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INVITED REVIEW

The Clinical Symptoms and Signs in Giant Cell Arteritis with the Preliminary Results of Turkish Multi-Centered GCA Registry

Fatma Alibaz Öner[1]
ORCID: 0000-0002-6653-1758

Giant cell arteritis (GCA) which is a granulomatous large vessel vasculitis, is characterized by the presence of ischemic signs such as headache, visual manifestations, scalp tenderness, jaw claudication, and stroke together with systemic symptoms such as weight loss or anorexia, fatigue, and fever.

GCA is the most frequent primary systemic vasculitis among patients ≥50 years of age [1], peaking in the seventh and eighth decade of life [2]. In a recent systematic review, the pooled incidence of GCA was 10 [9.22, 10.78] cases per 100,000 people over 50 years old. The incidence was threefold higher in Scandinavia relative to the rest of Europe and was 6 times higher in Scandinavia compared to East Asia. Pooled prevalence was 51.74 [42.04, 61.43] cases per 100,000 people over age 50 [3]. Mortality in GCA was found to generally decrease over time and showed no geographic variation [3].

GCA frequently begins insidiously. The severity of the symptoms gradually increases over a period of weeks or months. In some cases, the onset can be abrupt with a major complication such as losing eyesight. The spectrum of initial disease manifestations is quite broad, and physicians need to be alert to not miss subtle manifestations of vascular insufficiency or clinical symptoms. Most patients present with headaches, scalp tenderness, and polymyalgia rheumatica (PMR); fever, weight loss, malaise, and anorexia are also frequent disease manifestations. Suppose the arteritis affects the cranial vessels, headaches, and clinical findings of the eye, brain, and cranial muscles' ischemia. If extracranial arteries are involved, patients often have an aortic arch syndrome characterized by impaired blood flow to the upper extremities. If the major disease component is a systemic inflammatory syndrome, vascular complications may be subtle. Nevertheless, systemic inflammation findings are less specific but very useful for screening suspected cases.

Glucocorticoids (GC) are the mainstay of medical treatment in GCA. EULAR suggests starting with 40–60 mg/day prednisone-equivalent for induction of remission and tapering the GC dose to a target dose of 15–20 mg/day within 2–3 months and after one year to ≤5 mg/day. Slow tapering of GC with a withdrawal between 18 and 24 months is suggested to avoid relapse [4]. Tocilizumab and methotrexate, in some cases, are suggested as steroid tapering agents [5].

Recently, we assessed the clinical findings and the relapse rates of patients with GCA in the Turkish multi-centered GCA registry retrospectively. Our study included 330 (F/M: 196/134) patients with GCA. The mean age at disease onset was 68.9±9 years. The most frequent symptom was headache (Table 1). While the duration of headache was longer than one month in 57.8% of patients, the duration was shorter than one month in 42.2% of patients. Headache is mostly localized in the temporal region (82.1%). Ocular symptoms were present in 42.1% of the patients. Permanent vision loss developed in 70 (21.2%) patients. PMR was also present in 81 (24.5%) patients.

[1]Marmara University School of Medicine, Department of Internal Medicine, Division of Rheumatology, Istanbul, Turkey.

Note:
This manuscript was reviewed by Şule Apraş Bilgen.

The median duration of PMR symptoms before GCA diagnosis was 60 (2-3240) days. PMR was started within the last three months in 51 (62.9%) of 81 patients. The Turkish cohort's distribution of clinical signs and symptoms was compatible with the literature. Temporal artery the Doppler US was performed in 132 patients. 42 (31.9%) have a "halo sign" compatible with the GCA diagnosis. Temporal artery biopsy was available in 241 (73%) patients, and 180 of them had positive histopathological findings for GCA diagnosis. Inflammation markers were normal in 25 (7.6%) patients during diagnosis. In 12 of these 25 patients, GCA diagnosis was confirmed by temporal artery biopsy. PET-CT was done in 49 patients. 28 (57.1%) had increased vasculitic FDG uptake in the aorta and its main branches. Large vessel involvement was detected in 4 patients by CT/MR angiography. While all patients received 1 mg/kg/day GC treatment for remission induction, additional GC pulses (250-1000 mg) were given to 69 (20.9%) patients. Immunosuppressives as steroid-sparing agent was used in 252 (76.4%) patients (cyclophosphamide=2, methotrexate=187, azathioprine=54, tocilizumab=9). At third month after diagnosis, 92.7% of patients achieved remission (280/302).

In conclusion, Turkish multi-centered GCA patients' clinical signs and symptoms were similar to the literature data. The relapse rate is lower than the literature, possibly due to higher conventional immunosuppressive agent usage and corticosteroids at diagnosis.

Table 1. Clinical characteristics of patients with Giant-Cell Arteritis

	Giant-Cell Arteritis (n=330)
Manifestations of systemic inflammation	
Anemia (<12 mg/dL for female,<13 mg/dL for male)(n, %)	202 (61.2)
Erythrocyte sedimentation rate (mm/hour)(n=328)	79.7 ± 29.2 (9-159)
C-reactive protein (mg/l, n=325)	84.9 ± 69.3 (0.6-403)
Malaise (n,%)	261 (81.3)
Weight loss (n,%)	137 (41.5)
Fever (n,%)	80 (24.3)
PMR	81 (25.5)
Manifestations of Vascular Ischemia	
Headache (n,%)	294 (89.1)
Scalp tenderness (n,%)	156 (47.3)
Sensitivity on temporal artery region (n,%)	177 (53.6)
Jaw claudication (n,%)	128 (38.8)
Ocular symptoms (n,%)	139 (42.1)
Extremity claudication (n,%)	18 (5.9)
Absent or asymmetric pulses (n,%)	5 (1.5)
Asymmetric blood pressure (n,%)	4 (1.2)
Vascular bruit (n, %)	25 (7.6)
Neurological manifestations (n,%)	25 (7.9)

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