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Original Article

Clinical characteristics and courses of Korean patients with giant cell arteritis: a multi-center retrospective study

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Objective: Giant cell arteritis (GCA) is a large-vessel vasculitis that primarily affects elderly individuals. However, data regarding Korean patients with GCA are scarce owing to its extremely low prevalence in East Asia. This study aimed to investigate the clinical characteristics of Korean patients with GCA and their outcomes, focusing on relapse.

Methods: The medical records of 27 patients with GCA treated at three tertiary hospitals between 2007 and 2022 were retrospectively reviewed.

Results: Seventeen (63.0%) patients were females, and the median age at diagnosis was 75 years. Large vessel involvement (LVI) was detected in 12 (44.4%) patients, and polymyalgia rheumatica (PMR) was present in 14 (51.9%) patients. Twelve (44.4%) patients had fever at onset. The presence of LVI or concurrent PMR at diagnosis was associated with a longer time to normalization of the C-reactive protein level (p=0.039) or erythrocyte sedimentation rate (p=0.034). During follow-up (median: 33.8 months), four (14.8%) patients experienced relapse. Kaplan-Meier analyses showed that relapse was associated with visual loss (p=0.008) and the absence of fever (p=0.004) at onset, but not with LVI or concurrent PMR.

Conclusion: Concurrent PMR and LVI were observed in approximately half of Korean patients with GCA, and the elapsed time to normalization of inflammatory markers in these patients was longer. The relapse rate in Korean GCA is lower than that in Western countries, and afebrile patients or patients with vision loss at onset have a higher risk of relapse, suggesting that physicians should carefully monitor patients with these characteristics.

Keywords: Giant cell arteritis, Polymyalgia rheumatica, Recurrence

INTRODUCTION

Giant cell arteritis (GCA) is a medium and large sized vessel vasculitis (LVV) that involves the aorta and its major branches, with a predilection for the branches of the carotid and vertebral arteries, such as the temporal artery [1]. GCA is the most common primary vasculitis in Europe and North America among individuals aged ≥50 years [2]. In the United States, the lifetime risk of GCA is estimated to be 1.0% in females and 0.5% in males [3]. However, GCA is relatively rare in East Asia, where Takayasu arteritis, another type of LVV, is more commonly observed in young Asian females. In a Japanese, single-center, retrospective study, nine (9.5%) of 95 patients with LVV had GCA [4], and the nationwide GCA prevalence was 1.47 per 100,000

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individuals aged ≥50 years [5]. Therefore, studies regarding the clinical profiles and outcomes of East Asian patients with GCA are limited. Among the Korean population, one retrospective study investigated seven patients with arteritic anterior ischemic optic neuropathy (AAION) associated with GCA, but the study focused on the ophthalmological manifestations of the disease [6].

The clinical presentation of GCA is notably diverse, often accompanied by fever or polymyalgia rheumatica (PMR) at onset [7]. In addition, large vessel involvement (LVI), referring to the involvement of the aorta and its major proximal branches in the extremities, is detected in a significant portion of GCA patients [8,9]. Several studies have noted distinctive clinical patterns or phenotypes of GCA based on the presence of LVI, PMR, or fever at onset [7-12], although these findings are inconsistent and heterogeneous. For instance, the associations between LVI and a favorable outcome were contrary between Western and Japanese studies, suggesting the ethnic differences [8,9]. In addition, LVI, PMR, and fever at onset were associated with flare or relapse in previous studies [11,13,14]. To date, there has yet to be a study investigating these subtypes and outcomes, such as relapse, in the Korean GCA population.

Therefore, this study aimed to investigate the clinical profiles of Korean patients with GCA by comparing the clinical characteristics according to the presence of PMR, LVI, or fever at onset and to determine the factors associated with relapse.

MATERIALS AND METHODS

Patients and study design

The medical records of 27 Korean patients treated for GCA at three tertiary hospitals between January 2007 and December 2022 were retrospectively reviewed. The diagnosis of GCA was based on the fulfillment of the 1990 American College of Rheumatology (ACR) classification criteria for GCA [15] or the 2022 ACR/European League Against Rheumatism (EULAR) classification criteria for GCA [16]. This study was approved by the Institutional Review Board of Seoul National University Bundang Hospital and affiliated hospitals (IRB no. B-2012/654-112) and was conducted in compliance with good clinical practice and the Declaration of Helsinki. The requirement for informed patient consent was waived due to the retrospective nature of the study.

Data collection and definition of variables

Demographic data, such as patient age, sex, body mass index, smoking history, past medical history, and signs and symptoms related to GCA at presentation, were collected from the medical records. Fever was defined as an ear temperature ≥38°C. Initial laboratory findings, including complete blood count, erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), rheumatoid factor (RF), anti-nuclear antibody (ANA), and anti-neutrophil cytoplasmic antibodies (ANCA), histologic findings on temporal artery biopsy, and radiologic data were obtained from medical records.

The concurrence of PMR was defined as fulfillment of the 2012 ACR/EULAR provisional classification criteria [17]. LVI was based on the presence of vascular luminal damage (circumferential wall thickening, stenosis, occlusion, or aneurysm not attributable to atherosclerotic changes) on computed tomography (CT) angiography or abnormal fluorodeoxyglucose (FDG) uptake in the arterial wall throughout the aorta on positron emission tomography (PET) imaging [16,18].

Treatment decisions for each patient were made by the responsible rheumatologists. All patients were hospitalized at the time of diagnosis, and outpatient follow-up visits were conducted approximately two weeks after discharge and once a month thereafter. The clinical course of the study participants was reviewed until the last available outpatient visit prior to December 2022. Information regarding medications used during the disease course was retrieved, including anti-platelet agents, glucocorticoid (GC) pulse therapy, starting dose of oral GCs, methotrexate, azathioprine, cyclophosphamide, and biologics, such as tocilizumab. Complete remission was defined as the absence of GCA signs or symptoms, along with normal ESR and CRP levels, and achievement of complete remission at week 12 was specifically checked [19]. Discontinuation of GCs or immunosuppressants and the elapsed time to the normalization of ESR or CRP levels during follow-up were also investigated. Relapse was defined as follows: (1) the appearance of symptoms of GCA and/or PMR associated with an increase in ESR and/or CRP and (2) the rheumatologists' decision to escalate GCs or immunosuppressive therapy due to the increase in ESR and/or CRP levels without other causes and subsequent improvement, as previously described [9].

Statistical analysis

All statistical analyses were performed using R software (ver-

Table 1. Baseline characteristics of patients with giant cell arteritis (n=27)

Characteristic	Value
Age at diagnosis (yr)	75.0 [71.0~79.0]
Female	17 (63.0)
Body mass index (kg/m^2)	23.0±2.6
History of smoking	3 (11.5)
Duration of main presenting symptoms (wk)	5.5 [1.0~8.0]
Symptoms and signs at presentation	
Fever	12 (44.4)
Fatigue	10 (37.0)
Weight loss	7 (25.9)
Headache	23 (85.2)
Jaw claudication	9 (33.3)
Temporal artery pulsation	5 (18.5)
Temporal artery tenderness	17 (63.0)
Visual loss	9 (33.3)
Bilateral	3 (33.3)
Unilateral	6 (66.7)
Anterior ischemic optic neuropathy	8 (30.8)
Cerebrovascular ischemia	3 (11.1)
Polyarthralgia	10 (37.0)
Myalgia	17 (63.0)
Past medical history	
Diabetes mellitus	5 (18.5)
Hypertension	16 (59.3)
Dyslipidemia	10 (37.0)
Coronary artery disease	2 (7.4)
Hepatitis B virus infection	1 (3.7)
Concurrent polymyalgia rheumatica	14 (51.9)
Initial laboratory findings	
ESR (mm/hr)	98.0 [74.5~111.0]
CRP (mg/dL)	9.09 [5.91~15.86]
White blood cell count (/mm^3)	9,080.0 [8,085.0~12,970.0]
Hemoglobin (g/dL)	11.1±1.4
Platelet count (×10^3/mm^3)	398.0±136.0
Cr (mg/dL)	0.74±0.13
Albumin (g/dL)	3.41±0.48
RF positivity	3 (13.0)
ANA positivity	12 (48.0)
p-ANCA positivity	3 (11.1)
Temporal artery biopsy performed	16 (59.3)
Positive findings on temporal artery biopsy	15 (93.8)
Imaging modalities	
Temporal and axillary artery doppler US performed	11 (40.7)
Positive findings to suggest GCA	5 (45.5)
Enhanced CT angiography performed	24 (88.9)
Positive finding to suggest LVI	9 (37.5)
FDG-PET performed	10 (37.0)
Abnormal FDG uptake	4 (40.0)
LVI	12 (44.4)
Meeting ≥3 1990 ACR criteria	24 (88.9)

Values are presented as median [interquartile ranges], mean±standard deviation, or number (%). ESR: erythrocyte sedimentation rate, CRP: C-reactive protein, RF: rheumatoid factor, ANA: anti-nuclear antibody, p-ANCA: perinuclear anti-neutrophil cytoplasmic antibody, US: ultrasound, GCA: giant cell arteritis, CT: computed tomography, LVI: large vessel involvement, FDG-PET: fluorodeoxyglucose-positron emission tomography, ACR: American College of Rheumatology.

Table 2. Comparisons of clinical characteristics in patients with GCA with and without large vessel involvement

	Without LVI (n=15)	LVI (n=12)	p-value
Age at diagnosis (yr)	75.0 [72.0~77.5]	74.5 [70.0~80.0]	0.845
Female	10 (66.7)	7 (58.3)	0.964
Presenting signs & symptoms			
Fever	9 (60.0)	3 (25.0)	0.153
Fatigue	7 (46.7)	3 (25.0)	0.449
Weight loss	4 (26.7)	3 (25.0)	>0.999
Headache	15 (100.0)	8 (66.7)	0.060
Jaw claudication	5 (33.3)	4 (33.3)	>0.999
Limb claudication	1 (6.7)	5 (41.7)	0.088
Temporal artery pulsation	4 (26.7)	1 (8.3)	0.471
Temporal artery tenderness	5 (33.3)	6 (50.0)	0.397
Visual loss	5 (33.3)	4 (33.3)	>0.999
Anterior ischemic optic neuropathy	4 (26.7)	4 (33.3)	>0.999
Cerebral ischemia	1 (6.7)	2 (16.7)	0.837
Polyarthralgia	6 (40.0)	4 (33.3)	>0.999
Myalgia	10 (66.7)	7 (58.3)	0.964
Polymyalgia rheumatica	9 (60.0)	5 (41.7)	0.576
Laboratory findings			
ESR (mm/hr)	98.0 [74.0~116.0]	99.5 [77.0~110.0]	0.961
CRP (mg/dL)	7.7 [5.9~18.0]	9.5 [6.1~13.6]	0.905
TA biopsy performed	10 (66.7)	6 (50.0)	0.630
TA biopsy positive	10 (100.0)	6 (83.3)	0.790
Meeting ≥3 1990 ACR criteria	15 (100.0)	9 (75.0)	0.150
Age ≥50 year	15 (100.0)	11 (81.7)	0.909
New headache	14 (93.3)	8 (66.7)	0.203
Temporal artery abnormality	13 (86.7)	5 (41.7)	0.040
ESR ≥ 50 mm/hr	15 (100.0)	12 (100.0)	None
Abnormal TA biopsy	10 (66.7)	5 (41.7)	0.363
Treatment			
Initial GCs dose (mg)*	60.0 [50.0~60.0]	60.0 [45.0~60.0]	0.621
Steroid pulse therapy	5 (33.3)	3 (25.0)	0.962
Methotrexate	11 (73.3)	8 (66.7)	>0.999
Azathioprine	3 (20.0)	1 (8.3)	0.762
Cyclophosphamide	2 (13.3)	0 (0.0)	0.565
Tocilizumab	0 (0.0)	1 (8.3)	0.909
Anti-platelet drug	5 (33.3)	4 (33.3)	>0.999
Clinical course			
Time to ESR normalization (wk)	3.5 [3.0~7.0]	5.0 [3.5~7.5]	0.534
Time to CRP normalization (wk)	2.5 [1.0~4.0]	4.0 [3.5~7.5]	0.039
Time to main symptom resolution (wk)	1.5 [1.0~3.0]	2.0 [1.0~4.5]	0.421
Achievement of complete remission within 12 weeks	14 (93.3)	10 (83.3)	0.837
GC discontinuation	6 (42.9)	4 (33.3)	0.926

Values are present as median [interquartile ranges] or number (%). GCA: giant cell arteritis, LVI: large vessel involvement, ESR: erythrocyte sedimentation rate, CRP: C-reactive protein, TA: temporal artery, ACR: American College of Rheumatology, GCs: glucocorticoids. *Prednisolone-equivalent dose.

sion 4.1.3; R Foundation for Statistical Computing). Categorical variables are presented as frequencies and percentages, and continuous variables are reported as mean and standard deviation or median and interquartile ranges (IQR). The Mann-Whitney U test was used to compare continuous variables between the groups. Categorical variables were compared using the chi-square test or Fisher's exact test, as appropriate. The first relapse after GCA diagnosis was estimated using the Kaplan-Meier method, and log-rank tests were used to compare relapse-free survival between the groups. P<0.05 was considered statistically significant.

Table 3. Comparisons of clinical characteristics of patients with GCA according to the concurrent of polymyalgia rheumatica

	Without PMR (n=13)	With PMR (n=14)	p-value
Age at diagnosis (yr)	75.0 [71.0~77.0]	76.5 [70.0~80.0]	0.408
Female	4 (30.8)	13 (92.9)	0.003
Presenting signs & symptoms			
Fever	6 (46.2)	6 (42.9)	>0.999
Fatigue	4 (30.8)	6 (42.9)	0.802
Weight loss	2 (15.4)	5 (35.7)	0.444
Headache	11 (84.6)	12 (85.7)	>0.999
Jaw claudication	6 (46.2)	3 (21.4)	0.340
TA pulse	0 (0.0)	5 (35.7)	0.059
TA tenderness	7 (53.8)	10 (71.4)	0.585
Visual loss	7 (53.8)	2 (14.3)	0.077
AION	6 (46.2)	2 (14.3)	0.164
Cerebral ischemia	2 (15.4)	1 (7.1)	0.946
Polyarthralgia	0 (0.0)	10 (71.4)	0.001
Myalgia	4 (30.8)	13 (92.9)	0.003
Laboratory findings			
ESR (mm/hr)	99.0 [75.0~110.0]	96.0 [74.0~120.0]	0.922
CRP (mg/dL)	8.4 [7.1~13.3]	9.5 [5.1~19.8]	0.650
Albumin (g/dL)	3.5 [3.3~3.6]	3.3 [3.1~3.8]	0.715
Cr (mg/dL)	0.8 [0.8~0.9]	0.7 [0.6~0.8]	0.005
TA biopsy positivity	9 (69.2)	7 (50.0)	>0.999
Large vessel involvement	7 (53.8)	5 (35.7)	0.576
Meeting ≥3 1990 ACR criteria	11 (84.6)	13 (92.9)	0.946
Treatment			
Initial GC dose (mg)*	60.0 [60.0~60.0]	50.0 [30.0~60.0]	0.016
Steroid pulse therapy	6 (46.2)	2 (14.3)	0.164
Methotrexate	9 (69.2)	10 (71.4)	>0.999
Azathioprine	2 (15.4)	2 (14.3)	>0.999
Cyclophosphamide	1 (7.7)	1 (7.1)	>0.999
Tocilizumab	1 (7.7)	0 (0.0)	0.970
Anti-platelet drug	4 (30.8)	5 (35.7)	>0.999
Clinical course			
Time to ESR normalization (wk)	4.0 [2.0~6.0]	7.0 [3.0~12.0]	0.034
Time to CRP normalization (wk)	3.0 [1.0~4.0]	4.0 [3.0~7.0]	0.118
Time to main symptom resolution (wk)	2.5 [1.0~4.5]	1.0 [1.0~2.0]	0.317
Achievement of complete remission within 12 weeks	13 (100.0)	11 (78.6)	0.247
GC discontinuation	3 (23.1)	7 (53.8)	0.227

Values are present as median [interquartile ranges] or number (%). GCA: giant cell arteritis, PMR: polymyalgia rheumatic, TA: temporal artery, AION: anterior ischemic optic neuropathy, ESR: erythrocyte sedimentation rate, CRP: C-reactive protein, ACR: American College of Rheumatology, GCs: glucocorticoids. *Prednisolone-equivalent dose.

RESULTS

Baseline characteristics of the study population

The clinical characteristics of the patients with GCA are shown in Table 1. The median age of the study population was 75 years (IQR: 71 to 79 years), and 17 (63.0%) patients were females. The median duration of the main presenting clinical symptoms was 5.5 weeks (IQR: 1.0 to 8.0 weeks).

Twenty-three (85.2%) patients had headaches, including 17 (63.0%) patients with temporal artery tenderness and five (18.5%) patients with temporal artery pulsation. Twelve (44.4%) patients had fever at presentation. Vision loss was present in nine (33.3%) patients at onset, including three with bilateral vision loss. Of the nine patients with vision loss, eight had AAION and one had central retinal artery occlusion combined with branch retinal artery occlusion. Temporal artery biopsy was performed in 16 patients and revealed positive histological findings of GCA in 15 (93.8%) patients. Among the 11 patients who underwent temporal artery Doppler ultrasonography, five demonstrated GCA-specific ultrasonographic findings, such as the halo sign or compression sign. PMR was concurrent with GCA at diagnosis in 14 (51.9%) patients. Twelve (44.4%) patients had radiographic LVI, which was detected using CT angiography in nine out of 24 patients and FDG-PET in four out of 10 patients. All patients underwent either CT angiography or FDG-PET.

Clinical characteristics of patients with and without LVI at presentation

The clinical characteristics of GCA patients with and without LVI were compared and are presented in Table 2. All patients without LVI fulfilled the 1990 ACR criteria for GCA, while three of 12 (25.0%) patients with LVI did not. The frequency of limb claudication in the LVI group (41.7%, 5 of 12) tended to be higher than that in the non-LVI group (6.7%, 1 of 15, p=0.088). There were no significant differences in age, sex, other symptoms at presentation, laboratory findings, or occurrence of permanent vision loss between patients with and without LVI at presentation. As expected, temporal artery abnormalities based on the 1990 ACR criteria were less prevalent in patients with GCA and LVI than in those without LVI (41.7% vs. 86.7%, p=0.040). The time to CRP normalization was significantly longer in patients with LVI than in those without (median 4.0 vs. 2.5 weeks, respectively; p=0.039), although the treatment between the two groups was not different.

Clinical characteristics patients with and without PMR at presentation

Patients with GCA and PMR at presentation were more likely to be females (p=0.003) and have musculoskeletal symptoms, including polyarthralgia (p=0.001) and myalgia (p=0.003), than those without PMR (Table 3). Serum creatinine levels were significantly lower in GCA patients with PMR than in those without PMR (p=0.003), while other laboratory markers, such as ESR, CRP, and complete blood count, did not differ between the groups. The time to ESR normalization was significantly longer in patients with PMR than in those without (median; 7.0 vs. 4.0 weeks, respectively; p=0.034).

Clinical characteristics of patients with and without fever at presentation

The clinical features and frequencies of PMR and LVI were not significantly different between patients with GCA with fever and those without fever (Table 4). Patients with fever at the onset of GCA tended to have higher CRP levels (p=0.093) and significantly lower albumin levels (p=0.001) than those without fever.

Treatment outcomes and factors associated with relapse during follow-up

The median follow-up period was 33.8 months (IQR: 7.6 to 49.7 months). All patients with GCA were administered oral or intravenous GC immediately after suspicion or diagnosis of GCA. Twenty-two (81.5%) patients received GC-sparing agents along with GCs. Combined immunosuppressants included methotrexate, azathioprine, cyclophosphamide, or tocilizumab. Aspirin was administered to nine (33.3%) patients. Following the medical treatment of GCA, all patients achieved complete remission with a median duration of 5 weeks (range, 1 to 36 weeks), and 24 patients (88.9%) achieved remission within 12 weeks. Five of the nine patients with vision loss at presentation had permanent vision loss. Four (14.8%) patients experienced relapse during the follow-up period, although no patient experienced two or more recurrences. There were no significant differences in medication use between patients with and without relapse (Supplementary Table 1). Vision loss (p=0.008) and the absence of fever (p=0.044) at GCA onset were significantly associated with relapse (Figure 1A and 1B). However, there were no differences in relapse-free survival according to the presence of LVI or PMR (Figure 1C and 1D).

Table 4. Comparisons of clinical characteristics of GCA patients with fever at presentation and those without

	Without fever (n=15)	With fever (n=12)	p-value
Age at diagnosis (yr)	77.0 [72.5~79.0]	73.5 [70.5~78.0]	0.327
Female	10 (66.7)	7 (58.3)	0.964
Presenting signs & symptoms			
Fatigue	3 (20.0)	7 (58.3)	0.099
Weight loss	3 (20.0)	4 (33.3)	0.731
Headache	12 (80.0)	11 (91.7)	0.762
Jaw claudication	4 (26.7)	5 (41.7)	0.681
Limb claudication	4 (26.7)	2 (16.7)	0.877
TA pulse	3 (20.0)	2 (16.7)	>0.999
TA tenderness	8 (53.3)	9 (75.0)	0.447
Visual loss	7 (46.7)	2 (16.7)	0.218
AION	6 (40.0)	2 (16.7)	0.371
Cerebral ischemia	1 (6.7)	2 (16.7)	0.837
Polyarthralgia	7 (46.7)	3 (25.0)	0.449
Myalgia	9 (60.0)	8 (66.7)	>0.999
Laboratory findings			
ESR (mm/hr)	80.0 [73.0~115.0]	102.0 [94.0~111.0]	0.418
CRP (mg/dL)	8.4 [5.1~11.8]	15.4 [7.2~23.8]	0.093
Albumin (g/dL)	3.7 [3.4~4.0]	3.0 [2.8~3.4]	0.001
Cr (mg/dL)	0.8 [0.7~0.9]	0.7 [0.6~0.8]	0.364
TA biopsy positivity	7 (100.0)	8 (88.9)	>0.999
Large vessel involvement	9 (60.0)	3 (25.0)	0.153
Polymyalgia rheumatica	8 (53.3)	6 (50.0)	>0.999
Treatment			
Initial GCs dose (mg)*	60.0 [45.0~60.0]	60.0 [50.0~60.0]	0.848
Steroid pulse therapy	6 (40.0)	2 (16.7)	0.371
Methotrexate	12 (80.0)	7 (58.3)	0.423
Azathioprine	1 (6.7)	3 (25.0)	0.431
Cyclophosphamide	1 (6.7)	1 (8.3)	>0.999
Tocilizumab	1 (6.7)	0 (0.0)	>0.999
Anti-platelet drug	6 (40.0)	3 (25.0)	0.681
Clinical course			
Time to ESR normalization (wk)	4.0 [3.0~7.0]	5.5 [3.0~7.5]	0.517
Time to CRP normalization (wk)	3.5 [1.0~7.0]	3.5 [2.0~4.5]	0.896
Time to main symptom resolution (wk)	2.0 [1.0~4.0]	2.0 [1.0~3.5]	0.818
Achievement of complete remission within 12 weeks	13 (86.7)	11 (91.7)	>0.999
GCs discontinuation	6 (42.9)	4 (33.3)	0.926

Values are present as median [interquartile ranges] or number (%). GCA: giant cell arteritis, TA: temporal artery, AION: anterior ischemic optic neuropathy, ESR: erythrocyte sedimentation rate, CRP: C-reactive protein, GCs: glucocorticoids. *Prednisolone-equivalent dose.

DISCUSSION

The results of this study indicate that patients with GCA with LVI or PMR at presentation had a longer time to normalization of acute-phase reactants. During a median follow-up period of 34 months, approximately 15% of the patients in this study experienced relapse, which was more frequent in patients with vision loss and without fever at onset.

In our study, 93.8% of the patients who underwent temporal artery biopsy showed positive histological findings consistent with GCA. Although temporal artery biopsy is the diagnostic gold standard for GCA, its sensitivity has been reported to be

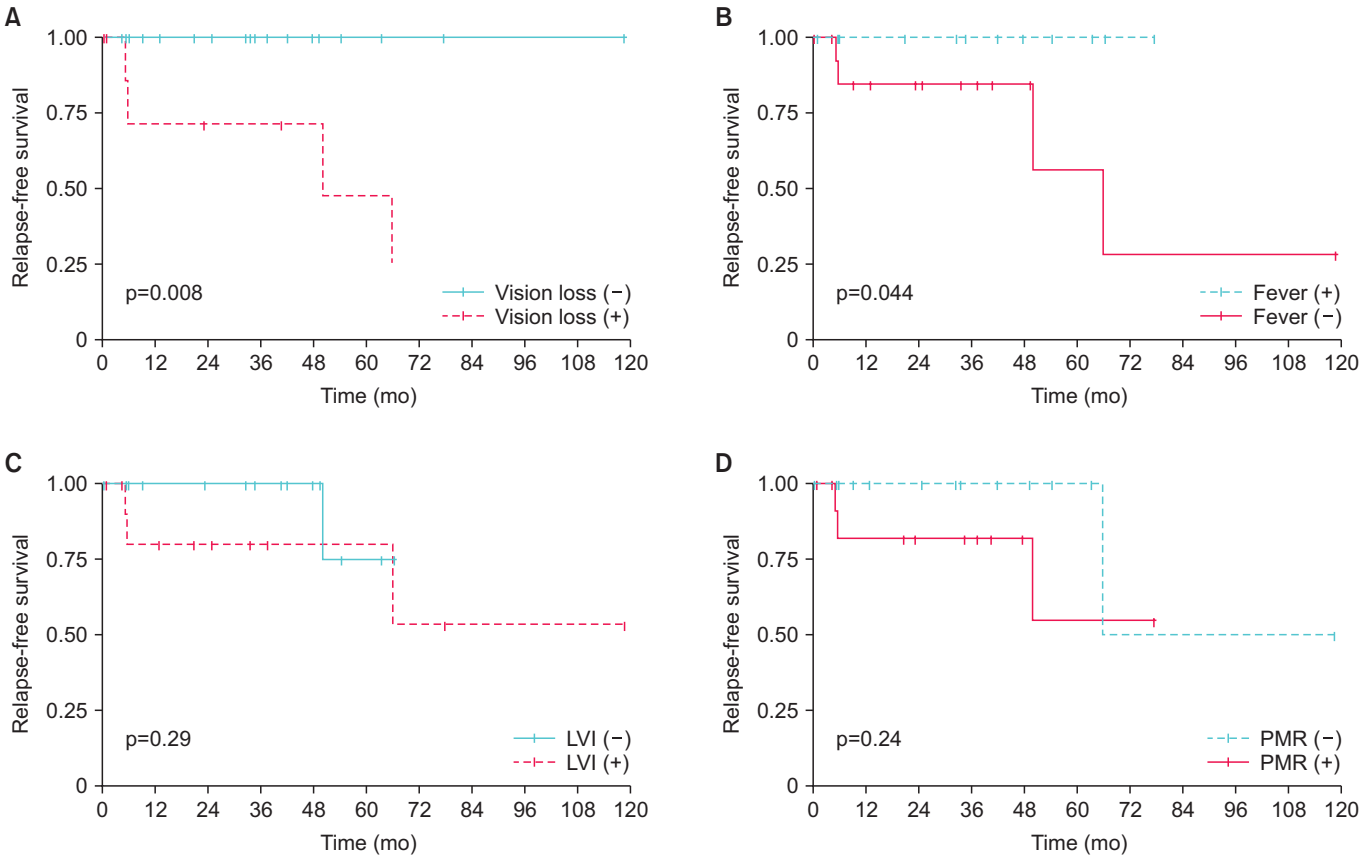

Figure 1. Kaplan-Meier curves for relapse-free survival of patients with giant cell arteritis. Relapse-free survival is estimated using the Kaplan-Meier method and is delineated according to the presence or absence of (A) vision loss at onset, (B) fever at onset, (C) LVI, and (D) PMR. LVI: large vessel involvement, PMR: polymyalgia rheumatic.

low [20]. In our GCA cohort, the small number of patients and selection bias for temporal artery biopsy might have led to the relatively high sensitivity of temporal artery biopsy.

LVI occurs in 40% to 80% of patients with GCA and can be associated with severe complications, such as aortic aneurysm, aortic dissection, and vascular stenosis [21,22]. Clinical phenotypes can differ between GCA patients with and without LVI; those with LVI tend to be younger, have fewer cranial symptoms, and face delayed diagnosis [9,23]. In our study, patients with LVI showed less temporal artery involvement, with no significant differences in age or clinical features, compared to those without LVI. Previous studies on the prognostic impact of LVI have been inconsistent; some reported poorer survival with LVI [21], while others found worse outcomes in GCA without LVI [8]. In the present study, the relapse rate appeared unaffected by LVI status, suggesting potential ethnic variations in LVI-GCA prognosis, with possibly better outcomes in East Asian populations.

The prevalence of concurrent PMR at the diagnosis of GCA ranges from 16% to 65% [24], with our study reporting a prevalence of 52%, similar to previous data. GCA with PMR is reported to present predominantly in younger individuals and females, but there was no age difference at diagnosis between those with and without PMR in our patients with GCA [2]. While some studies have linked PMR to underlying LVI in GCA [9,25], our findings did not show increased LVI in patients with concurrent PMR.

Acute-phase reactants, such as ESR or CRP, are key markers for monitoring GCA disease activity [26] and are integral to remission criteria in recent clinical trials [27,28]. In our study, all patients attained complete remission at various time points. Those with concurrent PMR and GCA experienced delayed ESR normalization, while GCA patients with LVI had a longer time to CRP normalization. However, there were no baseline differences in ESR or CRP levels, time to symptom resolution, or initial treatment between the groups. Therefore, physicians

should consider these characteristics when treating and monitoring Korean patients with GCA.

Fever is a common but challenging symptom in GCA diagnosis, with 44% of our patients presenting with fever at onset, aligning with previous studies [29,30]. In a study by Zhang et al. [10], patients with GCA and fever had more severe inflammation based on lower albumin levels and a lower risk of cerebrovascular ischemic accidents than those without fever. Consistent with this study, patients with fever at onset had lower albumin levels than afebrile patients. However, the incidence of cerebrovascular ischemic accidents was not significantly different between patients with and without fever.

The reported incidence of relapse or recurrence of GCA varies widely, ranging from 34% to 79% [12,31,32]. In our study, the relapse rate was 14.8% over a median follow-up period of 34 months, which was lower than the rates in Western studies. The high usage of GC-sparing agents (81.5%) in our cohort may have contributed to this reduced relapse rate. Previous studies have reported various factors for predicting relapse in GCA patients, including female sex, lower starting prednisolone doses, higher body mass index, scalp tenderness at diagnosis, and LVI [11,27,33]. However, our findings did not show a significant link between these factors and relapse. Instead, relapse was more commonly observed in patients who were afebrile at onset and those who experienced vision loss at presentation. The reasons for these associations remain unclear; however, a worse prognosis has been reported in GCA patients experiencing vision loss, typically resulting from anterior ischemic option neuropathy or retinal artery occlusion [34]. Additionally, the presence of any damage has been linked with relapse in a long-term, retrospective GCA cohort study [35]. The absence of systemic manifestations, including fever, has been frequently associated with vision loss in GCA [36]. Another study also demonstrated an association between lower circulating levels of IL-6, a cytokine responsible for inducing fever, and GCA with ischemic complications, potentially due to IL-6 driven neoangiogenesis [37]. These findings suggest that patients without fever at onset and those with initial vision loss in our study might share similar pathophysiological traits. The increased risk of relapse in these groups could be related to a diminished protective effect of IL-6 in compensating for vascular ischemia or occlusive events. This hypothesis warrants further investigation.

This study had some limitations. First, the patient population was small, which may have limited the statistical power. Multivariate analyses on relapse could not be conducted. However, as GCA has an extremely low prevalence in East Asian countries, the sample size is considerable and is the largest in Korea to date. Second, due to the retrospective nature of the study, the data retrieved from the medical records may be incomplete. Third, as patient information was collected over a period of 16 years and the patients were not continuously treated by a single physician, the treatment strategies may have differed depending on the time period and physicians. However, this reflects actual clinical practice, and all patients were evaluated and managed at tertiary referral centers. Lastly, because not all patients underwent both CT angiography and FDG-PET, the LVI may have been underestimated. Despite these limitations, this is the largest multicenter study of GCA in the Korean population. Additionally, this is the first study to compare GCA phenotypes according to several accompanying conditions, the prevalence of relapse, and factors associated with relapse in Korean patients with GCA. In addition, the observed differences in the clinical aspects of GCA between East Asian and Western populations provide data regarding regional variations in GCA, guiding the clinical management of patients with GCA in Korea and other East Asian populations. Further multinational studies are required to validate these findings.

CONCLUSION

In conclusion, concurrent PMR and LVI were present in approximately half of Koreans with GCA in this study, and the time to normalization of inflammatory markers was longer in these patients. Moreover, patients with vision loss or no fever at the time of GCA onset showed a higher risk of relapse, suggesting that physicians should carefully monitor the progress and consider aggressive treatment in these patients. This study provides valuable insights into the clinical characteristics and outcomes of Korean patients with GCA.

SUPPLEMENTARY DATA

Supplementary data can be found with this article online at https://doi.org/10.4078/jrd.2024.0007.

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CONFLICT OF INTEREST

No potential conflict of interest relevant to this article was reported.

AUTHOR CONTRIBUTIONS

Concept and design: Y.J.H. Administrative, technical, or material support: J.J.Y. Acquisition, analysis, or interpretation of data: J.I.L., J.W.P., Y.J., K.S., E.H.K., and Y.J.H. Statistical analysis: J.I.L. and S.R.C. Drafting of the manuscript: J.I.L. and Y.J.H. Supervision: Y.J.L. All authors were involved in drafting and revising the manuscript critically for important intellectual content and final approval of the version to be published.

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