

A Case Report of Patient with Takayasu's Arteritis Complicated by Reversible Cerebral Vasoconstriction Syndrome

Seung-Hoon Lee, Min Jung Lee, Byungju Kang, Hyoin Choi, You Jae Kim,
Bon San Koo, Min Wook So, Chang-Keun Lee, Bin Yoo

*Division of Rheumatology, Department of Internal Medicine,
Asan Medical Center, University of Ulsan College of Medicine, Seoul, Korea*

Takayasu's arteritis (TA) is a chronic inflammatory vascular disease that mainly affects large vessels. Central nervous system involvement occurs in about 20% of cases with rare involvement of intracranial vessel, and its typical manifestation is cerebral ischemia or stroke. Reversible cerebral vasoconstriction syndrome (RCVS) is a group of disorders with prolonged, but reversible vasoconstriction of the cerebral arteries with acute-onset, severe, recurrent headaches with or without neurologic signs or symptoms. We report a case of TA in a 17-year old girl who presented with secondary RCVS. She complained of thunderclap headache, seiz-

ure and acute stroke. 3-dimensional computed tomography scan and magnetic resonance angiography of head revealed irregular thickening of aortic wall and its main branches with multifocal narrowing of intracranial basilar artery, which improved after oral nimodipine intake. This case highlights RCVS as an unusual manifestation of TA and demonstrates the diagnosis, treatment and response to therapy of RCVS in TA, which resolved after treatment with calcium channel blocker.

Key Words. Takayasu's arteritis, Reversible cerebral vasoconstriction syndrome

Introduction

Takayasu's arteritis (TA) is a chronic, idiopathic, inflammatory vascular disease that mainly affects large vessels such as the aorta and its main branches (1). It is common in Asia and usually affects adolescents and young woman (2). TA presents with variety of manifestations like arm pain, visual disturbance, dizziness, syncope, and stroke by involvement of common carotid and vertebral arteries in extracranial portions, but involvement of intracranial arteries are rare (3).

Reversible cerebral vasoconstriction syndrome (RCVS) often presents with acute-onset, excruciating headache with or without additional neurological symptoms (4). Although the pathophysiology is not clearly understood, many medical conditions like pregnancy, migraine and vasoactive drugs are known to be associated with RCVS (4). In 2007, Calabrese et al. proposed the diagnostic criteria of RCVS that includes the normalization of arteriographic abnormalities within 12 weeks (4).

There is only 1 case report of RCVS associated with TA in Japan in the literature, which occurred in a 15-year-old girl with thunderclap headache (5). We report the case of RCVS in a patient with TA with involvement of intracranial basilar artery, which is the first case in Korea.

Case Report

A 17-year old girl with acute-onset, severe headache for the last 7 days came to the emergency room complaining of tonic-clonic seizure with impaired consciousness. The headache was like hammer striking and lasted for 3 to 4 hours once it occurred. It deteriorated in a supine position and relieved when standing. She was taking pain killer for recent headache from local clinic, and there was no other medical history. No family history of seizure or stroke existed. Her blood pressure was 154/95 mmHg, heart rate was 95 beats/minute, respiration rate was 20/minute, and body temperature was 36.9°C.

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Corresponding to : Chang-Keun Lee, Division of Rheumatology, Department of Internal Medicine, Asan Medical Center, University of Ulsan College of Medicine, 88, Olympic-ro 43-gil, Songpa-gu, Seoul 138-736, Korea. E-mail : cklee@amc.seoul.kr

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Breathing sound was clear and bowel sound was normoactive with soft abdomen. She was drowsy, but orientations for time, place and persons were intact. In the emergency room, general tonic-clonic seizure occurred 3 times more with duration of 1 minute and post-ictal confusion. Her brain magnetic resonance imaging (MRI) showed faintly high signal intensity at bilateral cerebral hemisphere in T2 weighted images. Her laboratory data showed WBC count of 10,500/uL and hemoglobin of 9.8 g/dL in blood. Lumbar tapping was conducted and cerebrospinal fluid (CSF) tapping pressure was 12 cmH₂O. CSF analysis was normal in cell count and protein. Considering the possibility of viral encephalitis and encephalopathy, empirical therapy with acyclovir and 1st intravenous corticosteroid pulse therapy was started with 1,000 mg of methylprednisolone for 3 days. The results of CSF culture was negative. The patient's consciousness and general condition were improving with therapy. No neurological deficit remained and the corticosteroid was tapered out.

On the 10th hospital day, she had severe thunderclap headache again and decreased bilateral visual acuity, visual field defects and left hemiparesis occurred. The patient said she used to feel pain and numbness on both hands when she raised her arms to grab the handle in a subway from 9 months ago. On Physical examination, there was no arterial pulses in her bilateral upper extremities and blood pressures in her arms were reduced (right arm: 70/49 mmHg, left arm: 76/59 mmHg, right leg: 134/70 mmHg, left leg: 131/61 mmHg). Laboratory finding of blood showed negative results in anti-neutrophil antibody, antinuclear antibody, antiphospholipid antibody and normal in protein C, protein S and antithrombin III. Her CSF fluid analysis result was normal in cell count and protein, but the initial CSF pressure was 40 cmH₂O. Her brain MRI showed a new area of high signal intensity at bilateral occipital lobes and right frontal lobe in diffusion

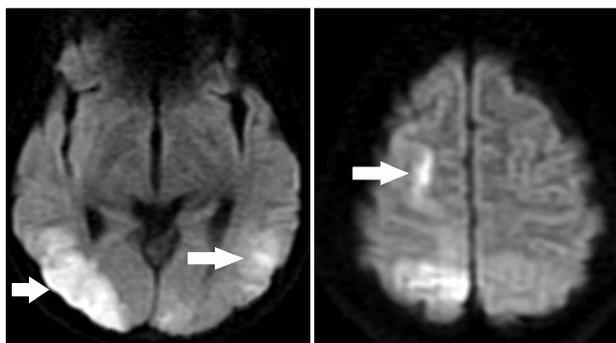


Figure 1. Diffusion weighted image of brain MRI shows high signal intensity at bilateral occipital lobes and right frontal lobe (arrows).

weighted image (Figure 1) suggesting cortical blindness. Aspirin 100 mg per day and intravenous heparin were started to prevent further ischemic stroke. In addition to brain MRI, 3-dimensional computed tomography (CT) scan of the aorta was conducted because the pulses in both arms were not palpable, and stenosis of subclavian arteries were considered. There were obstructions on both subclavian arteries and diffuse concentric wall thickening in distal ascending aorta, proximal descending aorta, bilateral common carotid arteries, subclavian arteries, vertebral arteries and right brachiocephalic artery (Figure 2). Considering the age of the patient, history of arm claudication, decreased bilateral brachial arterial pulses and abnormal findings of 3D CT scan of aorta and its main branches, TA was diagnosed. She was treated with 2nd intravenous corticosteroid pulse with 1,000 mg of methylprednisolone for 5 days and 28 mg per day after that.

On the 16th hospital day, brain MR angiography was conducted to evaluate the cerebral vessels and it showed multifocal segmental narrowing in basilar artery (Figure 3A). Because involvement of intracranial vasculature in TA is unusual, and the patient had acute-onset symptoms which is not the common feature of TA, we thought other etiology other than TA could contribute to the stenosis of basilar artery. She did not complain fatigue, weight loss, arthralgia, abdominal pain or fever recently. Further, her blood ESR level was 6 mm/hr and CRP was 0.1 mg/dL. We thought the activity of Takayasu's arteritis was adequately suppressed and clinically controlled. Rather, high possibility of RCVS was raised due to the following reasons; acute-onset thunderclap headache, multifocal segmental arterial narrowing of intracerebral vessel and normal CFS fluid



Figure 2. 3D CT scan of aorta shows obstruction of bilateral subclavian arteries (arrows).

analysis results. Assessed as RCVS associated with Takayasu's arteritis, oral nimodipine 30 mg q 8 hours was administered with 3rd intravenous corticosteroid pulse therapy with 1,000 mg of methylprednisolone for 3 days.

On the 28th hospital day, her visual agnosia and left side hemiparesis improved, and she was able to read a book in a comfortable manner and walk by herself. No more thunderclap headache occurred with oral nimodipine and methylprednisolone 16 mg per day.

MRI of cerebral vessels were followed up at 2 and 4 weeks each after 3rd corticosteroid pulse therapy, and there were gradual improvements of previously found multifocal segmental narrowing of basilar artery (Figure 3B), suggesting that vasospasm had been responsible for the transient stenosis of the vessels. RCVS was confirmed and she is now on follow up on outpatient clinic for 6 months with aspirin, nimodipine and maintenance therapy of methylprednisolone 12 mg per day without headache or neurologic dysfunction. CT scans were also followed with interval of 6 months to evaluate the

status of aorta and its main branches, and there was no change of wall thickening and narrowing of the vessels.

Discussion

Our case is of a 17-year-old girl who presented with convulsion, thunderclap headache, left hemiparesis and visual agnosia with features of Takayasu's arteritis. MRI of the brain showed multiple cerebral infarct and segmental narrowing of basilar artery which could not be explained by TA. We made a diagnosis of RCVS, based on reversibility of basilar artery stenosis and good response to nimodipine.

In 2007, Calabrese et al. proposed the diagnostic criteria of RCVS (4), and the criteria as follows: 1) transfemoral angiography or indirect CT angiography or MR angiography documenting multifocal segmental cerebral artery vasoconstriction. 2) no evidence of aneurysmal subarachnoid hemorrhage. 3) normal or near-normal cerebral fluid analysis. 4) severe, acute headache, with or without additional neurologic signs or symptoms. 5) reversibility of angiographic abnormalities within 12 weeks after onset. The symptoms, laboratory and radiological findings of our patient met all five diagnostic criteria of RCVS.

There are many findings to support that the patient's cerebral events were associated with RCVS, rather than primary angiitis of central nervous system (CNS) or intracranial vascular involvement of systemic vasculitis. The autoimmune markers related to vasculitic diseases such as anti-neutrophil cytoplasmic antibody, antinuclear antibody and antiphospholipid were all negative and ESR and CRP levels in blood were not increased. Unlike the subacute and progressive course of primary angiitis of CNS, the patient had acute-onset thunderclap headache. And, our patient's CSF analysis was normal in cell count and protein. In Singhal's review of patients with RCVS without subarachnoid hemorrhage in 2002, 95% of patients showed CSF cell count of less than 10/mm³ and CSF protein levels below 80 mg/dL (6). This finding helps to differentiate RCVS not only from subarachnoid hemorrhage but also from other cerebral vasculitic diseases. Intracranial involvement of TA is known to be very rare. There was a systematic review of clinical features and management of TA in 2005, and there was no intracranial involvement in 272 patients (7). In another case report, TA with intracranial vessel involvement was reported (8). However this case was associated with elevated ESR and CRP levels in serum. Lastly, it took only 2 weeks for the vascular stenosis to improve and 4 weeks to be completely resolved. The reversibility of vasoconstriction over days to weeks is the feature that best distinguishes RCVS from CNS vasculitis (4), and this point argues compellingly

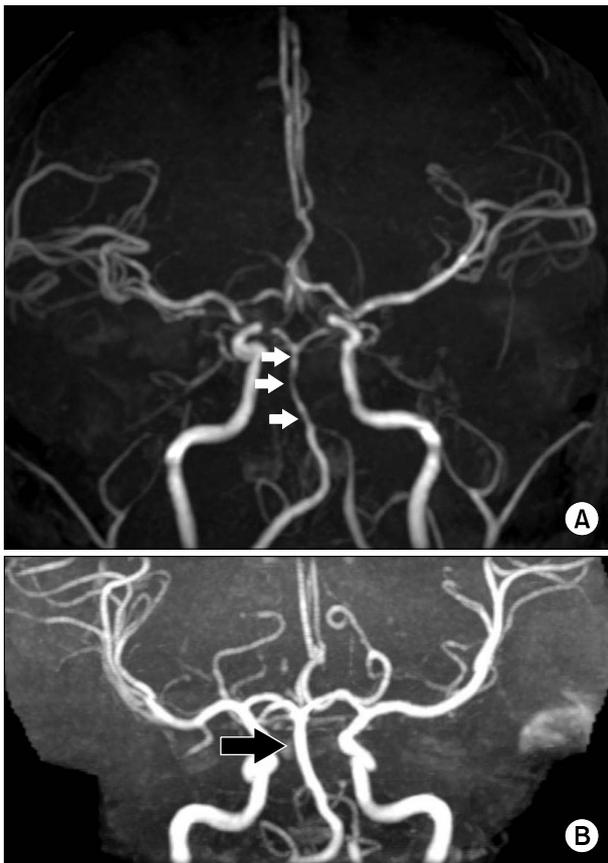


Figure 3. MR angiography (A). Multifocal segmental narrowing of basilar artery (B). Previously shown multifocal segmental narrowing of basilar artery (white arrows) was improved (black arrow) after 2 weeks of 3rd corticosteroid pulse therapy.

for RCVS rather than primary angiitis of CNS or systemic vasculitis with CNS involvement. All the above findings raise the possibility that RCVS might have been involved in the stenosis of intracranial arteries in the current case.

Various clinical conditions are known to be associated with RCVS (4). Sympathomimetics and serotonergic drugs, catecholamine secreting tumors like pheochromocytoma or bronchial carcinoid tumors, pregnancy-related conditions like pre-eclampsia or late pregnancy are the clinical settings that were associated with RCVS. The pathophysiology is not clearly understood but disturbance in the control of cerebral vascular tone seems to be a key element.

It is recommended to initiate therapy of RCVS when there is moderate risk of ischemic stroke and poor outcome (4). Calcium channel blocker is known to be the first choice of therapy, and high-dose glucocorticoid is also reported to be effective (9). Our patient is currently taking oral nimodipine 30mg q 12 hours and methylprednisolone 12 mg q 24 hours, and is now being followed on outpatient clinic with favorable clinical course.

Summary

We report a patient with TA complicated by RCVS. If a patient with TA complains of thunderclap headache with or without additional neurological symptoms, and the vascular abnormality in image study is transient, RCVS should be considered in the differential diagnosis before other primary angiitis of CNS. Evaluation of intracranial vessels such as angiography or MR angiography should be considered, and post-treatment follow up of angiographic studies might be needed to confirm the improvement of vascular lesions.

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