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Is the Presence of Headache Indispensable in Diagnosing Reversible Cerebral Vasoconstriction Syndrome?

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Dear Editor,

Reversible cerebral vasoconstriction syndrome (RCVS) is defined as a clinical and radiological syndrome comprising a diverse group of conditions including thunderclap headache (TCH) and reversible vasoconstriction of multifocal intracranial arteries.[1] TCH is the most prominent clinical feature of RCVS, but it has recently been recognized that a subset of RCVS patients present without the typical TCH.[2] The purpose of this report is to describe an atypical manifestation of RCVS that presented as a progressive cryptogenic stroke without a headache and to briefly review the current literature on the absence of headache in RCVS.

A 46-year-old woman visited an emergency room due to the sudden development of a visual field defect on the previous day. She had no medical history of conventional vascular risk factors or headache. She was not taking any medication, had not experienced recent trauma or abortion, and had not performed intense exercise at or before the time of presentation. Initial diffusion-weighted imaging (DWI) revealed a wedge-shaped acute cerebral infarction in the borderzone region between the left middle cerebral artery (MCA) and the posterior cerebral artery (Fig. 1A). Magnetic resonance angiography (MRA) showed diffuse multifocal intracranial stenoses with a strings-and-beads appearance. Perfusion MRI (time-to-peak map) showed multiple areas of perfusion delay that were mainly located in the bilateral borderzone regions. She had never complained of headache before or after her stroke event. We started her on dual antiplatelet therapy that included 300-mg loading doses of aspirin and clopidogrel.

On the 2nd day she reported sudden-onset lower limb weakness on her left side. Follow-up DWI showed a new ischemic stroke in the right anterior cerebral artery (ACA) territory, which was consistent with her new neurological deficit (Fig. 1B). Conventional angiography showed multifocal stenoses in the bilateral branches of the MCA and ACA, with poststenotic dilatation giving a beaded appearance (Fig. 1B). In addition to antithrombotic therapy, she was empirically treated with nimodipine. She took oral nimodipine (30 mg) three times daily, and there was no subsequent neurological deterioration or new neurological deficits. Routine stroke workup did not produce any finding related to cardioembolism or systemic embolism. Laboratory investigations yielded no evidence of either systemic vasculitis or other autoimmune diseases. CT angiography performed 2 weeks later revealed persistent diffuse intracranial stenoses (Fig. 1C). Antithrombotic and nimodipine therapy were continued for a 3-month period after the initial ischemic stroke. MRA performed at a 3-month follow-up showed complete resolution of the multifocal intracranial stenoses, and her treatment was discontinued. At 5 years after the index stroke she has not experienced a recurrent stroke or any headaches.

Given that vasoconstriction was reversed within 3 months, the ischemic stroke in this patient was certainly due to RCVS. A French study found that reversible vasoconstriction without the typical TCH was the only plausible cause in 13% of ischemic stroke patients aged

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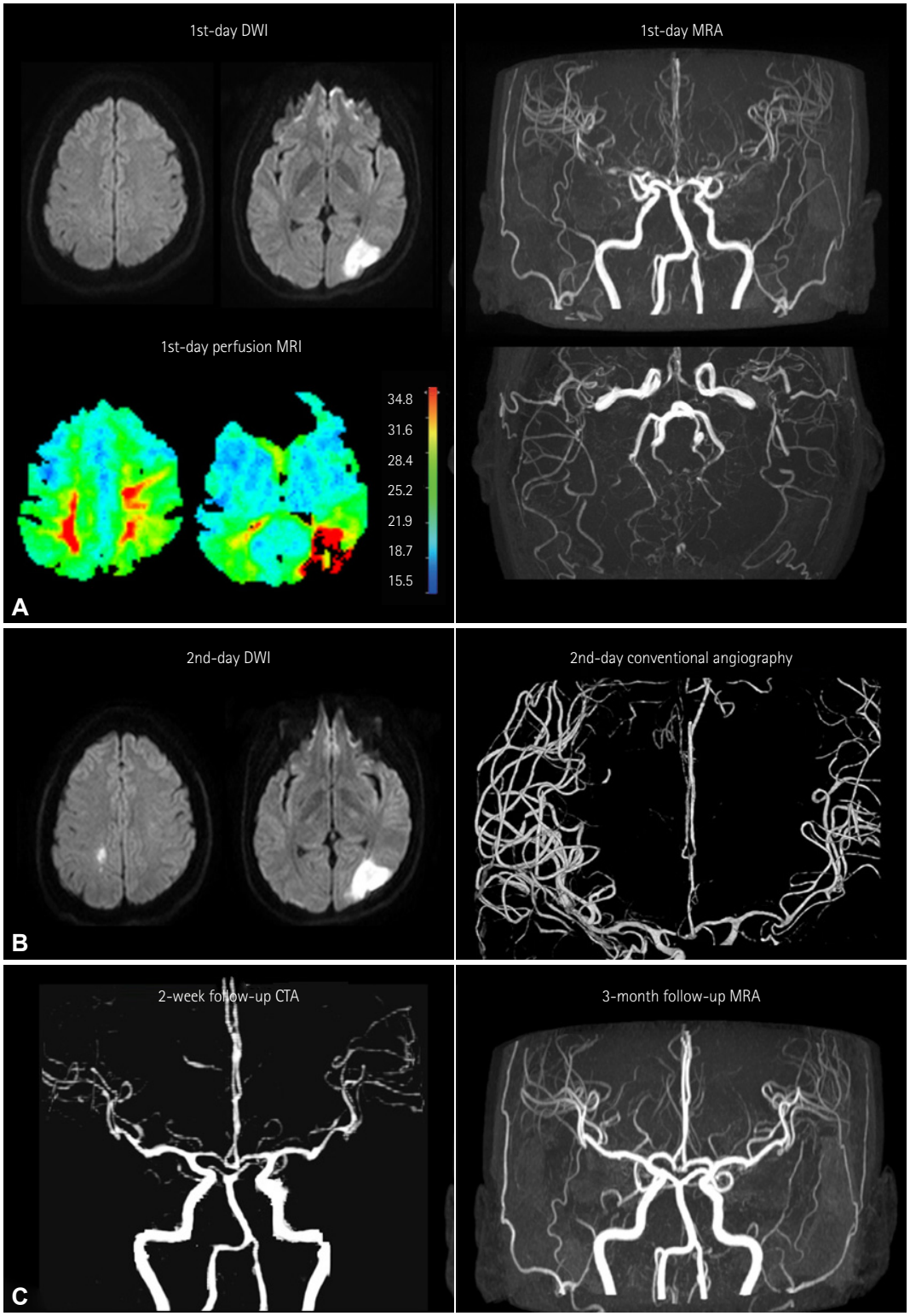

Fig. 1. Neuroimaging findings. A: Initial DWI revealed a wedge-shaped acute cerebral infarction in the borderzone region between the left MCA and posterior cerebral artery, and MRA revealed multifocal intracranial stenoses. Perfusion MRI (time-to-peak map) showed multiple areas with perfusion delay that were mainly located in the bilateral borderzone regions. B: DWI on the 2nd day showed a new ischemic stroke in the right ACA territory. There were multifocal stenoses in the bilateral branches of the MCA and ACA, with poststenotic dilatation presenting as a strings-and-beads appearance on conventional cerebral angiography. C: CTA performed 2 weeks after nimodipine treatment showed persistent multifocal intracranial stenoses, which had completely resolved in the 3-month follow-up MRA. ACA: anterior cerebral artery, CTA: computed tomography angiography, DWI: diffusion-weighted imaging, MCA: middle cerebral artery, MRA: magnetic resonance angiography.

<45 years.[3] Contrary to our patient, those other patients received only antithrombotic therapy instead of nimodipine, and no subsequent ischemic stroke occurred. Our case suggests that nimodipine is useful in stopping progressive ischemic stroke by RCVS, but the efficacy of nimodipine against the associated ischemic or hemorrhagic complications has not been proven.[4] Given that a subset of RCVS patients experience fulminant progressive strokes that produce a severely negative outcome,[1,2,4,5] further studies are required to identify the best treatment for such patients.

A recent review identified 87 RCVS patients without the typical TCH in 2 large series and 8 single-case reports.[2] Fifteen of these patients (17.2%) reported no headache. Among the 57 patients for whom detailed information was available on clinical and radiological features, various cerebral complications of ischemic stroke, subdural hematoma, cortical subarachnoid hemorrhage, intracerebral hemorrhage, and posterior reversible encephalopathy syndrome were reported in 54 patients (94.7%). Seven (87.5%) of eight patients without headache had ischemic stroke, and most of them had an excellent clinical outcome. However, 14 (28.5%) of 49 patients with headache had a poor outcome (modified Rankin Scale score of 3, persistent deficit, or death).

This report indicates that RCVS comprises a wider spectrum of headache and cerebrovascular disorders than previously though. RCVS should be considered a possible diagnosis in patients with cryptogenic stroke and other cerebral complications, with reversible angiographic abnormalities consistent with RCVS, regardless of the presence of headache.

Author Contributions

Conceptualization: Byung-Su Kim, Yun Kyung Park, Mun Kyung Sunwoo, Hyun-Jeung Yu, Eun Hye Jeong, Dae Yoon Kim. Investigation: Byung-Su Kim, Dae Yoon Kim. Supervision: Byung-Su Kim. Writing—original draft: Byung-Su Kim. Writing—review & editing: Byung-Su Kim, Yun Kyung Park, Mun Kyung Sunwoo, Hyun-Jeung Yu, Eun Hye Jeong, Dae Yoon Kim.

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Conflicts of Interest

The authors have no potential conflicts of interest to disclose.

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