Patterns of large-vessel lesions are associated with treatment outcomes in large-vessel giant cell arteritis

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Abstract

Objective

To evaluate whether the distribution of large-vessel lesions (LVLs) in giant cell arteritis (GCA) is associated with poor treatment outcomes.

Methods

In a retrospective, multi-centric, nationwide registry of GCA patients treated with glucocorticoids between 2007 and 2014, 68 newly-diagnosed patients with LVLs were identified by imaging. Non-achievement of clinical remission by week 24 and/or relapse within 104 weeks were primarily evaluated. Factors influencing the poor treatment outcome were analyzed using Cox proportional hazard modeling. Cumulative rates and median time to the first event were analyzed by the Kaplan-Meier method and log-rank testing.

Results

Aortic lesions were detected in 72.1% of the 68 GCA patients with LVLs (defined as group 2). Patients without aortic lesions were classified as having large-vessel GCA with subclavian lesions (group 1) or atypical large-vessel GCA without subclavian lesions (group 3). The mean age and proportions of PMR in group 3 were higher than those in the other two groups. Cranial lesions were observed in 66.7%, 55.1%, and 80.0% of patients in groups 1, 2 and 3, respectively. In group 2, 73.5% had lesions in both the aorta and aortic branches. Group 1 had axillary lesions in 33.3%, and carotid lesions in 44.4%. Atypical LVLs in group 3 included pulmonary, hepatic or mesenteric lesions in addition to carotid lesions. Baseline doses of GCs were not different across the groups. Mean time to achievement of low-dose GC treatment (prednisolone ≤ 5 mg/day) was also not significantly different between the groups. The cumulative rate of poor treatment outcome over the two years was 11.1%, 55.3% and 88.0% in the groups 1, 2 and 3, respectively; mean time to the events was significantly different among the groups. Multivariable analysis showed that the risk of poor treatment outcome was significantly higher in the group 3.

Conclusions

The distribution of LVLs was associated with treatment outcomes in large-vessel GCA. In addition to subclavian arteries, lesions in aorta and aortic branches other than subclavian arteries should be evaluated by imaging for large-vessel GCA. The pattern of LVLs determined by imaging should be considered when determining treatment strategies for GCA.

Background

Giant cell arteritis (GCA) is characterized by cranial symptoms, polymyalgia rheumatica (PMR), and large-vessel lesions (LVLs) in the aorta or its branches. The subclavian artery is a key location for LVLs in GCA (1). Aortic dilatation or aneurysm is also an important clinical feature of GCA (2, 3) that is related to
mortality (4, 5). Aortic dissection or rupture of aneurysm was reported in previous studies (6–8), and aortic inflammation detected by imaging was associated with aortic dilatation (9). Based on previous reports on imaging of LVLs in patients with Takayasu arteritis (TAK) and GCA from the Diagnostic and Classification Criteria for Vasculitis cohort, it was shown that GCA patients were more likely to present with widespread lesions from the subclavian artery to the thoracic and abdominal aorta than TAK patients. In contrast, carotid lesions and/or lesions in renal, celiac or mesenteric arteries are infrequent in GCA patients (10).

Increasing dose of glucocorticoid (GC) for GCA led to GC-related complications (11, 12), which were associated with increased mortality rate of GCA (13), and risk factors for prolonged treatment course of glucocorticoids (GCs) are important in determining the indication of combination therapy of tocilizumab and GCs (14–16). We reported that clinical characteristics of Japanese patients newly diagnosed with GCA are similar to those of Western countries (17). In addition, imaging revealed that LVLs were present in approximately half of all GCA patients, and that they were significantly associated with an increased probability of poor treatment outcome (17). We collectively hypothesize that the distribution of LVLs determines the response to treatment in patients with GCA. To test this hypothesis, we investigated whether the distribution of LVLs was associated with poor treatment outcome in patients with GCA using two-year follow-up data from our multi-center retrospective cohort study.

**Methods**

**Database**

The members of the Japan Research Committee of the Ministry of Health, Labour, and Welfare for Intractable Vasculitis (JPAVS) participated in this retrospective multi-center study, which was approved by the institutional review board of Tokyo Medical and Dental University (approval number: M2000-2084-01). The details were described in a previous study (17). The 68 newly-diagnosed GCA patients with LVLs were diagnosed between 2007 and 2014 in each facility based on imaging of LVLs with and without temporal arterial biopsy (TAB). Data for two-year follow-up post-initiation of GC treatment were collected, using pre-defined case-report forms at 4, 8, 24, 52, 76 and 104 weeks after starting treatment.

**Outcomes**

The primary endpoint was an event related to a poor treatment outcome (classified as failure to achieve clinical remission by week 24 or relapse within 104 weeks). Clinical remission was defined as absence of active disease as described in a previous report (17). Active disease at baseline was defined as having clinical signs and symptoms in cranial and large-vessel areas, or suffering from PMR, and/or elevation of CRP levels. We distinguished persistent ischemic signs and symptoms (i.e., visual manifestations or claudication) from GCA damage at week 24 after starting treatment as follows: if the signs and symptoms of active disease at baseline persisted without worsening for six months or longer and the CRP level was normalized, these were considered to reflect the damage at week 24 after starting treatment. A patient was determined to have a relapse as described previously (17); if they had either one
of the signs or symptoms newly appearing or worsening after achievement of clinical remission, or if they showed deterioration in the LVLs by imaging. Re-elevation of the CRP level above the limit of the normal range (<0.3 mg/dl) but without any clinical manifestations was considered as a relapse only if other causes of increased CRP such as infection were excluded and at that time treatment was intensified. Three investigators (HAU, HY, YN) independently confirmed clinical findings at a time of relapse as described in the previous study (17).

**Imaging of LVLs at baseline**

The site investigators reported wall thickening, stenosis, aneurysm, or dissection in anatomical sites of lesions of aortic branches and aortic lesions based on the results of at least one of the following techniques: computed tomography (CT), CT angiography (CTA), magnetic resonance imaging (MRI), or magnetic resonance angiography (MRA). Fluorodeoxyglucose (FDG) uptake in the arterial wall on positron emission tomography (PET)-CT were also reported. Based on the imaging findings, the GCA with LVLs were categorized into two phenotypes: GCA with aortic lesions (group 2) or without aortic lesions. The latter were subdivided into large-vessel GCA (LV-GCA) with subclavian lesions (group 1: LV-GCA without aortic lesions) and that with lesions of aortic branches without subclavian lesions (group 3: atypical LV-GCA without aortic lesions).

**Statistics**

Student’s t test and the Mann-Whitney test were used to compare continuous variables depending on their distribution, and the chi-squared test and Fisher’s exact test were used for categorical variables. One-way analysis of variance was used to compare three groups. Cumulative rates and median time to the first event of the poor treatment outcome or the achievement of low-dose GC (prednisolone ≤5 mg/day) treatment within 104 weeks were analyzed using the Kaplan-Meier method and the log-rank testing. Patients who did not achieve clinical remission by week 24 were deemed to have had an event of the poor treatment outcome at week 0 as described in the previous study (17, 18). Univariable and multivariable analysis for associated factors with the event of poor treatment outcomes during 104 weeks were conducted by using the Cox proportional hazard modeling. All analyses were performed using SPSS version 26 (IBM, Armonk, NY, USA). All reported p-values are two-tailed and the level of significance is $p<0.05$.

**Results**

**Patients’ characteristics**

Case report forms of 68 newly-diagnosed GCA patients with LVLs were assessed. All patients were of Asian ethnicity. The mean (standard deviation [S.D.]) age was 70.5 (7.0) years, and 70.6% were women. Twenty-seven (39.7%) of the 68 patients were diagnosed by both positive TAB and positive imaging of LVLs, and 41 (60.3%) by positive imaging of LVLs only. Twenty-nine (42.6%) did not meet the ACR GCA classification criteria. Cranial lesions and PMR were observed in 41 (60.3%) and 23 (33.8%) of the 68
patients with LVLs, respectively. Wall thickening or FDG uptake in the arterial wall were common (70.6%), but the proportion of aortic aneurysms was low (8.8%) at baseline. Subclavian lesions were also frequently observed (57.4%), and 25% had stenosis of the aortic branches (Table 1). The initial mean dose (S.D.) of prednisolone was 0.74 (0.26) mg/kg/day, and 20.6% received MTX for remission induction therapy, 4.4% cyclophosphamide, and 13.2% azathioprine.
Table 1
Clinical characteristics and imaging findings of three groups of LV-GCA phenotype.

|                     | Enrolled patients (n=68) | Group 1 (n=9) | Group 2 (n=49) | Group 3 (n=10) | P-value |
|---------------------|--------------------------|---------------|----------------|----------------|---------|
| Age, years, mean (S.D.) | 70.5 (7.0)               | 70.6 (7.3)    | 69.9 (6.7)     | 73.6 (8.0)     | 0.842   |
| Female patients, %   | 70.6                     | 77.8          | 69.4           | 70.0           | 0.878   |
| Cranial lesions at baseline, % | 60.3                  | 66.7          | 55.1           | 80.0           | 0.312   |
| PMR, %               | 33.8                     | 33.3          | 30.6           | 50.0           | 0.498   |
| CRP at baseline, mg/dl, mean (S.D.) | 7.3 (5.1)                | 3.5 (3.5)     | 8.0 (5.3)      | 7.6 (4.1)      | 0.248   |
| Left carotid, %      | 39.7                     | 44.4          | 38.8           | 40.0           | 0.950   |
| Right carotid, %     | 32.4                     | 33.3          | 36.7           | 10.0           | 0.257   |
| Vertebral, %         | 7.4                      | 22.2          | 4.1            | 10.0           | 0.150   |
| Brachiocephalic, %   | 30.9                     | 33.3          | 36.7           | 0              | -       |
| Any subclavian lesions, % | 57.4                  | 100           | 61.2           | 0              | -       |
| Left subclavian, %   | 52.9                     | 88.9          | 57.1           | 0              | -       |
| Right subclavian, %  | 44.1                     | 55.6          | 51.0           | 0              | -       |
| Left axillary, %     | 20.6                     | 33.3          | 20.4           | 10.0           | 0.454   |
| Right axillary, %    | 16.2                     | 33.3          | 16.3           | 0              | 0.143   |
| Pulmonary, %         | 1.5                      | 0             | 0              | 10.0           | -       |
| Ascending aorta, %   | 30.9                     | 0             | 42.9           | 0              | -       |
| Aortic arch, %       | 50.0                     | 0             | 69.4           | 0              | -       |
| Descending thoracic aorta, % | 50.0                | 0             | 69.4           | 0              | -       |
| Abdominal aorta, %   | 54.4                     | 0             | 73.5           | 0              | -       |

One-way analysis of variance was used to compare three groups.

Group 1: subclavian artery lesions without aortic lesions (typical LV-GCA without aortic lesions);
Group 2: aortic lesions with or without subclavian artery lesions; Group 3: Lesions of aortic branches without aortic lesions and subclavian artery lesions (atypical LV-GCA without aortic lesions)

AZA: azathioprine; CRP: C-reactive protein; CY: cyclophosphamide; LV: large-vessel; LVLs: large-vessel lesions; PMR: polymyalgia rheumatica; S.D.: standard deviation.
| Clinical characteristics and imaging findings of patients stratified by the three groups of LVLs. | Enrolled patients (n=68) | Group 1 (n=9) | Group 2 (n=49) | Group 3 (n=10) | P-value |
|---|---|---|---|---|---|
| Renal, % | 5.9 | 11.1 | 6.1 | 0 | 0.584 |
| Hepatic, % | 1.5 | 0 | 0 | 10.0 | - |
| Mesenteric, % | 1.5 | 0 | 0 | 10.0 | - |
| Iliac or femoral artery, % | 11.8 | 22.2 | 10.2 | 10.0 | 0.579 |
| Stenosis of aortic branches, % | 25.0 | 55.6 | 18.4 | 30.0 | 0.056 |
| Aneurysm of aorta, % | 8.8 | 0 | 12.2 | 0 | - |
| Initial dose of prednisolone, mg/kg/day, mean (S.D.) | 0.74 (0.26) | 0.59 (0.23) | 0.77 (0.24) | 0.75 (0.31) | 0.743 |
| MTX for induction therapy, (%) | 20.6 | 0 | 24.5 | 20.0 | 0.248 |
| MTX for relapse, % | 19.1 | 0 | 24.5 | 10.0 | 0.167 |
| CY for induction therapy, % | 4.4 | 11.1 | 2.0 | 10.0 | 0.309 |
| CY for relapse, % | 2.9 | 0.0 | 2.0 | 0.0 | 0.821 |
| AZA for induction therapy, % | 13.2 | 11.1 | 16.3 | 0.0 | 0.374 |
| AZA for relapse, % | 5.7 | 0.0 | 4.1 | 0.0 | 0.671 |

One-way analysis of variance was used to compare three groups.

Group 1: subclavian artery lesions without aortic lesions (typical LV-GCA without aortic lesions);
Group 2: aortic lesions with or without subclavian artery lesions; Group 3: Lesions of aortic branches without aortic lesions and subclavian artery lesions (atypical LV-GCA without aortic lesions)

AZA: azathioprine; CRP: C-reactive protein; CY: cyclophosphamide; LV: large-vessel; LVLs: large-vessel lesions; PMR: polymyalgia rheumatica; S.D.: standard deviation.

Based on the imaging findings, patients with LVLs were stratified into three groups as described in the Methods. Group 1 (LV-GCA without aortic lesions) consisted of 9 patients (13.2%), group 2 (GCA with aortic lesions) of 49 (72.1%), and group 3 (atypical LV-GCA without aortic lesions) of 10 (14.7%). The mean age and proportion of PMR in group 3 was higher than in the other two groups (Table 1). Cranial lesions were observed in 66.7%, 55.1%, and 80.0% of patients in groups 1, 2 and 3, respectively. In group 2, 36 of the 49 patients had lesions in both the aorta and aortic branches, with left subclavian lesions reported in 28 (57.1%), and right subclavian lesions in 25 (51.0%). Thirteen (26.5%) of the 49 had isolated aortic lesions. There were axillary lesions in 33.3% of group 1, and carotid lesions in 44.4%. Stenosis of aortic branches was more frequently observed in group 1 (55.6 %), compared to group 2 (18.4%) and
group 3 (30.0%). Atypical large-vessel lesions in group 3 included pulmonary, hepatic or mesenteric lesions in addition to carotid or vertebral lesions. Baseline doses of GCs were not different across the groups. Mean time to achievement of low-dose GC treatment (prednisolone ≤ 5 mg/day) was also not significantly different between the groups as follows: group 1: 459 days (95% confidence interval [CI] 314-604); group 2: 531 days (95% CI 471-591); and group 3: 497 days (95% CI 361-634) (Figure 1A). Methotrexate (MTX) was administered for initial treatment in 0% in group 1, 24.5% in group 2, 20% in group 3, and for relapse in 0% in group 1, 24.5% in group 2, and 10.0% in group 3 (Table 1). No patients received biologic agents.

**Treatment Outcomes Of Gca With LvlS**

Overall, 35 (51.5%) of the 68 GCA patients with LVLs had an event of the poor treatment outcome. Eleven patients failed to achieve clinical remission by week 24. Relapse after achieving clinical remission was reported in 24 patients, 9 between week 0 and 24, 12 between week 24 and 52, and 3 between week 52 and 104 (Figure 2). Imaging progression of LVLs were reported in 9 of the 49 in the group 2 and in 2 of the 10 in the group 3. Progression of thoracic aortic lesions, abdominal aortic lesions, and subclavian lesions were reported in 3, 3, 3 of the group 2 and 1, 0, 0 of the group 3, respectively, at the time of event of poor treatment response. One of the group 2 had cranial signs and symptoms, and one of the group 2 and one of the group 3 had PMR at the event. The elevation of CRP without clinical signs and symptoms was most frequently reported as clinical signs and symptoms at the time of event of poor treatment response (Table 2).

Table 2 Clinical signs and symptoms of patients at the time of event of poor treatment outcome
|                        | Group 1 n=1 | Group 2 n=26 | Group 3 n=8 |
|------------------------|-------------|--------------|-------------|
| **Thoracic aortic lesions** | None        | • Rupture of ascending aorta (n=1) | • Dissection of descending thoracic aorta (n=1) |
|                        |             | • Progression of stenosis of left subclavian and ascending aorta (n=1*) | |
|                        |             | • Newly detected wall thickening of ascending aorta (n=1) | |
| **Abdominal aortic lesions** | None        | • Progression of abdominal aneurysm (n=1) | None |
|                        |             | • Expansion of abdominal aorta (n=1) | |
|                        |             | • Newly detected wall thickening of abdominal aorta (n=1) | |
| **Subclavian lesions** | None        | • Progression of stenosis of left subclavian and ascending aorta (n=1*) | None |
|                        |             | • Newly detected wall thickening of subclavian artery (n=1) | |
|                        |             | • Expansion of right subclavian artery (n=1) | |
| **Other large-vessel lesions** | None        | • Stenosis of vertebral artery (n=1) | • Stenosis of iliac artery (n=1) |
| **Cranial signs and symptoms** | None        | • Headache (n=1) | None |
| **Others**             | Persistent CRP elevation (n=1) | • PMR (n=1) | • PMR (n=1) |
|                        |             | • Systematic symptoms (n=1) | • Systematic symptoms (n=1) |
|                        |             | • Persistent CRP elevation (n=14) | • Persistent CRP elevation (n=4) |

*clinical signs and symptoms of a same patient

CRP: C-reactive protein; PMR: polymyalgia rheumatica.

**Cumulative rate of poor treatment outcomes in patients stratified by the three groups of LVLs**
The cumulative rate of events of poor treatment outcome over the two-year follow-up was 11.1% for patients in group 1, 55.3% in group 2, and 88.0% in group 3. Mean time to an event of the poor treatment outcome was significantly different within each pair of the groups (Figure 1B). Univariable and multivariable Cox proportional hazards modeling showed that patients in group 1 were likely to have a reduced risk (hazard ratio [HR] 0.14, 95% CI 0.02-1.03, p=0.054), while group 3 patients had a significantly increased risk of poor treatment outcome (HR 2.22, 95% CI 1.06-4.68, p=0.054) (Table 3).

### Table 3

| Phenotype of LVLs | Univariable Analysis | Multivariable Analysis |
|------------------|----------------------|------------------------|
|                  | Hazard ratio (95% CI) | P-value                | Hazard ratio (95% CI) | P-value |
| Group 1          | 0.61 (0.30-1.23)      | 0.167                  | 0.14 (0.02-1.03)      | 0.054   |
| Group 2          | 0.97 (0.57-1.64)      | 0.899                  | 1.03 (0.60-1.77)      | 0.923   |
| Group 3          | 2.27 (1.14-4.51)      | 0.020                  | 2.22 (1.06-4.68)      | 0.035   |

Univariable and multivariable analyses of factors associated with an event of poor treatment outcome within 104 weeks were conducted using the Cox proportional hazard model. Age, any cranial symptoms, and polymyalgia rheumatica were selected as covariates of interest.

CI: confidence interval; LVLs: large-vessel lesions.

### Discussion

In the current study, approximately 70% of GCA patients with LVLs confirmed by imaging exhibited aortic lesions. One half of these patients with aortic lesions (group 2) failed to achieve clinical remission by 24 weeks or relapsed after achieving clinical remission within the two-year follow-up. Patients with subclavian arteritis without aortic lesions (group 1) had the better treatment response than the group 2, and atypical large vessel-GCA without both aortic and subclavian artery involvement (group 3) had the worst prognostic phenotype of LV-GCA. Interestingly, the mean age of onset in the atypical LV-GCA (group 3) was older compared to the typical LV-GCA with subclavian lesions (group 1) or aortic lesions (group 2), and cranial lesions and PMR were common findings in the atypical LV-GCA (group 3).

Prolonged aortic inflammation might contribute to slowly progressive vascular damage in GCA patients who have prior LVLs (9, 19, 20), and serious complications in the aortas of patients with GCA could result in increased mortality (4, 6, 7, 20, 21). LVLs were predictive factors of new cardiovascular events of GCA (22). Our JPVAS cohort showed that LVLs were associated with an increased probability of poor treatment outcome of GCA, especially when present in the aorta rather than its branches (17). Notably, the present study revealed that GCA patients with aortic lesions, mainly due to aortic wall inflammation, were more resistant to initial therapy than patients with subclavian arteritis without aortic lesions. Our results
indicate that the aortic wall inflammation served as a factor predicting poor response to initial treatment. Subclavian/axillary artery was easier to assess by ultrasonography than aortic lesions, but the aortic wall inflammation by MRI or PET-CT should be also assessed to determine disease activity of GCA (23, 24).

Patients with subclavian artery involvement with or without aortic lesions had a higher relapse rate than in patients with cranial GCA without LVLs (25). Our JPVAS cohort found a better treatment response in cranial GCA without LVLs (17) and subclavian arteritis without aortic lesions (group1). However, arm claudication due to subclavian artery stenosis at baseline was most frequently counted as damage at week 24 in the present study (Figure 2). Recent imaging studies also showed arm claudication was associated with subclavian artery damage, but not inflammation (26). This is in line with the results of the evaluation of damage in previous prospective studies (27).

Recent meta-analysis showed the overall prevalence of GCA relapse was about 50 % with a high heterogeneity, and shorter GC regimens in randomized controlled trials was associated with the higher relapse rate (28). In our observational studies, patients with aortic lesions (group 2) had similar relapse rate with the meta-analysis, and group 1 and group 3 had clearly different relapse rate, even though mean time to achievement of low-dose GC treatment was similar among 3 groups.

Previous study has shown that new lesions by imaging may appear even in the absence of typical signs and symptoms, underscoring the necessity of comprehensive vascular imaging (29). Vessel wall signals by MRI (30) or vascular inflammation by PET-CT (31) persisted even after the disappearance of clinical signs and symptoms. Our study also indicated the elevation of CRP without clinical signs and symptoms was a common finding in GCA patients with LVLs, emphasizing the importance of imaging in evaluating vascular inflammation (32–34), although CRP was not useful to evaluate cranial signs and symptoms and PMR at the time of relapse of GCA (35, 36).

Gribbons et al. sought to identify subsets of GCA, and showed that GCA with LVLs was divisible into two groups based on the involvement of temporal artery (37). TCZ improved clinical outcomes not only in GCA patients with cranial lesions but also in patients who presented with LVLs and PMR without cranial lesions (38). The present study showed proportion of cranial lesions were similar between LV-GCA patients with and without poor treatment outcome.

Group 3 in the present study was considered atypical LV-GCA because the patients did not have both aortic and subclavian artery lesions. Interestingly, the pattern of LVLs in group 3 had imaging features similar to TAK (10), while the mean age of onset was older compared to the other two groups, and high proportions of cranial lesions and PMR were present. A recent prospective study also documented progression of arterial stenosis or dilation in the relatively infrequent vascular lesions of GCA (29). Thus, the older age of onset and higher proportion of cranial lesions in group 3 were likely to be those of cranial GCA (1, 25), but these had atypical LVLs.
There are some limitations to this study associated with its retrospective design, as described in the previous report (17). First, there was no uniform treatment protocol and imaging examination for assessment of LVLs in the 3 groups. Second, there was a potential indication bias in selecting treatment because the attending physician might intensify treatment for patients with atypical lesions, such as pulmonary vasculitis. However, we did not find a significant difference among groups regarding the dose of GCs and the choice of immunosuppressive drugs. Third, although there might be some imprecision due to the relatively small sample size, significant differences among the three groups were obvious.

**Conclusions**

The distribution of LVLs was associated with treatment outcomes in large-vessel GCA. In addition to the conventionally screened subclavian artery, involvement of aorta and other large arteries should be evaluated in patients with GCA. The pattern of LVLs determined by imaging should be considered when determining treatment strategies for GCA.

**Abbreviations**

ACR  
American College of Rheumatology  
AEs  
adverse events  
AZA  
azathioprine  
CI  
confidence interval  
CRP  
C-reactive protein  
CY  
cyclophosphamide  
FDG  
18fluorodeoxyglucose  
GCA  
giant cell arteritis (GCA)  
GCs  
Glucocorticoids  
JPVAS  
Japan Research Committee of the Ministry of Health Labour and Welfare for Intractable Vasculitis  
LVLs
Large-vessel lesions
LV
large-vessel
MTX
methotrexate
PET
positron emission tomography
PMR
polymyalgia rheumatica
PSL
prednisolone
S.D.
standard deviation
TAB
temporal arterial biopsy.

Declarations

Ethics approval and consent to participate

This study was conducted in accordance with the Declaration of Helsinki and the Ethical Guidelines for Epidemiological Research in Japan. The institutional review board of Tokyo Medical and Dental University as main center (approval number: M2000-2084-01) and the additional institutions approved our retrospective study without personally identifiable information. Patients received posters informing the present study, or the posters were displayed in outpatient clinic of each facility.

Consent for publication

Not applicable

Availability of data and materials

All of the data supporting the conclusions of this article are included within the article.

Competing interests

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**Authors' contributions**
T sugihara, Y Nakaoka and M Harigai were responsible for conception and design, data collection and analysis, critical revision, and manuscript writing. HAU, HY, and YN were responsible for conception and design, data collection and analysis, and critical revision. TN, YK, TO, JI, YM, NO, HD, TH, YT, SF, TT, and YK were responsible for data collection and analysis, and critical revision. All authors read and approved the final manuscript.

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Figures
Figure 1

Differential treatment response among 3 groups Cumulative rate of achievement of low-dose GCs (PSL ≤5 mg/day) (A) and event of poor treatment response (B) were assessed by the Kaplan-Meier method and the log-rank test. Group 1: subclavian artery lesions without aortic lesions (LV-GCA without aortic lesions); Group 2: aortic lesions with or without subclavian artery lesions (GCA with aortic lesions); Group 3: atypical LV-GCA without aortic lesions.
3. Lesions of aortic branches without aortic lesions and subclavian artery lesions (atypical LV-GCA without aortic lesions). GCs: glucocorticoids; LV: large-vessel; PSL: prednisolone.

**Figure 2**

Screening, follow-up of the patients, and treatment outcomes. Clinical remission and relapse were evaluated in 68 newly-diagnosed patients with LVLs. Eleven had worsening of clinical signs and symptoms or persisted elevation of CRP and were not able to achieve clinical remission. Nine had relapse...
after achievement of clinical remission between week 0 and 24, and 48 had no relapse at week 24 after achievement of clinical remission. Twelve had relapse between week 24 and 52, and three between 52 and 104. Finally, 29 had no relapse throughout 104 weeks after achievement of clinical remission at week 24. Overall, 35 had poor treatment outcome. GCs: glucocorticoids; LV: large-vessel; LVLs: large-vessel lesions.