

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

Toshihiko HAISA,<sup>1</sup> Tokutaro TSUDA,<sup>2</sup> Kiyofumi HAGIWARA,<sup>2</sup> Takeshi KIKUCHI,<sup>3</sup> and Kunihiko SEKI<sup>4</sup>

*Departments of <sup>1</sup>Neurosurgery, <sup>2</sup>Rheumatology, <sup>3</sup>Neurology, and <sup>4</sup>Clinical 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, Hutchinson<sup>1)</sup> described a patient with a clinical presentation quite similar to that of GCA, but Horton et al.<sup>2)</sup> 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, Gilmour<sup>3)</sup> 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

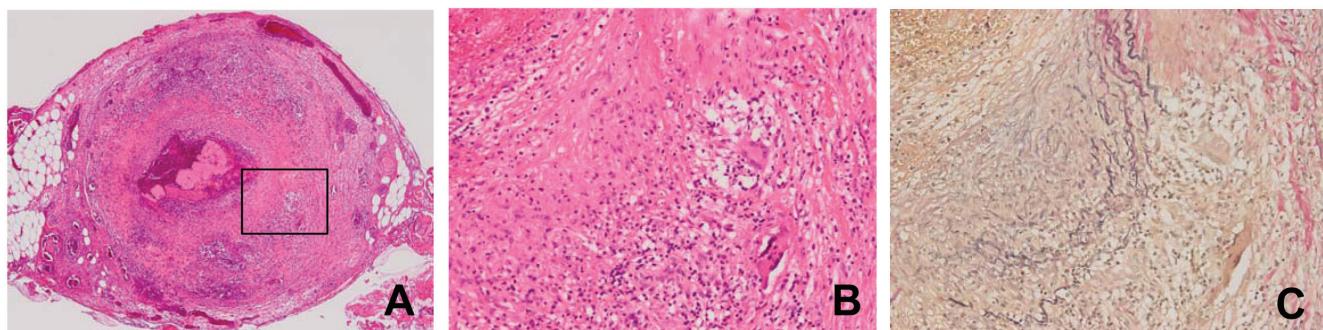
An 84-year-old male with a 3-month history of bilateral occipital and frontal headache along with elevated C-reactive protein (CRP) levels of 12.12 mg/dL was admitted to our hospital for biopsy of the superficial temporal artery. The patient had no history of hypertension, diabetes mellitus, dyslipidemia, 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,  $7.3 \times 10^3 / \mu\text{L}$ ; and platelet count,  $29.3 \times 10^4 / \mu\text{L}$ . 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).

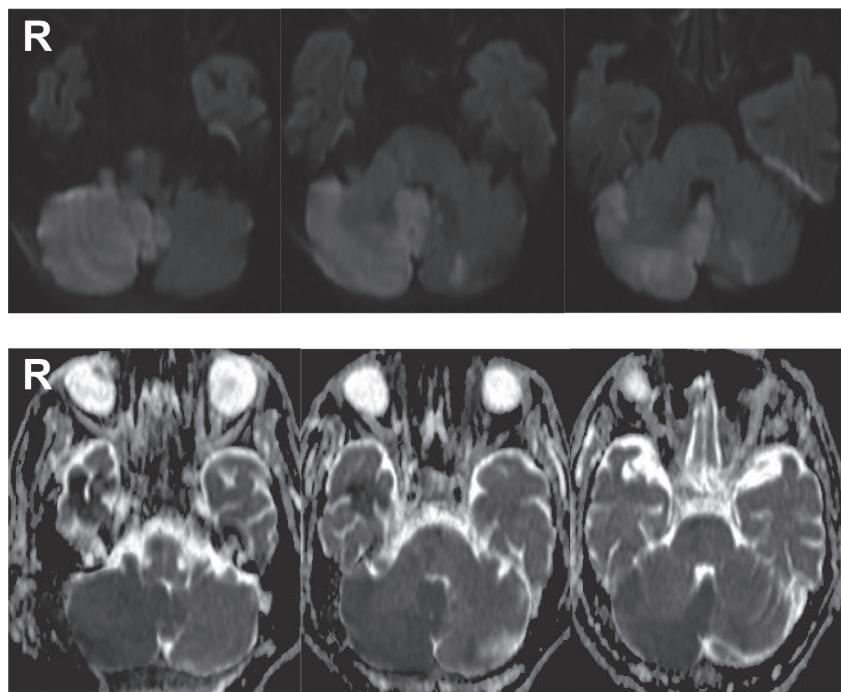
On day 4, oral prednisolone therapy was initiated at a dose of 15 mg/day. The pain subsided, but transient vertigo appeared on day 6. On day 7, perspiration, vomiting with recurrent vertigo, and minimal motor weakness of the left limbs developed, but emergency computed tomography (CT) of the head revealed 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  $\times 40$ . B: The media and adventitia are infiltrated by inflammatory cells including multinucleated giant cells. Hematoxylin and eosin stain, original magnification  $\times 200$  (high magnification of the black square in Fig. 1A). C: The internal elastic lamina is disrupted. Elastica-van Gieson stain, original magnification  $\times 200$ .



**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.<sup>4)</sup> Almost all patients with GCA are aged  $\geq 50$  years, as indicated by the American College of Rheumatology (ACR) 1990 criteria for the classification of GCA which include the following: age  $\geq 50$  years at disease onset; new onset of localized headache; temporal artery tenderness or decreased pulse; elevated ESR  $\geq 50$  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.<sup>5)</sup> 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.<sup>6)</sup> Although GCA is generally a self-limiting disease,<sup>7)</sup> it has proven fatal in some cases.<sup>8-13)</sup>

Though ischemic stroke is relatively rare in patients with GCA, recognition of the potential for stroke is important

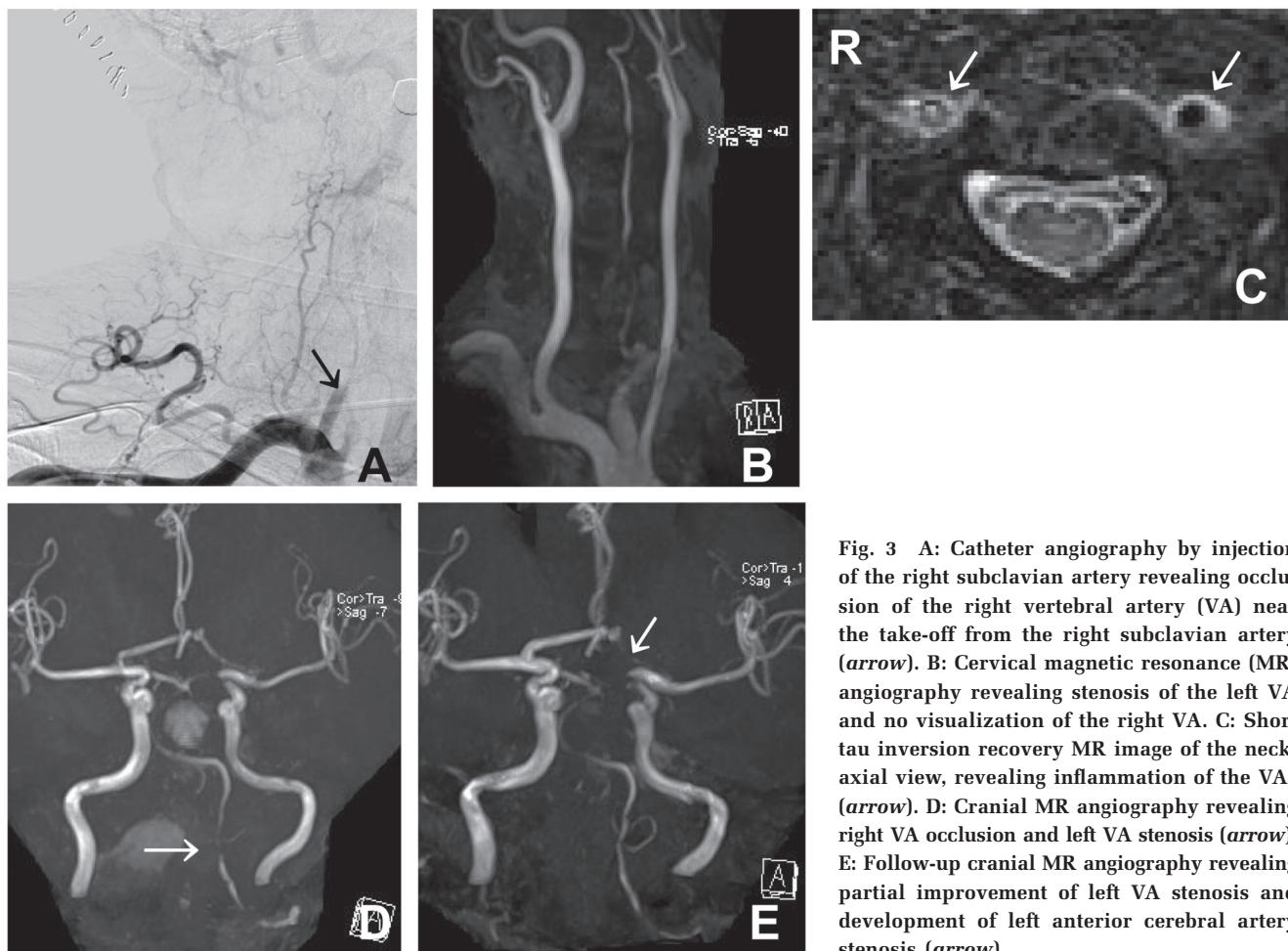


Fig. 3 A: Catheter angiography by injection of the right subclavian artery revealing occlusion of the right vertebral artery (VA) near the take-off from the right subclavian artery (arrow). B: Cervical magnetic resonance (MR) angiography revealing stenosis of the left VA and no visualization of the right VA. C: Short tau inversion recovery MR image of the neck, axial view, revealing inflammation of the VAs (arrow). D: Cranial MR angiography revealing right VA occlusion and left VA stenosis (arrow). E: Follow-up cranial MR angiography revealing partial improvement of left VA stenosis and development of left anterior cerebral artery stenosis (arrow).

because cerebrovascular disease is considered to be one of the predominant causes of death.<sup>14)</sup> 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.<sup>15)</sup> This frequency was 2.8% in the studies of Salvarani et al.<sup>16)</sup> and Gonzalez-Gay et al.<sup>17)</sup> During the disease course, transient ischemic attacks, or brain infarctions occurred in 12 (7.2%) out of 166 patients in a study<sup>15)</sup> and cerebrovascular accidents occurred in 30 (14.3%) out of 210 patients in another study.<sup>18)</sup> 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.<sup>19)</sup> Compared to atherosclerosis-related ischemic stroke, the vertebrobasilar territory is more commonly affected than the carotid territory in patients with GCA.<sup>11,16,17)</sup>

In regard to treatment of GCA, the first-choice therapy is corticosteroid administration.<sup>6,14,20-23)</sup> However, several studies have reported development or deterioration of GCA-related vertebrobasilar stroke despite corticosteroid therapy.<sup>4,8-10,12-14,21,24-32)</sup> We have reviewed 31 similar cases in the literature.<sup>4,8-10,12-14,21,24-32)</sup> Surprisingly, ischemic stroke developed or deteriorated within 1 week of steroid initiation in 14 out of 31 cases,<sup>4,9,10,14,26,28-31)</sup> 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.<sup>31)</sup> 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<sup>27)</sup> 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,<sup>9,14,21)</sup> whereas others have pointed out the potentially deleterious effects of corticosteroids.<sup>8,25,28,31)</sup> 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.<sup>33)</sup> hypothesized that glucocorticoids 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.<sup>8,10,20,22,25,28-30)</sup> One recent report advocated angioplasty using the endovascular approach as another promising option.<sup>24)</sup>

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

Finally, we would like to underline the following four points: ESR and/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 anti-platelets 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

**Table 1** Characteristics of 31 patients with histologically confirmed giant cell arteritis in whom vertebrobasilar infarction developed or deteriorated despite steroid therapy

	Death group	Survival group	Total
Number of cases	20	11	31
Mean age (years)	74.4 $\pm$ 6.75	71.6 $\pm$ 8.40	73.4 $\pm$ 7.31
Duration of symptoms (days)	5-365 mean: 81 median: 38	10-104 mean: 54 median: 53	5-365 mean: 71 median: 45
Interval from steroid use until ischemic symptoms (days)	0-240 mean: 18 median: 3	1-730 mean: 88 median: 7	0-730 mean: 43 median: 6

the article. All authors who are members of The Japan Neurosurgical Society (JNS) have registered online Self-reported COI 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
- 2) Horton BT, Magath TB, Brown GE: An undescribed form of arteritis of the temporal vessels. *Mayo Clin Proc* 7: 700–701, 1932
- 3) Gilmour JR: Giant-cell chronic arteritis. *J Pathol Bacteriol* 53: 263–277, 1941
- 4) Wilkinson IMS, Russel RWR: Arteries of the head and neck in giant cell arteritis. A pathological study to show the pattern of arterial involvement. *Arch Neurol* 27: 378–391, 1972
- 5) Hunder GG, Bloch DA, Michel BA, Stevens MB, Arend WP, Calabrese LH, Edworthy SM, Fauci AS, Leavitt RY, Lie JT, Lightfoot RW, Masi AT, McShane DJ, Mills JA, Wallace SL, Zvaifler NJ: The American College of Rheumatology 1990 criteria for the classification of giant cell arteritis. *Arthritis Rheum* 33: 1122–1128, 1990
- 6) Hayreh SS, Zimmerman B: Management of giant cell arteritis. Our 27-year clinical study: new light on old controversies. *Ophthalmologica* 217: 239–259, 2003
- 7) Meadows SP: Temporal or giant cell arteritis. *Proc R Soc Med* 59: 329–334, 1966
- 8) Boettinger M, Sebastian S, Gamulescu MA, Grauer O, Ritzka M, Schuierer G, Bogdahn U, Steinbrecher A, Schlachetzki F: Bilateral vertebral artery occlusion with retrograde basilar flow in three cases of giant cell arteritis. *BMJ Case Rep* 2009; 2009.
- 9) Büttner T, Heye N, Przuntek H: Temporal arteritis with cerebral complications: report of four cases. *Eur Neurol* 34: 162–167, 1994
- 10) Collazos J, García-Moncó C, Martín A, Rodriguez J, Gómez MA: Multiple strokes after initiation of steroid therapy in giant cell arteritis. *Postgrad Med J* 70: 228–230, 1994
- 11) Missen GAK: Involvement of the vertebro-carotid arterial system in giant-cell arteritis. *J Pathol* 106: 2–3, 1972
- 12) Salvarani C, Giannini C, Miller DV, Hunder G: Giant cell arteritis: Involvement of intracranial arteries. *Arthritis Rheum* 55: 985–989, 2006
- 13) Sheehan MM, Keohane C, Twomey C: Fatal vertebral giant cell arteritis. *J Clin Pathol* 46: 1129–1131, 1993
- 14) Säve-Söderbergh J, Malmvall BE, Andersson R, Bengtsson BA: Giant cell arteritis as a cause of death. Report of nine cases. *JAMA* 255: 493–496, 1986
- 15) Caselli RJ, Hunder GG, Whisnant JP: Neurologic disease in biopsy-proven giant cell (temporal) arteritis. *Neurology* 38: 352–359, 1988
- 16) Salvarani C, Della Bella C, Cimino L, Macchioni P, Formisano D, Bajocchi G, Pipitone N, Catanoso MG, Restuccia G, Ghinai A, Boiardi L: Risk factors for severe cranial ischaemic events in an Italian population-based cohort of patients with giant cell arteritis. *Rheumatology (Oxford)* 48: 250–253, 2009
- 17) Gonzalez-Gay MA, Vazquez-Rodriguez TR, Gomez-Acebo I, Pego-Reigosa R, Lopez-Diaz MJ, Vazquez-Triñanes MC, Miranda-Filloy JA, Blanco R, Dierssen T, Gonzalez-Juanatey C, Llorca J: Strokes at time of disease diagnosis in a series of 287 patients with biopsy-proven giant cell arteritis. *Medicine (Baltimore)* 88: 227–235, 2009
- 18) Pego-Reigosa R, Garcia-Porrúa C, Piñeiro A, Dierssen T, Llorca J, Gonzalez-Gay MA: Predictors of cerebrovascular accidents in giant cell arteritis in a defined population. *Clin Exp Rheumatol* 22(6 Suppl 36): S13–17, 2004
- 19) Nesher G, Berkun Y, Mates M, Baras M, Nesher R, Rubinow A, Sonnenblick M: Risk factors for cranial ischemic complications in giant cell arteritis. *Medicine (Baltimore)* 83: 114–122, 2004
- 20) Ahdab R, Thabuy F, Menager de Froberville E, Brugieres P, Hosseini H: Reversible vertebral artery stenosis following corticotherapy in giant cell arteritis. *Eur Neurol* 59: 331, 2008
- 21) Caselli RJ: Giant cell (temporal) arteritis: a treatable cause of multi-infarct dementia. *Neurology* 40: 753–755, 1990
- 22) Garcia-Porrúa C, Pego-Reigosa R, Martínez-Vazquez F, Armesto V, Gonzalez-Gay MA: Bilateral vertebral artery occlusion in giant cell arteritis. *Clin Exp Rheumatol* 24(2 Suppl 41): S101, 2006
- 23) Sutter R, Renaud S, Bonati L, Lyrer P, Tolnay M, Wetzel S, Rüegg S, Engelert S: Bilateral vertebral giant cell arteritis—favourable outcome in two cases. *J Neurol* 255: 133–134, 2008
- 24) Dementovych N, Mishra R, Shah QA: Angioplasty and stent placement for complete occlusion of the vertebral artery secondary to giant cell arteritis. *J Neurointerv Surg* 4: 110–113, 2012
- 25) FitzGerald AJ, Ironside JW, Summers DM, Dennis MS, McRorie ER: Two cases of recurrent stroke in treated giant cell arteritis: diagnostic and therapeutic dilemmas. *J Clin Rheumatol* 16: 225–228, 2010
- 26) González-Gay MA, Blanco R, Rodríguez-Valverde V, Martínez-Taboada VM, Delgado-Rodríguez M, Figueroa M, Uriarte E: Permanent visual loss and cerebrovascular accidents in giant cell arteritis: predictors and response to treatment. *Arthritis Rheum* 41: 1497–1504, 1998
- 27) Kumar A, Costa DD: Insidious posterior circulation stroke with rapid deterioration due to vertebral giant cell arteritis. *Age Ageing* 36: 695–697, 2007
- 28) Polomat K, Chausson N, Olindo S, Smadja D: [Reversibility of vertebrobasilar stenoses following treatment with corticosteroid therapy in patients with giant cell arteritis]. *Rev Neurol (Paris)* 166: 940–943, 2010 (French)
- 29) Rüegg S, Engelert S, Jeanneret C, Hetzel A, Probst A, Steck AJ, Lyrer P: Bilateral vertebral artery occlusion resulting from giant cell arteritis: report of 3 cases and review of the literature. *Medicine (Baltimore)* 82: 1–12, 2003
- 30) Solans-Laqué R, Bosch-Gil JA, Molina-Catenario CA, Ortega-Aznar A, Alvarez-Sabin J, Vilardell-Tarres M: Stroke and multi-infarct dementia as presenting symptoms of giant cell arteritis: report of 7 cases and review of the literature. *Medicine (Baltimore)* 87: 335–344, 2008
- 31) Staunton H, Stafford F, Leader M, O'Riordain D: Deterioration of giant cell arteritis with corticosteroid therapy. *Arch Neurol* 57: 581–584, 2000

32) van Laar JM, Verschueren JJGM, de Meijer PHEM: [Clinical thinking and decision making in practice. An elderly patient with vertigo and high sedimentation rate]. *Ned Tijdschr Geneesk* 143: 2190–2196, 1999 (Dutch)

33) Conn DL, Tompkins RB, Nichols WL: Glucocorticoids in the management of vasculitis—a double edged sword? *J Rheumatol* 15: 1181–1183, 1988

34) Smeeth L, Cook C, Hall AJ: Incidence of diagnosed polymyalgia rheumatica and temporal arteritis in the United Kingdom, 1990–2001. *Ann Rheum Dis* 65: 1093–1098, 2006

35) Gran JT, Myklebust G: The incidence of polymyalgia rheumatica and temporal arteritis in the county of Aust Agder, south Norway: a prospective study 1987–94. *J Rheumatol* 24: 1739–1743, 1997

36) González-Gay MA, Garcia-Porrúa C, Rivas MJ, Rodriguez-Ledo P, Llorca J: Epidemiology of biopsy proven giant cell arteritis in northwestern Spain: trend over an 18 year period. *Ann Rheum Dis* 60: 367–371, 2001

37) Salvarani C, Crowson CS, O'Fallon WM, Hunder GG, Gabriel SE: Reappraisal of the epidemiology of giant cell arteritis in Olmsted County, Minnesota, over a fifty-year period. *Arthritis Rheum* 51: 264–268, 2004

38) Kobayashi S, Yano T, Matsumoto Y, Numano F, Nakajima N, Yasuda K, Yutani C, Nakayama T, Tamakoshi A, Kawamura T, Ohno Y, Inaba Y, Hashimoto H: Clinical and epidemiologic analysis of giant cell (temporal) arteritis from a nationwide survey in 1998 in Japan: the first government-supported nationwide survey. *Arthritis Rheum* 49: 594–598, 2003

39) Harigai T, Hoshino S, Kawakami A, Higuchi M: [Temporal arteritis with recurrent attacks of cerebral infarction. A case report]. *Shinkeinaika* 38: 575–580, 1993 (Japanese)

40) Inafuku T, Watanabe M, Takagi M, Hoshino H, Morinaga S, Koto A: [Giant cell arteritis with bilateral obstruction of the internal carotid artery—report of an autopsy case]. *Rinsho Shinkeigaku* 38: 323–328, 1998 (Japanese)

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