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Aggravation of Acute Ischemic Stroke with Cerebral Hypoperfusion after Intravenous Propacetamol

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Dear Editor,

A 66-year-old male visited the emergency room due to the sudden onset of right hemiparesis. The patient reported that he had experienced intermittent right hemiparesis lasting 1−2 hours 2 months previously, and had been taking medication for diabetes mellitus. His muscle strength in the right lower extremity was measured as Medical Research Council (MRC) grade 4+. Brain magnetic resonance imaging (MRI) revealed an acute infarction in the border zone of the left middle cerebral artery (MCA). Total occlusion of the left internal carotid artery (ICA) and severe stenosis of the right proximal ICA were confirmed in brain magnetic resonance angiography. Severe hypoperfusion of the left MCA was also confirmed (Fig. 1A-C).

The patient had a first-ever fever reaching 38°C, and his blood pressure was 123/60 mm Hg on the third day of hospitalization. On the day of the visit, his high-sensitivity C-reactive protein level was 8.68 mg/L, the erythrocyte sedimentation rate was 52 mm/h, hemoglobin was 11.3 g/dL, and the lactate level was 2.5 mmol/L, which were all within the normal ranges. A chest X-ray obtained on the same day did not reveal any evidence of pneumonia. There was also no evidence of systemic dehydration. The quick sequential organ failure assessment score of the patient was 0 prior to intravenous propacetamol administration.

Two grams of intravenous propacetamol was administered to curb the patient's fever. After 2.5 hours his blood pressure had reduced to 88/50 mm Hg and his heart rate was 44 beats/minute. The only medication that could explain the decrease in blood pressure was propacetamol. At that time the patient was alert, his orientation was normal, SpO2 was 99% when breathing air, and his respiration rate was 17 breaths/min. Blood glucose was measured at 149 mg/dL in the random glucose test. Upon the occurrence of hypotension (systolic blood pressure <90 mm Hg), the subject did not show any skin symptoms (e.g., hives, itchiness, or tongue swelling), respiratory symptoms, or digestive symptoms. Additionally, unlike general allergic reactions, the hypotension of the subject occurred 2.5 hours after administering intravenous propacetamol. All these results suggested a low likelihood of anaphylaxis.

The muscle strengths of the patients in the right upper and lower extremities decreased to MRC grades 0 and 2, respectively, following the decrease in blood pressure. We increased the previously normal saline infusion rate by 40 mL/h, and 30 minutes later the muscle strengths in the right upper and lower extremities had improved to MRC grades 2 and 3, respectively. After 1 hour of infusion, the blood pressure had improved to 126/68 mm Hg. We performed brain MRI 20 minutes after the onset of motor aggravation, which revealed that the previous lesion now further extended around the MCA border zone (Fig. 1D).

Propacetamol is an antipyretic, nonopioid analgesic, and nonsteroidal anti-inflammatory drug (NSAID) that suppresses the cyclo-oxygenase pathway, but is associated with small peripheral anti-inflammatory and antiplatelet responses. Propacetamol induces hypoten-

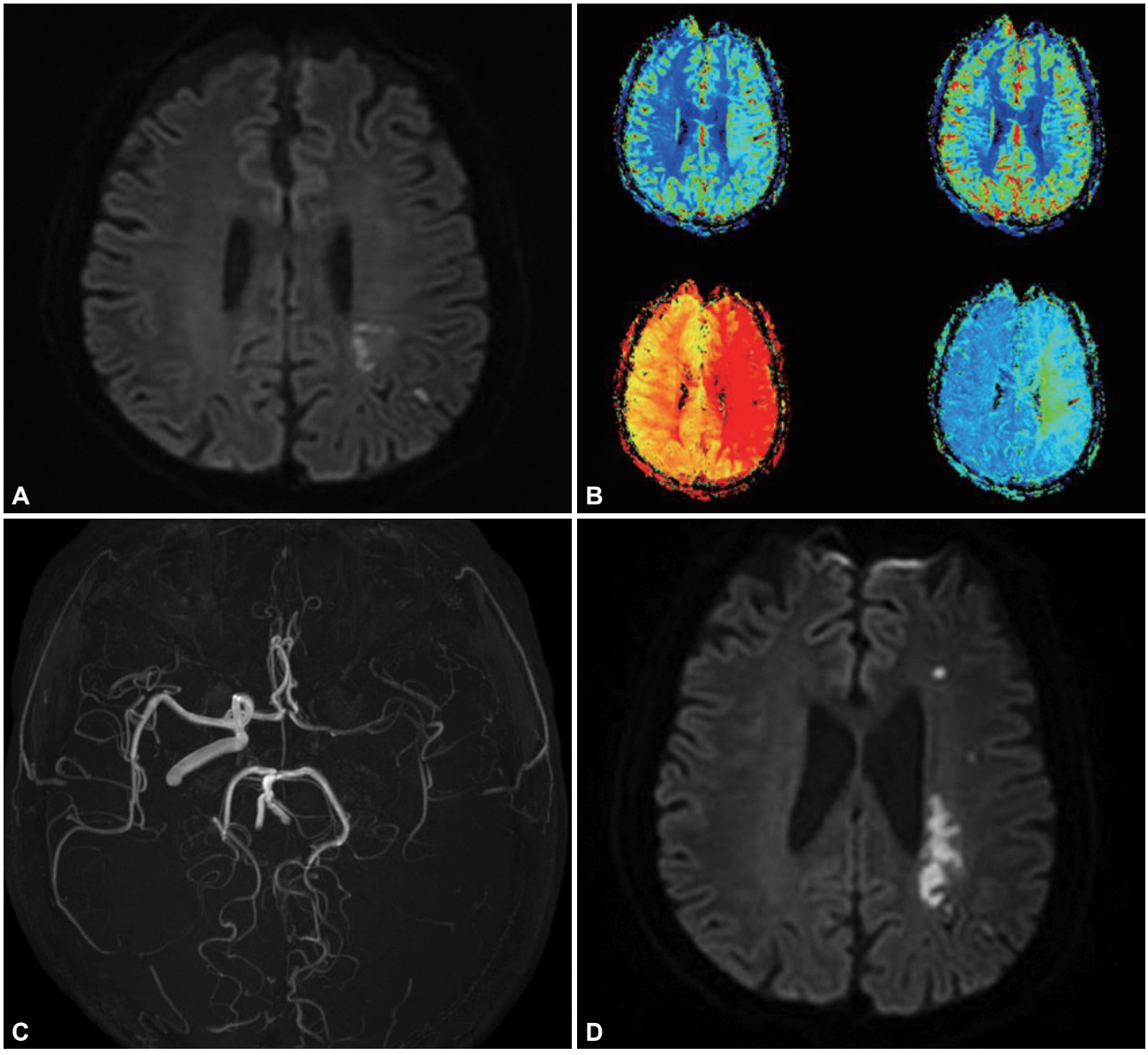

Fig. 1. Brain magnetic resonance imaging (MRI) upon entering the emergency room, and a blood-pressure-lowering event. A: Diffusion-weighted image shows a watershed-pattern high-signal-intensity lesion in the left parietal lobe. B: Brain perfusion image shows a decrease in perfusion in the left internal carotid artery region (left upper, negative integral; right upper, index map; left lower, time to peak; right lower, mean transit time). C: The left internal carotid artery was not visible on intracranial magnetic resonance angiography. D: Diffusion-weighted image taken after the blood-pressure-lowering event shows enlargement of the lesion in the left parietal region.

sion in approximately 1% of all patients,[1] but in up to 3.9% of patients with brain injury and 8.0% of those with severe sepsis.[2] The mechanism of propacetamol-induced hypotension has not yet been elucidated, but several hypotheses exist. Boyle et al.[3] proposed that the occurrence hypotension after administering intravenous paracetamol (a derivative of propacetamol) is associated with an increase in skin blood flow. Intravenous paracetamol reset the thermoregulatory set point in the body to radiate heat through vasodilation and sweating, and changes in skin blood flow can lead to changes in core blood pressure.

An ischemic lesion of the brain impairs autoregulation of the systemic blood pressure[4] so that it does not effectively respond to abrupt fluctuations of the blood pressure, leading to further brain damage. Hyperperfusion in the brain increases the risk of cerebral edema and hemorrhagic transformation.[5] On the other hand, hypoperfusion enlarges the area of the cerebral infarction, which can be devastating in patients with acute ischemic lesions and underlying hypoperfusion caused by ipsilateral ICA steno-occlusion. Fever commonly occurs in patients with cerebral infarction, and propacetamol is widely used as an antipyretic. In clinical practice, NSAIDs

are also widely used as antipyretics. However, NSAIDs can induce nephropathy, and they increase the risk of gastrointestinal bleeding when used with an antiplatelet agent. For these reasons, caution is needed when considering the administration of NSAIDs. A study of acute ischemic stroke found that the function outcome was better in the paracetamol administration group than in the placebo group.[6] However, propacetamol should be used with caution in patients with severe hypoperfusion and ipsilateral ICA stenosis or occlusion, since ischemic lesions may be aggravated by propacetamol-induced hypotension.

Author Contributions

Conceptualization: Chan-Hyuk Lee, Hyun Goo Kang. Data curation: Sang Yeon Kim, Byoung-Soo Shin. Formal analysis: Seung Jae Lee. Investigation: Sang Yeon Kim, Chan-Hyuk Lee, Seung Jae Lee. Methodology: Byoung-Soo Shin, Hyun Goo Kang. Supervision: Byoung-Soo Shin, Hyun Goo Kang. Validation: Chan-Hyuk Lee, Hyun Goo Kang. Visualization: Seung Jae Lee. Writing—original draft: Chan-Hyuk Lee, Sang Yeon Kim. Writing—review & editing: Byoung-Soo Shin, Hyun Goo Kang.

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Conflicts of Interest

The authors have no potential conflicts of interest to disclose.

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