Case Studies

Spontaneous Bilateral Cervical Internal Carotid and Vertebral Artery Dissection in a Japanese Patient without Collagen Vascular Disease with Special Reference to Single-Nucleotide Polymorphisms

Arata Abe, MD,* Chikako Nito, MD,* Yuki Sakamoto, MD,* Akane Nogami, MD,* Hiroyuki Hokama, MD,* Shiro Takahashi, MD,* Kumiko Kirita, MD,* Masayuki Ueda, MD,* Yoshiro Ishimaru,† and Kazumi Kimura, MD*

Spontaneous cervical artery dissection (sCAD) is a major cause of ischemic stroke in young adults. Frequently, sCAD involves multiple neck arteries, accounting for 13%-28% of the total sCAD cases. However, little is known about factors related to multiple sCAD. In this case, a 52-year-old man was admitted due to headache without aura. There was a personal history of migraine with aura and a family history of similar symptoms. The patient's younger brother had a left vertebral artery (VA) dissecting aneurysm and underwent endovascular occlusion of his parent artery at the age of 48. Magnetic resonance imaging of our admitted patient showed hyperintensities in the right internal carotid artery (ICA) without acute infarction, and magnetic resonance angiography revealed a narrowing of the right ICA. Angiography was then performed, which showed a trace of dissection of the left ICA and both VAs as well as the right ICA. The patient did not fulfill any major criteria of collagen vascular disease such as Ehlers–Danlos syndrome type IV or Loeys–Dietz syndrome. The data in our patient are quite similar to those reported in patients with single-nucleotide polymorphism (SNP) of *PHACTR1*. Obtaining the patient's informed consent, we analyzed a common SNP variation in the rs9349379[G] allele (*PHACTR1*), which has been reported to be associated with a lower risk of sCAD. **Key Words:** Carotid artery dissection—vertebral artery dissection—PHACTR1—migraine.

From the *Department of Neuro-pathophysiological Imaging, Graduate School of Medicine, Nippon Medical School, Tokyo, Japan; and †Department of Applied Biological Chemistry, Graduate School of Agricultural and Life Sciences, The University of Tokyo, Tokyo, Japan.

Received January 22, 2016; revision received March 28, 2016; accepted April 29, 2016.

Authors' contributions: Drs. Abe, Hokama, Takahashi, and Kirita, the patient's attending doctors, performed neurological and imaging examinations, prescribed medicines, and made decisions about the patient's management. Dr. Abe prepared the manuscript with the other authors' suggestions. Drs. Nito, Nogami, and Sakamoto supervised the management of the patient. Dr. Ishimaru took part in genome analysis with no disclosures. Drs. Kimura and Ueda served as overall scientific advisors.

Address correspondence to Arata Abe, MD, Department of Neurological Science, Graduate School of Medicine, Nippon Medical School, 1-1-5, Sendagi, Bunkyo-ku, Tokyo 113-8603, Japan. E-mail: abe@nms.ac.jp.

1052-3057/$ - see front matter

http://dx.doi.org/10.1016/j.jstrokecerebrovasdis.2016.04.027

Case Report

Spontaneous cervical artery dissection (sCAD) is a major cause of ischemic stroke in young adults.[1] Frequently, sCAD involves multiple neck arteries, accounting for 13%-28% of the total sCAD cases.[2-5] However, little is known about factors related to multiple sCAD.

In this case, a 52-year-old man was admitted due to headache without aura. There was a personal history of migraine with aura and a family history of similar symptoms. The patient's younger brother had a left vertebral artery (VA) dissecting aneurysm and underwent endovascular occlusion of the parent artery at the age of 48. Magnetic resonance imaging of our admitted patient showed hyperintensities in the right internal carotid artery (ICA) without acute infarction, and magnetic resonance angiography revealed a narrowing of the right ICA (Fig 1). Angiography was then performed, which showed a trace of dissection of the left ICA and of both VAs as well as the right ICA (Fig 2). Connective tissue disorders, such as Ehlers–Danlos syndrome type IV and Loeys–Dietz syndrome, were suspected because of multiple dissections of the cervical and intracranial arteries. However, our patient did not satisfy the clinical diagnostic criteria of Ehlers–Danlos syndrome type IV, including (1) easy bruising, (2) thin skin with visible veins, (3) characteristic facial features, and (4) rupture of arteries, the uterus, or intestines.[6] Therefore, Ehlers–Danlos syndrome type IV was unlikely. We additionally confirmed neither abnormal type III procollagen molecules from cultured fibroblasts or type III procollagen (*COL3A1*) gene mutation. Loeys–Dietz syndrome was characterized by ascending aortic aneurysm and aortic dissection, abnormally long limbs and fingers, and dural ectasia,[7] and de novo mutation in *TGFB3*, a ligand of the transforming growth factor (TGF)-β pathway, was also identified in the disorder.[8] However, these clinical and genetic characteristics were not found in our patient. Moreover, the findings in our patient were quite similar to those reported in patients with single-nucleotide polymorphism (SNP) of *PHACTR1*.[9] Obtaining the patient's informed consent, we analyzed a common SNP variation in the rs9349379[G] allele (*PHACTR1*), which has been reported to be associated with a higher risk of sCAD.[9]

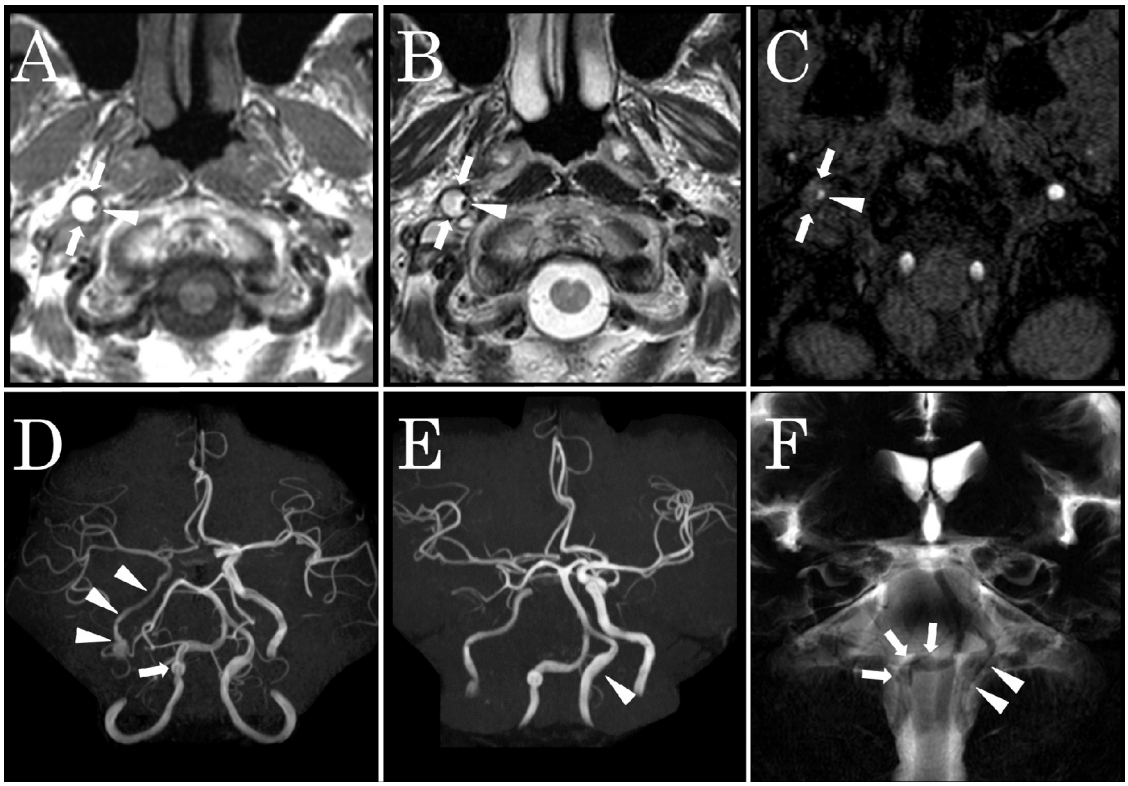

Figure 1. *Magnetic resonance image on admission. Right ICA dissection on axial T1-weighted imaging (A) and T2-weighted imaging (B) showing a typical eccentric hyperintense signal of the ICA in correspondence with the mural hematoma (arrow) surrounding the residual lumen (arrowhead). The external diameter of the right ICA is markedly enlarged in comparison with the left ICA. Additionally, MRA source imaging reveals hypointense signal of the mural hematoma in the right ICA (C, arrowhead). MRA shows a narrowing and reduced signal intensity in the right ICA and middle cerebral artery (D, arrowhead), a dissecting aneurysm of the right VA (D, arrow), and dilatation of the left VA (E, arrowhead) at the skull base. Basiparallel anatomical scanning shows bilateral VA dilatation (F; right VA, arrows; left VA, arrowheads). Abbreviations: ICA, internal carotid artery; MRA, magnetic resonance angiography; VA, vertebral artery.*