual complications in GCA. However, 2 other retrospective studies have demonstrated the usefulness of antiplatelet and anticoagulation treatment for reducing the rate of ischemic (including visual) complications in patients with GCA[42,43].

As expected, patients with visual complications were treated with higher doses of glucocorticosteroids at diagnosis compared with other patients with GCA. Still, although IV glucocorticosteroid treatment for patients with GCA and visual symptoms is now standard in our area, only 24% of this subset of patients received such treatment. This may reflect that patients had been diagnosed during a period of 14 years and were treated at a number of departments and hospitals in the region. Further, the benefits of IV glucocorticoids in this context may not have been fully recognized until after the publication of the randomized clinical trial by Mazlumzadeh, *et al*[44]. Patients with visual complications were also more likely to receive adjunctive immunosuppressives during followup. This is compatible with a more treatment-resistant disease subset overall, and a perceived greater risk of severe consequences of relapses during steroid tapering.

The incidence rate of visual complications in our population-based study was 3-times higher in patients with biopsy-proven GCA than in the reference persons without GCA from the background population. To our knowledge, no previous studies compared the rate of visual complications among patients with GCA with the background population.

Our current study has a number of limitations. Ours is a retrospective study and is thus associated with the biases of such a design, including some missing data. Because the first identification of cases with visual complication was carried out entirely by screening the diagnosis registry for the relevant ICD codes, the possibility of missing cases cannot be excluded. However, our study also has a number of strengths. Our study cohort is based on one of the largest population-based cohorts of GCA in which all cases were verified by TAB. In addition, the diagnosis of ophthalmological complication was verified by review of case records and only cases with complications verified by an ophthalmologist were included.

Our study demonstrated that patients with biopsy-proven GCA with a higher inflammatory response at the disease onset had a lower risk of visual complications. Patients with current use of β-adrenergic inhibitors had a higher risk of developing visual complications, a finding that needs further study. The incidence rate of visual complications was 3-fold higher among patients with biopsy-proven GCA compared with a reference population.

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