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Case Report

A Child with Paradoxical Cerebral Embolism in Whom Mechanical Thrombectomy Led to a Favorable Outcome

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Objective: We report a case of paradoxical cerebral embolism caused by patent foramen ovale (PFO) that was treated by the direct aspiration first pass technique (ADAPT).

Case Presentation: The case involved a 12-year-old boy who had symptoms of dizziness and vomiting the day prior to being admitted to the emergency department. The following morning, consciousness disorder, dysarthria, and right paresis were observed, and he was transferred to our hospital. Computed tomography (CT) and magnetic resonance imaging (MRI) lead to the diagnosis of acute cerebral infarction due to basilar artery (BA) occlusion. Mechanical thrombectomy was performed, and Thrombolysis in Cerebral Infarction (TICI) 3 was obtained. Postoperatively, his consciousness was improved, but echocardiography revealed PFO. Percutaneous PFO closure was performed at our department of pediatric cardiology.

Conclusion: For our patient with paradoxical cerebral embolism of the BA caused by PFO more than 6 hours after onset, mechanical thrombectomy with ADAPT using a Penumbra 5MAX ACE68 resulted in a good outcome.

Keywords ▶ pediatric acute ischemic stroke, mechanical thrombectomy, basilar artery occlusion

Introduction

Currently, it is recommended that mechanical thrombectomy be preferentially performed to treat acute cerebral embolism related to anterior circulation major artery occlusion (internal carotid artery, middle cerebral artery) within 6 hours after onset by the guidelines established in Japan. Based on the results of the DAWN[1] and DEFUSE3[2] trials, acute-phase mechanical thrombectomy is indicated even for patients with anterior circulation occlusion ≥6 hours after onset when they meet the indication criteria. However, this applies to adult patients aged ≥18 years; in the field of pediatrics, only a few case reports have been published. Furthermore, the incidence of childhood cerebral infarction is approximately 1.6/100000 persons/year[3]; this disease is rare, and the possibility that diagnosis may be delayed has been proposed. We report a patient in whom the direct aspiration first pass technique (ADAPT) was selected to treat paradoxical cerebral embolism of the basilar artery (BA) related to the patent foramen ovale (PFO) ≥6 hours after onset.

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Case Presentation

Patient: A 12-year-old boy.
Complaints: Consciousness disorder, and weakness of the right upper and lower limbs.
Medical history: Not contributory.
Height: 159 cm, Body weight: 52 kg.
Early developmental history: No developmental disorder.
Present illness: On Y-month Z-day, X-year, vertigo and vomiting were noted during chorus training at an elementary school at 15:00. He rested at home. He fell asleep at 22:00. Consciousness disorder and right incomplete paralysis were observed upon waking up at 6:00 the following day, and he was brought to the Emergency Outpatient Unit of our hospital by ambulance at 6:56.

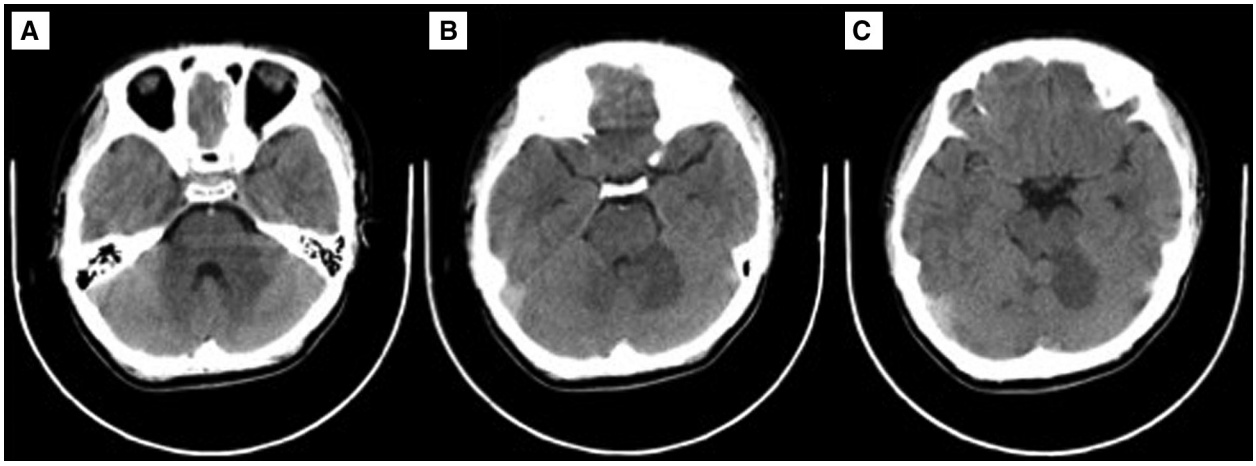

Fig. 1 Plain CT showed a hyper-dense sign at the BA end. (**A**) In the left SCA region, a low-density area was observed. (**B**) In the left cerebral peduncle, a low-density area was also detected. BA: BA: basilar artery; CT: computed tomography; SCA: superior cerebellar artery

Physical examination on arrival: The Japan Coma Scale (JCS) score was I-1. Dysarthria, left ataxia, and right incomplete paralysis were observed. The National Institutes of Health Stroke Scale (NIHSS) score was 7.

Imaging procedures on arrival: Cephalic computed tomography (CT) demonstrated a low-density area in the left superior cerebellar artery (SCA) region and a hyper-dense sign of the BA (**Fig. 1A–1C**). The posterior circulation Alberta Stroke Programme Early CT Score (pc-ASPECTS) was 8. Considering the need for more accurate evaluation of the condition, cephalic magnetic resonance imaging (MRI) was subsequently performed. On diffusion-weighted imaging, diffuse high signal intensities in the bilateral midbrain cerebral peduncles, left SCA region, and bilateral cerebellar hemispheres were observed. T2-weighted fluid-attenuated inversion recovery (FLAIR) images also exhibited high signal intensities at the same sites. Magnetic resonance angiography (MRA) revealed a defect in the signal intensity involving the BA trunk to the end. On basi-parallel anatomical scanning (BPAS), wall irregularity of the left or right vertebral arteries (VAs) to BAs was not noted (**Fig. 2A–2F**).

Course after admission: These examinations suggested posterior circulation cerebral infarction. As diseases to be differentiated, embolism or BA dissection was suspected, and cerebral angiography was scheduled. As the interval from onset until arrival to our hospital was 16 hours, intravenous thrombolysis with recombinant tissue plasminogen activator (IV-rtPA) was not conducted. At 11:01, cerebral angiography was performed under general anesthesia. At this point, the consciousness level was reduced to a JCS score of II-10. The right inguinal region was punctured. On left subclavian arteriography, the left VA was visualized, but the BA trunk to end was not visualized, as demonstrated on MRA. Three-dimensional (3D) angiography revealed a crab-claw-like defect at the BA end, leading to a diagnosis of embolism (**Fig. 3A** and **3B**). On left and right common carotid angiography, the posterior communicating artery-mediated visualization of the posterior cerebral artery was favorable on both sides, and collateral pathways were advanced. However, there was a gradual decrease in the consciousness level (JCS score: ≥10) in comparison with that on arrival, suggesting top of the BA syndrome. Mechanical thrombectomy using ADAPT was selected. As a suction catheter, a Penumbra 5MAX ACE68 (outer diameter: 2.06 mm, MEDICO'S HIRATA INC., Osaka) was used because the vascular lumen diameter of the left VA to BA access route was approximately 2.2–2.4 mm on 3D angiography. A 6Fr FUBUKI (Asahi Intecc Co., Ltd., Aichi, Japan) was inserted into the left VA through the right inguinal region. As a microguidewire, a CHIKAI BLACK 18 (Asahi Intecc Co., Ltd.) was selected and a Marksman microcatheter (Japan Medtronic, Tokyo, Japan) was guided to the site of occlusion (**Fig. 3C**). Following this system, the ACE68 was carefully guided to the site of suction to prevent a thrombus from being pushed in (Fig. 3D). Suction was conducted, and the system was slowly pulled to not miss a thrombus. A dark red thrombus was retrieved (12:01). A single session of this procedure led to complete recanalization (Thrombolysis in Cerebral Infarction (TICI) grade: 3) (**Fig. 3E** and **3F**). The onset to door time was 956 minutes. The door to puncture time was 245 minutes. The puncture to recanalization time was 60 minutes.

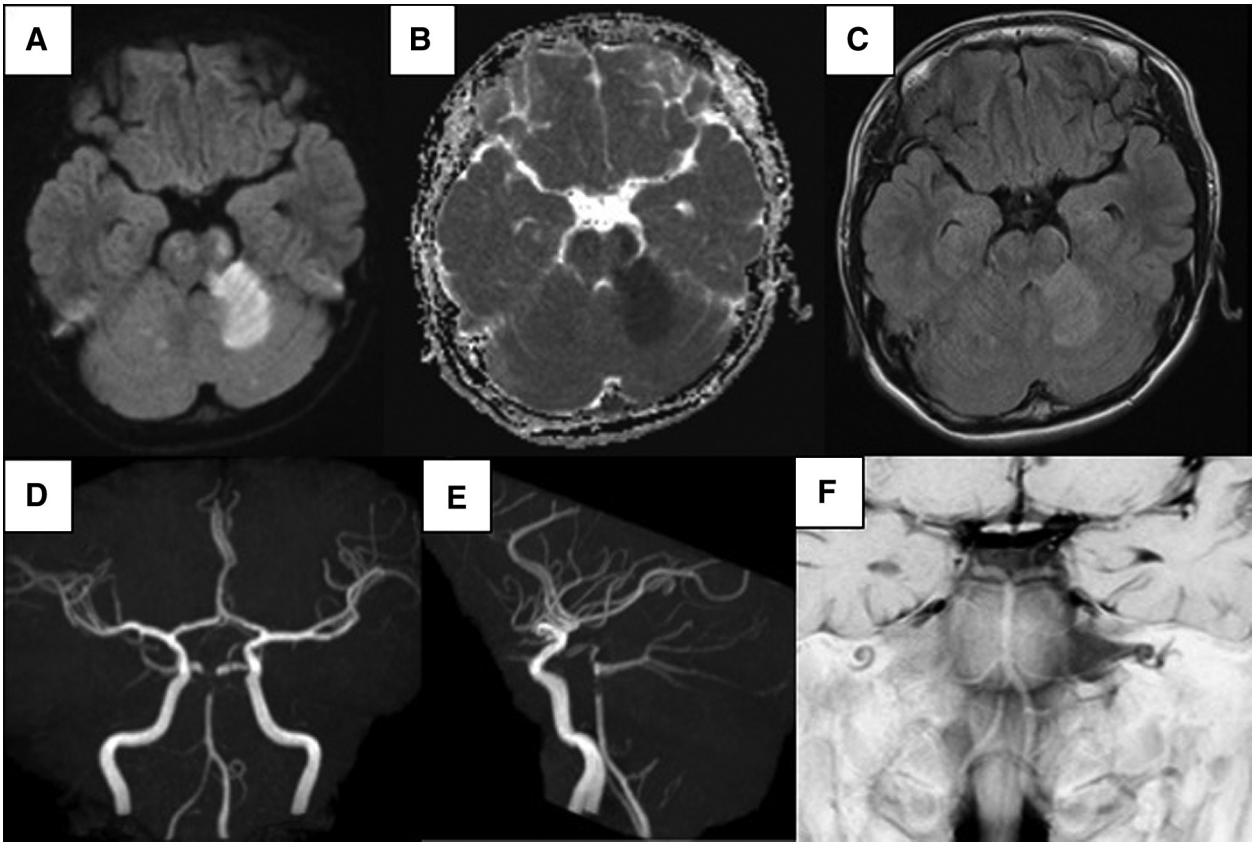

Fig. 2 DWI showed high-signal-intensity areas in the left SCA region and left cerebral peduncle. (**A**) ADC showed low-signal-intensity areas in the left SCA region and left cerebral peduncle. (**B**) T2-FLAIR showed high-signal-intensity areas in the left SCA region and left cerebral peduncle. (**C**) On MRA, the BA end was not visualized. (**D**) Similar to C. (**E**) BPAS did not show wall irregularity of the left or right VAs to BAs. ADC: apparent diffusion coefficient; BAs: basilar arteries; BPAS: basi-parallel anatomical scanning; DWI: diffusion-weighted imaging; FLAIR: fluid-attenuated inversion recovery; MRA: magnetic resonance angiography; SCA: superior cerebellar artery; VAs: vertebral arteries

Pathologically, the embolus was diagnosed as a fibrin thrombus. Postoperative cephalic MRI-diffusion-weighted imaging (DWI) did not demonstrate any new high-signal-intensity areas in comparison with the preoperative findings (**Fig. 4A**). Cephalic MRA confirmed recanalization of the BA (**Fig. 4B** and **4C**).

After surgery, the presence of lower limb venous thrombosis, arrhythmia, or aortic lesions, and thrombotic predispositions were investigated, but there was no significant finding. However, transesophageal ultrasonography was performed at the pediatric cardiovascular department of our hospital considering the possibility of intracardiac shunt disease. PFO was detected. Furthermore, a bubble test with the Valsalva maneuver demonstrated shunt blood flow from the right atrium to the left atrium under an intrathoracic pressure of PEEP 30 cmH2O, suggesting the involvement of PFO-mediated paradoxical embolism in cerebral infarction. Subsequently, percutaneous closure of the foramen ovale was performed, and the oral administration of aspirin, as an antiplatelet drug, was started.

Immediately after surgery, the JCS score was 10 under the influence of general anesthesia. The consciousness level improved to a JCS score of 0 the day after surgery, but left ataxia remained. The modified Rankin Scale (mRS) score was 3 and the boy was referred to a rehabilitation hospital 30 days after surgery.

Outcome: After discharge from the rehabilitation hospital, follow-up was performed at the outpatient clinic. The oral administration of aspirin was completed 6 months after surgery. Functional recovery was achieved, with an mRS score of 0. The course involving his school life has been favorable.

Discussion

The number of case reports or reviews on mechanical thrombectomy in children is limited. However, according to a review on mechanical thrombectomy in children published by Satti et al.,[4] TICI 2b/3 recanalization was achieved in 75.9% of 29 anterior/posterior-circulation-affected children,

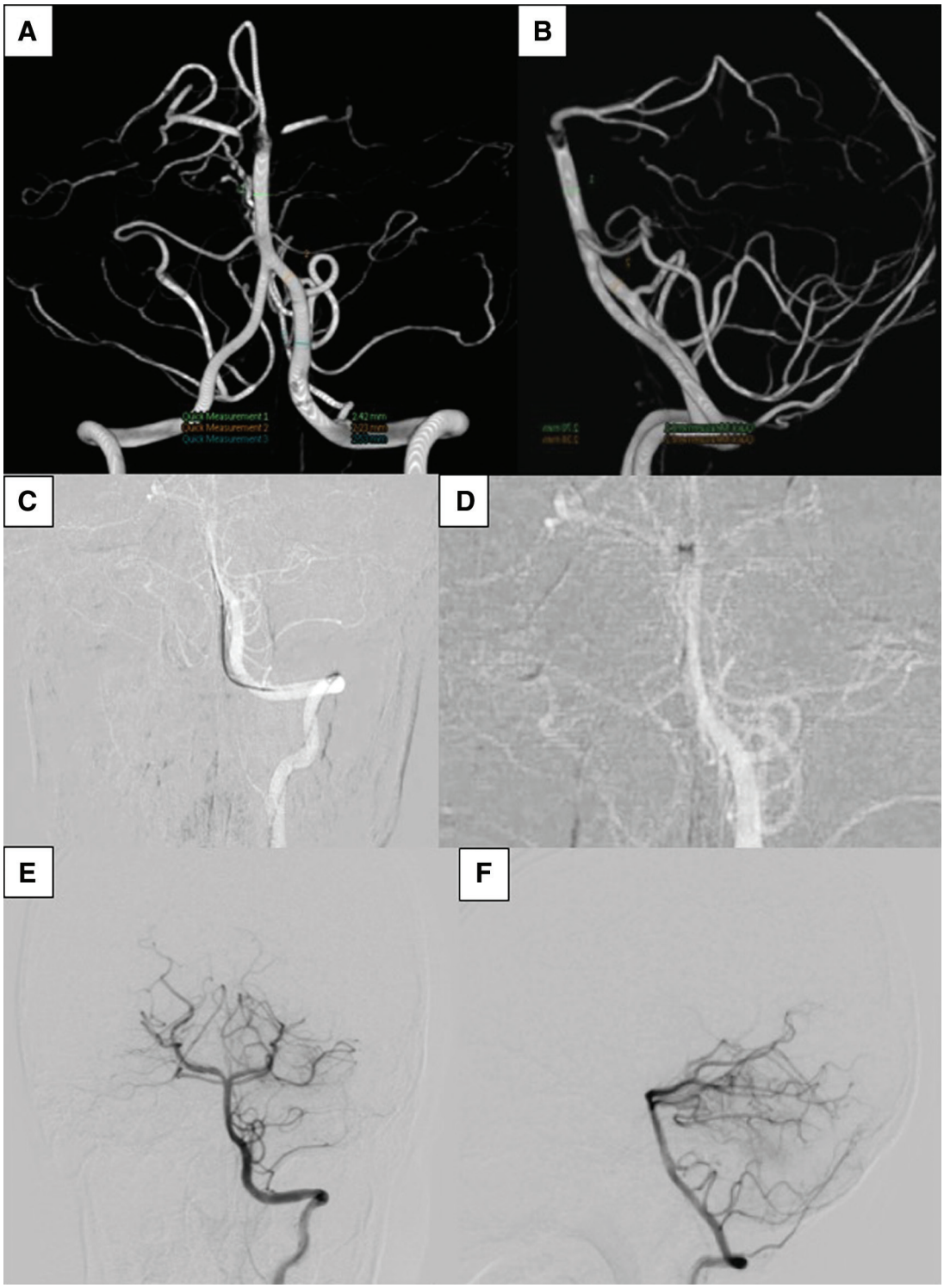

Fig. 3 (**A**) 3D angiography showed a crab-claw-like defect at the BA end. Furthermore, the vascular lumen diameter was measured on frontal and lateral views. (**B**) Similar to A. (**C**) An ACE68 was guided using a system consisting of a CHIKAI black and Marksman. (**D**) An ACE68 was guided using a system consisting of a CHIKAI black and Marksman such that it was not guided beyond the site of embolism. It was gently guided to avoid pushing in a thrombus. (**E**) Final postoperative DSA for confirmation. Frontal view. (**F**) Final postoperative DSA for confirmation. Lateral view. BA: basilar artery; DSA: digital subtraction angiography

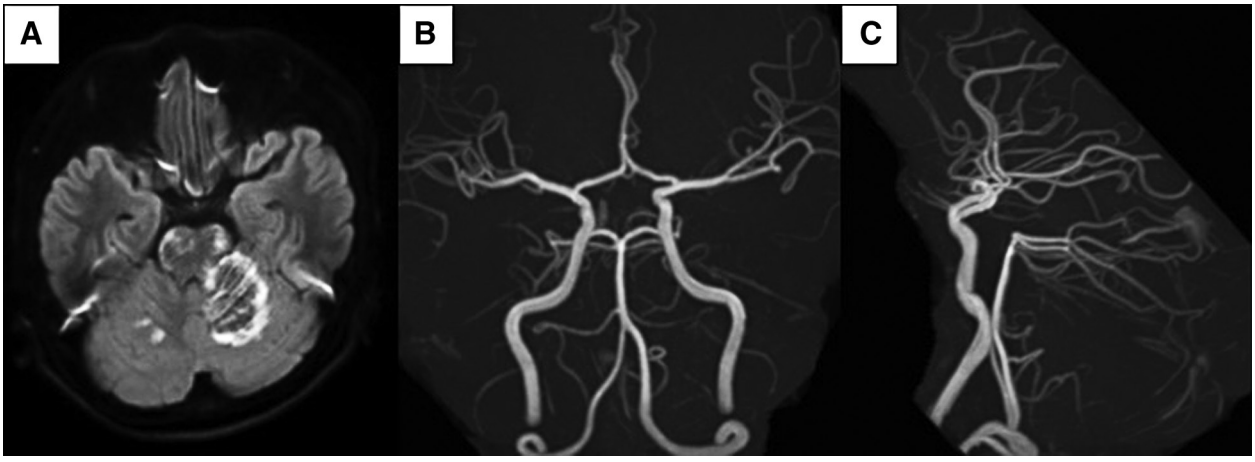

Fig. 4 (**A**) Postoperative MRI-DWI revealed no fresh infarcted focus in the brain. (**B**) MRA confirmed that recanalization at the BA end was maintained. (**C**) Similar to B. BA: basilar artery; MRA: magnetic resonance angiography; MRI-DWI: magnetic resonance imaging diffusion-weighed imaging

and there were no procedure-related complications. Concerning the functional prognosis, it was reported that the mRS score was ≤2 in 86.7%. Even in children, mechanical thrombectomy may improve the prognosis. Furthermore, as a background factor in such a small number of patients, childhood cerebral infarction is rare, and its incidence in Japan is reportedly approximately 1.6/100000 persons/year,[3] being low. As such, detection may be delayed in comparison with adults with cerebral infarction. The possibility of a diagnosis of major artery occlusion being made within 6 hours after onset, as described in the guidelines, may be low. According to the above review, ≥24 hours were required until mechanical thrombectomy in 3 children. In the present case, the interval from onset until mechanical thrombectomy was 21 hours.

Regarding the time window for indicating mechanical thrombectomy, the DAWN[1]/DEFUSE3[2] trials, whose results were published in 2018, revealed that the prognosis in the mechanical thrombectomy group was favorable, depending on the penumbra region, even when the interval from onset until mechanical thrombectomy was 6–24 or 6–16 hours, although these trials involved only anterior-circulation-system-affected adults. Based on these trials, the indication of mechanical thrombectomy for a larger number of patients is described as follows in the treatment guidelines in Japan[5]: "Among patients with cerebral infarction possibly associated with acute occlusion of the internal carotid artery (ICA) or at the M1 segment of the middle cerebral artery (MCA) >6 hours after the final confirmation of a healthy state, the start of this therapy within 16 hours after the final confirmation of a healthy state is strongly recommended for those with an mRS score of 0 or 1 before onset, NIHSS score of ≥10, and ASPECTS of ≥7 on diffusion-weighted MRI (Grade A). Furthermore, the start of this therapy within 24 hours after the final confirmation of a healthy state is recommended for patients in whom there is a mismatch between the core volume of ischemia on cephalic CT perfusion or diffusion-weighted MRI and neurological symptoms or a perfusion-delayed area on perfusion images (Grade B)." Regarding the time window for indicating mechanical thrombectomy for major artery occlusion of the posterior circulation system, as demonstrated in the present case, there is little evidence. However, Lindsberg et al.[6] reported that when posterior communicating artery-mediated blood flow from the anterior circulation system was sufficient, thrombosis of the BA did not frequently lead to embolism at the BA end due to blood flow, suggesting that posterior circulation system ischemia progression over time is slower than anterior circulation system ischemia progression. Furthermore, Alemseged et al.[7] evaluated the thrombus size and collateral pathway using scoring systems, such as the Basilar Artery on Computed Tomography Angiography (BATMAN) score and Posterior Circulation Collateral Score (PC-CS), with respect to the visualization of the posterior communicating artery and posterior circulation blood vessels on contrast-enhanced cephalic CT at the time of onset, and suggested that the functional prognosis after mechanical thrombectomy is improved when the score is high even in patients with an interval of ≥6 hours from onset. In the present case, CT angiography (CTA) was not conducted and the scoring of MRA findings on arrival demonstrated sufficient collateral flow. As the pathogenesis, a thrombus of the BA may have initially induced occlusion of the left SCA, leading to cerebellar infarction, and

causing vomiting and vertigo. In addition, there may have been a time lag until the thrombus reached the distal BA with the development of a collateral pathway from the posterior communicating artery, resulting in top of the BA syndrome the day after onset. Therefore, mechanical thrombectomy may improve the prognosis based on the imaging and physical findings.

In the present case, consciousness disorder progressed after arrival; therefore, a thrombus may have gradually led to embolism at the BA end. Based on digital subtraction angiography (DSA) findings concerning posterior circulation system blood flow, a collateral pathway from the anterior circulation system may have been maintained. This may also have been a factor for the widened time window for indicating mechanical thrombectomy. On the other hand, Puetz et al.[8] prepared the pc-ASPECTS, which reflects the scoring of prognostic factors for the posterior circulation system, and reported that the prognosis was poor despite recanalization in patients with a score of ≤8. In the present case, the pc-ASPECTS was 8 and the possibility of a poor prognosis despite recanalization was considered, but the above findings suggested sufficient collateral flow and mechanical thrombectomy was performed.

In addition, Gory et al.[9] found that the complete recanalization rate after mechanical thrombectomy for BA embolism using ADAPT as a first-choice technique was higher than that after mechanical thrombectomy with a stent retriever, and that the incidence of complications was lower. In the present case, mechanical thrombectomy using ADAPT was also performed and one pass led to TICI 3 complete recanalization. According to the above report, new embolism in a non-occluded vascular area (embolism to new territory (ENT)) accounted for the greater proportion of complications, and its incidence was significantly lower after mechanical thrombectomy using ADAPT. In the present case, when guiding an ACE68 to the thrombus and pulling out a Marksman, attention was paid to avoid the ACE68 pushing a thrombus into the BA end through migration to the periphery. Furthermore, the ACE68 was slowly pulled to prevent the thrombus from separating, thereby preventing ENT.

Delgado Almandoz et al.[10] previously reported that the use of a suction catheter with a larger diameter for ADAPT led to a reduction in the interval until recanalization and an increase in the recanalization rate in patients with anterior circulation major artery embolism. In the present case, we measured the vascular diameter of an access route to the thrombus using 3D angiography considering the risk of vascular injury related to suction-catheter insertion, which may depend on the vascular diameter of the access route in children, and confirmed that a suction catheter with the largest diameter (ACE68) among such catheters available in our hospital at that time was available.

Only a few studies have reported percutaneous PFO closure for PFO-related paradoxical cerebral embolism in children with cerebral infarction, as demonstrated in the present case. Benedik et al.[11] performed percutaneous PFO closure in children, aged 2–17 years, with PFO and idiopathic cerebral infarction, and emphasized that this procedure should be considered in such patients. Furthermore, Sondergaard et al.[12] reported that the recurrence rate after the combination of PFO closure and antiplatelet therapy was lower than that after the latter alone in adults aged 18–60 years with paradoxical cerebral embolism complicated by PFO. In the present case, transesophageal ultrasonography revealed PFO and percutaneous PFO closure was performed at the pediatric cardiovascular department of our hospital. Aspirin was orally administered for 6 months. There was no recurrence.

Conclusion

We performed mechanical thrombectomy using ADAPT with a Penumbra 5MAX ACE68 for PFO-related childhood paradoxical cerebral embolism of the BA ≥6 hours after onset, leading to a favorable outcome.

Disclosure Statement

The authors declare no conflicts of interest.

References

1) Nogueira RG, Jadhav AP, Haussen DC, et al: Thrombectomy 6 to 24 hours after stroke with a mismatch between deficit and infarct. *N Engl J Med* 2018; 378: 11–21.
2) Albers GW, Marks MP, Kemp S, et al: Thrombectomy for stroke at 6 to 16 hours with selection by perfusion imaging. *N Engl J Med* 2018; 378: 708–718.
3) Satoh S, Shirane R, Yoshimoto T: Clinical survey of ischemic cerebrovascular disease in children in a district of Japan. *Stroke* 1991; 22: 586–589.
4) Satti S, Chen J, Sivapatham T, et al: Mechanical thrombectomy for pediatric acute ischemic stroke: review of the literature. *J Neurointerv Surg* 2017; 9: 732–737.
5) The Japan Stroke Society, et al: Guidelines for the adequate use of devices for percutaneous transluminal mechanical thrombectomy. Third version. 2018. (in Japanese)

6) Lindsberg PJ, Pekkola J, Strbian D, et al: Time window for recanalization in basilar artery occlusion: Speculative synthesis. *Neurology* 2015; 85: 1806–1815.
7) Alemseged F, Van der Hoeven E, Di Giuliano F, et al: Response to late-window endovascular revascularization is associated with collateral status in basilar artery occlusion. *Stroke* 2019; 50: 1415–1422.
8) Puetz V, Sylaja PN, Coutts SB, et al: Extent of hypoattenuation on CT angiography source images predicts functional outcome in patients with basilar artery occlusion. *Stroke* 2008; 39: 2485–2490.
9) Gory B, Mazighi M, Blanc R, et al: Mechanical thrombectomy in basilar artery occlusion: influence of reperfusion on clinical outcome and impact of the first-line strategy (ADAPT vs stent retriever). *J Neurosurg* 2018; 129: 1482–1491.
10) Delgado Almandoz JE, Kayan Y, Wallace AN, et al: Larger ACE 68 aspiration catheter increases first-pass efficacy of ADAPT technique. *J Neurointerv Surg* 2019; 11: 141–146.
11) Benedik MP, Zaletel M, Meglic NP, et al: Patent foramen ovale and unexplained ischemic cerebrovascular events in children. *Catheter Cardiovasc Interv* 2007; 70: 999–1007.
12) Søndergaard L, Kasner SE, Rhodes JF, et al: Patent foramen ovale closure or antiplatelet therapy for cryptogenic stroke. *N Engl J Med* 2017; 377: 1033–1042.