Vertebrobasilar Infarction Related to Giant Cell (Temporal) Arteritis: Case Report

Toshihiko HAISA,1 Tokutaro TSUDA,2 Kiyofumi HAGIWARA,2 Takeshi KIKUCHI,3 and Kunihiko SEKI4

Departments of 1Neurosurgery, 2Rheumatology, 3Neurology, and 4Clinical Pathology, JR Tokyo General Hospital, Tokyo

Abstract

An 84-year-old male with a 3-month history of headache and elevated C-reactive protein levels was admitted for biopsy of the superficial temporal artery, which led to the diagnosis of giant cell arteritis (GCA). Two days after prednisolone therapy was initiated, the patient began to experience transient vertigo attacks. Two days later, dysarthria, left-sided hemiparesis, right abducens palsy, and horizontal nystagmus developed. Magnetic resonance (MR) imaging disclosed fresh infarctions in the vertebrobasilar territory. Since the patient became drowsy because of brainstem compression and hydrocephalus due to cerebellar swelling, emergency suboccipital decompression surgery and ventricular drainage were performed. Subsequently, the patient's consciousness levels improved. MR angiography revealed right vertebral artery (VA) occlusion and left VA stenosis due to arteritis. Ischemic stroke is a serious though relatively rare complication of GCA. Similar cases have been reported, in which ischemic stroke developed despite or possibly due to steroid therapy. To our knowledge, this is the first description of vertebrobasilar infarction associated with GCA in the Japanese population. The merits and potential demerits of steroid therapy are briefly discussed.

Key words: giant cell arteritis, temporal arteritis, brain infarction, vertebral artery occlusion, steroid

Introduction

Giant cell arteritis (GCA) is an autoimmune vasculitis of obscure etiology, primarily affecting large- and medium-sized extracranial vessels and rarely affecting intracranial vessels. In 1890, Hutchinson1) described a patient with a clinical presentation quite similar to that of GCA, but Horton et al.2) were the first to report the histopathological features of granulomatous and round cell-rich periarteritis and thrombosing arteritis of the temporal artery in 1932. As a result of their report, GCA has also been called Horton’s disease or temporal arteritis (TA). Subsequently, Gilmour3) introduced the term “giant-cell chronic arteritis” in 1941.

Ischemic stroke is a serious though relatively rare complication of GCA. In patients with GCA-related ischemic stroke, corticosteroids might be sometimes ineffective or even adverse. We report a case of GCA in which vertebrobasilar stroke developed shortly after initiation of corticosteroid therapy. To our knowledge, this is the first description of vertebrobasilar infarction associated with GCA in the Japanese population.

Case Report

An 84-year-old male with a 3-month history of bilateral occipital and frontal headache along with elevated C-reactive protein (CRP) levels of 12.12 mg/dL was admitted to our hospital for biopsy of the superficial temporal artery. The patient had no history of hypertension, diabetes mellitus, dyslipidemia, or arrhythmia. The vital signs were as follows: body temperature, 36.4°C; pulse rate, 84 beats/min; and blood pressure, 124/66 mmHg. Ocular examination revealed slight anemia. Pain was evident in the proximal parts of the limbs. The results of neurological and ophthalmological examinations were unremarkable. However, laboratory tests revealed signs of inflammation and, the results were as follows: erythrocyte sedimentation rate (ESR), 90 mm/h; CRP, 13.38 mg/dL; hemoglobin, 10.6 g/dL; hematocrit, 33.2%; white blood cell count, 7.3 × 10³ /μL; and platelet count, 29.3 × 10⁴ /μL. A biopsy of the superficial temporal artery was performed on the
day 3 of hospitalization, and a diagnosis of GCA was confirmed on day 11 (Fig. 1).

On day 4, oral prednisolone therapy was initiated at a dose of 15 mg/day. The pain subsided, but transient vertigo appeared on day 6. On day 7, perspiration, vomiting with recurrent vertigo, and minimal motor weakness of the left limbs developed, but emergency computed tomography (CT) of the head revealed no abnormality. Thereafter, on day 8, the patient was alert, but dysarthria with left-sided 3/5 hemiparesis, right abducens palsy, and horizontal nystagmus developed. Repeat CT revealed no definite abnormality, but cranial magnetic resonance (MR) imaging disclosed fresh infarctions in the cerebellar hemispheres and vermis, and the medulla oblongata (Fig. 2). Unfractionated heparin, edarabone, and fructose-added glycerol were commenced, and prednisolone therapy was continued. On day 11, the patient became drowsy, and CT disclosed cerebellar swelling leading to brainstem compression and hydrocephalus.

He was emergently taken to the operating room, and underwent right-sided suboccipital decompressive craniectomy, internal decompression, and ventricular drainage. Consciousness levels returned to normal, and left-sided hemiparesis gradually improved. Catheter angiography revealed occlusion of the right vertebral artery (VA) near the take-off from the right subclavian artery (Fig. 3A). Cervical MR

Fig. 1 Photomicrographs of the resected specimen. A: All three layers of the artery wall are severely affected by arteritis, and the artery wall architecture is destroyed. Hematoxylin and eosin stain, original magnification ×40. B: The media and adventitia are infiltrated by inflammatory cells including multinucleated giant cells. Hematoxylin and eosin stain, original magnification ×200 (high magnification of the black square in Fig. 1A). C: The internal elastic lamina is disrupted. Elastica-van Gieson stain, original magnification ×200.

Fig. 2 Diffusion-weighted magnetic resonance images (upper row) and apparent diffusion coefficient maps (lower row) revealing fresh multiple infarcts in the cerebellar hemispheres and vermis, and the medulla oblongata.
angiography revealed left VA stenosis with no visualization of the right VA (Fig. 3B), and short tau inversion recovery (STIR) images revealed inflammation of both VAs (Fig. 3C). Cranial MR angiography revealed right VA occlusion and left VA stenosis (Fig. 3D). Follow-up cranial MR angiography obtained approximately 3 months after surgery revealed partial improvement of left VA stenosis and development of left anterior cerebral artery stenosis (Fig. 3E).

The patient was discharged home after about 4 months’ rehabilitation with a score of 4 on the modified Rankin scale. At 6-month follow-up, he was neurologically stable under treatment with prednisolone (6 mg/day), methotrexate (6 mg/week), and cilostazol (200 mg/day).

**Discussion**

GCA is a systemic arteritis that involves not only the superficial temporal, ophthalmic, and posterior ciliary arteries, but also the vertebral and carotid arteries, extracranially up to a few millimeters of dural penetration as a rule. The reason the intracranial arteries are rarely involved is that they have little or no elastic tissue in the media and adventitia mainly targeted by GCA. Almost all patients with GCA are aged ≥ 50 years, as indicated by the American College of Rheumatology (ACR) 1990 criteria for the classification of GCA which include the following: age ≥ 50 years at disease onset; new onset of localized headache; temporal artery tenderness or decreased pulse; elevated ESR ≥ 50 mm/h; and biopsy sample including an artery, showing necrotizing arteritis, characterized by a predominance of mononuclear cell infiltrates or a granulomatous process with multinucleated giant cells. Supplementary diagnostic tools, including catheter angiography, MR angiography, CT angiography, and ultrasonography, aid in identifying involvement of the aorta and its proximal branches. STIR images might provide evidence of vessel wall inflammation, as in the present case. The mainstay of treatment consists of corticosteroid administration. Various immunosuppressants, such as cyclophosphamide and methotrexate, are additionally used as steroid-sparing agents. Although GCA is generally a self-limiting disease, it has proven fatal in some cases.

Though ischemic stroke is relatively rare in patients with GCA, recognition of the potential for stroke is important...
because cerebrovascular disease is considered to be one of the predominant causes of death.\(^{14}\) The frequency of ischemic stroke between disease onset or biopsy-based GCA diagnosis and 1 month after diagnosis was 2.4% according to Caselli et al.\(^{15}\) This frequency was 2.8% in the studies of Salvarani et al.\(^{16}\) and Gonzalez-Gay et al.\(^{17}\) During the disease course, transient ischemic attacks, or brain infarctions occurred in 12 (7.2%) out of 166 patients in a study,\(^{15}\) and cerebrovascular accidents occurred in 30 (14.3%) out of 210 patients in another study.\(^{18}\) In a series of 175 cases, including 152 biopsy-proven and 23 ACR-diagnosed patients, cranial ischemic complications were evident in as many as 43 (24.6%) patients at the time of presentation, and new complications developed in 8.4% during follow-up.\(^{19}\) Compared to atherosclerosis-related ischemic stroke, the vertebrobasilar territory is more commonly affected than the carotid territory in patients with GCA.\(^{11,16,17}\)

In regard to treatment of GCA, the first-choice therapy is corticosteroid administration.\(^{8,14,20–23}\) However, several studies have reported development or deterioration of GCA-related vertebrobasilar stroke despite corticosteroid therapy.\(^{3,4,8,10,12–14,21,24–32}\) We have reviewed 31 similar cases in the literature.\(^{3,4,8,10,12–14,21,24–32}\) Surprisingly, ischemic stroke developed or deteriorated within 1 week of steroid initiation in 14 out of 31 cases,\(^{3,4,8,10,12–14,21,24–32}\) although the average duration of GCA-related symptoms was approximately 10 weeks (Table 1). Considering the duration of GCA-related symptoms and the short time interval between corticosteroid initiation and development of ischemic symptoms, it is rather difficult to regard neurological deterioration as merely coincidental in these cases. In this regard, the case reported by Staunton et al.\(^{31}\) is illustrative: a 64-year-old patient with a 3-month history of headache, night sweats, malaise, weight loss, and jaw claudication developed cerebellar infarcts on the first day after prednisolone therapy (60 mg/day). In the present case, vertebrobasilar stroke developed 2 days after prednisolone initiation. The case reported by Kumar and Costa\(^{27}\) resembles the present case in that posterior circulation stroke was followed by hydrocephalus. Their patient did not undergo neurosurgical intervention because of brainstem involvement later and died, whereas the present patient survived decompression surgery and ventricular drainage. Thus, in selected cases, aggressive intervention might be indicated for favorable prognosis.

Corticosteroids are sometimes ineffective or even deleterious in GCA-related ischemic stroke, the reason of which is unclear. Some researchers have supposed that corticosteroid dosage might have been insufficient,\(^{9,12,14}\) whereas others have pointed out the potentially deleterious effects of corticosteroids.\(^{5,23,28,33}\) Therefore, clinicians should be careful in tapering and discontinuing corticosteroids, and bear in mind their potential deleterious effects as well. The mechanism by which corticosteroids provoke and worsen ischemic stroke is unclear, but Conn et al.\(^{32}\) hypothesized that gluccorticoids would usually control inflammation and inhibit endothelial cell products including prostacyclin, but would not inhibit the generation of platelet-derived thromboxane, contributing to vascular occlusion. In cases of GCA with evidence of vascular occlusion/stenosis, use of antithrombotic agents should be considered in addition to corticosteroid therapy.\(^{8,10,20,22,25,28–30}\) One recent report advocated angioplasty using the endovascular approach as another promising option.\(^{24}\)

The incidence and prevalence of GCA differs greatly according to geographic location.\(^{34}\) The annual incidence of TA among people aged ≥ 50 years was estimated to be 29.0/100,000 in south Norway\(^{35}\) and that of GCA in northwestern Spain was 10.24/100,000.\(^{36}\) The annual incidence of TA among people aged ≥ 40 years was 22/100,000 in the United Kingdom.\(^{34}\) The prevalence of GCA among people aged ≥ 50 years was 278/100,000 in Olmsted County, Minnesota, the United States.\(^{37}\) On the other hand, its prevalence among people aged ≥ 50 years in 1997 was 1.47/100,000 in Japan.\(^{38}\) Thus, GCA is extremely rare in Japan, compared with European and North American countries.\(^{38}\) Only 3 cases of GCA-related ischemic stroke have been presented as a case report in the Japanese population.\(^{39,40}\)

Finally, we would like to underline the following four points: ESR or CRP levels merit evaluation in elderly patients complaining of intractable headache; vertebrobasilar stroke in elderly patients with signs of inflammation might be related to GCA; vessel study of branches of the aortic arch is advisable in patients with GCA; and additional use of anticoagulants and/or antiplatelets should be taken into consideration in cases of GCA with evidence of vascular occlusion/stenosis.

### Conflicts of Interest Disclosure

The authors have no personal, financial, or institutional interest in any of the drugs, materials, or devices in

Neurol Med Chir (Tokyo) 55, January, 2015
the article. All authors who are members of The Japan Neurosurgical Society (JNS) have registered online self-reported CDI Disclosure Statement Forms through the website for JNS members.

References

1) Hutchinson J: Diseases of the arteries. 1. On a peculiar form of thrombotic arteritis of the aged which is sometimes productive of gangrene. Arch Surg 1: 323–329, 1890

Neurol Med Chir (Tokyo) 55, January, 2015
32) van Laar JM, Verschuuren JJGM, de Meijer PHEM: [Clinical thinking and decision making in practice. An elderly patient with vertigo and high sedimentation rate]. *Ned Tijdschr Geneeskd* 143: 2190–2196, 1999 (Dutch)

Address reprint requests to: Toshihiko Haisa, MD, PhD, Department of Neurosurgery, JR Tokyo General Hospital, 2-1-3 Yoyogi, Shibuya-ku, Tokyo 151-8128, Japan.

*e-mail*: haisat-kkr@umin.ac.jp