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Case report

Primary mechanical thrombectomy for anterior circulation stroke in children: Report of two cases and literature review

Ayu Yoniko Christi [a], Nur Setiawan Suroto [a,*], Zaky Bajamal [b], Asra Al Fauzi [a]

[a] Department of Neurosurgery, Faculty of Medicine, Universitas Airlangga - Dr. Soetomo General Academic Hospital, 60286 Surabaya, Indonesia
[b] Department of Neurosurgery, PHC Hospital, 60165 Surabaya, Indonesia

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ABSTRACT

Introduction and importance: Pediatric acute ischemic stroke is a rare but devastating condition with substantial rates of morbidity and mortality. Endovascular treatment is standard acute revascularization therapy for stroke in adults, but it is not well-studied in pediatrics. We report the successful treatment of two pediatric cases of anterior circulation stroke with primary mechanical thrombectomy.

Case presentation: Two Asian children, aged 13 and 8 years, presented to Dr. Soetomo General Academic Hospital in September 2020 and April 2021, respectively, with hemiplegia and significant Pediatric National Institutes of Health Stroke Scale (Ped NIHSS) scores. Head CT scans demonstrated hyperdense middle cerebral artery signs, suggesting large-vessel occlusion stroke. Both patients underwent emergent thrombectomy within 5 and 10 h after initial onset, and successful recanalization was achieved within an hour. Both demonstrated good neurological recovery and there was no recurrent stroke during follow-up.

Clinical discussion: Thrombectomy has appeal for childhood acute ischemic stroke (AIS) due to a longer post-stroke time window for intervention. As the short-term outcome, a significantly reduced Ped NIHSS score is achieved. Long-term outcomes are measured by modified Rankin Scale (mRS) scores. A literature review from 2016 to 2021 yielded 21 pediatric case reports of primary mechanical thrombectomy for anterior circulation stroke (including the present cases). We compare our cases with the published literature to discuss the short-term and long-term outcomes.

Conclusion: Mechanical thrombectomy holds promise as a treatment modality in pediatric AIS. These case reports described successful primary mechanical thrombectomy for AIS treatment in children.

1. Introduction

Pediatric acute ischemic stroke (AIS) is uncommon, affecting only an estimated 2 to 6 per 100,000 children annually [1]. However, the rates of mortality and neurological morbidity in childhood stroke are substantial [2]. Stroke is among the top 10 causes of death in children, with a reported mortality for AIS ranging from 7% to 28% [2]. Sixty percent of the children who survive stroke have residual neurological deficits that cause social and personal burdens [1,2]. The etiologies of AIS in children differ significantly from stroke in adults, with congenital or acquired heart disease as the most common risk factors; hypercoagulable or autoimmune disorders and arteriopathies (arterial dissection, Moyamoya syndrome, and vasculitis) are less frequent risk factors [1]. Endovascular treatment (EVT) is the standard acute revascularization therapy for AIS in adults and has potential appeal for childhood AIS due to its longer post-stroke time window for intervention [3]. In this article, we presented two cases of pediatric stroke with large vessel occlusion (LVO) that were successfully treated with mechanical thrombectomy. We also conducted a review of the published literature on primary mechanical thrombectomy in pediatric stroke. Although complete individual patient data from the published literature are not available for all patients, our aim was to summarize and discuss the EVT characteristics, as well as the neurological outcomes. The work has been reported according to SCARE 2020 criteria [4]. Written consent was obtained from the patients' families for publication of this case report and accompanying images.

* Corresponding author at: Department of Neurosurgery, Faculty of Medicine, Universitas Airlangga - Dr. Soetomo General Academic Hospital, 6-8, Prof. Dr. Moestopo, Surabaya 60286, Indonesia.
E-mail address: nur.setiawan.suroto-2016@fk.unair.ac.id (N.S. Suroto).

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2. Presentation of cases

2.1. Case 1

A previously healthy 13-year-old Asian girl presented to the emergency department (ED) of Dr. Soetomo General Academic Hospital in September 2020 with a chief complaint of sudden headache, followed by left-sided face, arm, and leg weakness. She also complained of difficulty swallowing while drinking. The patient arrived at our ED 1 h after initial onset. The patient had a history of varicella infection (chickenpox) one month prior to admission that healed without any medicine. She did not have any other past illnesses or surgical history. On examination, her initial Pediatric National Institutes of Health Stroke Scale (Ped NIHSS) score was 10. Her weight was 40 kg, her blood pressure was 122/70 mmHg, her pulse was 72 beats/min, her respiratory rate was 20 breaths/min, and the patient was afebrile. Neurological examination showed left hemiplegia. Cranial nerve examination showed slightly anisocoric pupils with diameters of 3 mm and 3.5 mm on the right and left pupil, respectively. She also demonstrated minor paralysis of the facial nerve. A head computed tomography (CT) scan without contrast (Fig. 1) performed within 1 h of arrival demonstrated hyperdensity of 55 Hounsfield units (HU) of the distal right M1 middle cerebral artery (MCA) around the bifurcation, suggestive of a hyperacute thromboembolic stroke.

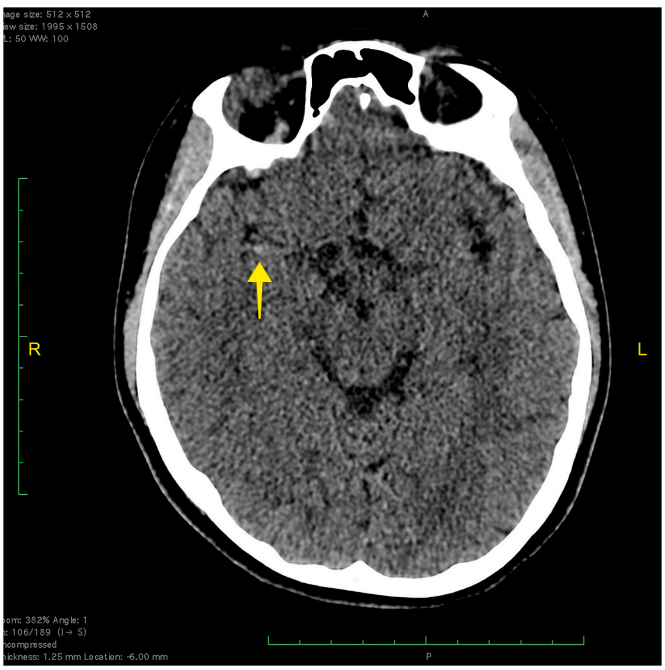

Fig. 1. Head CT scan (non-contrast) showed hyperdensity (yellow arrow) of the distal right M1 segment of the MCA.

The patient was taken for EVT, and a groin puncture was performed 5 h after her presentation to the ED. Digital subtraction angiography (DSA) was conducted under general anesthesia. An angiogram of the right internal carotid artery confirmed occlusion on the superior M2 division of the right MCA (white arrow, Fig. 2A). Primary mechanical thrombectomy (MT) was performed by our endovascular neurosurgeon, and a successful recanalization (modified thrombolysis in cerebral infarction 2B, mTICI 2B) was achieved (white arrow, Fig. 2B) in 64 min.

In the pediatric intensive care unit (PICU) of Dr. Soetomo General Academic Hospital, the patient underwent a head CT scan evaluation within 24 h after thrombectomy and showed no abnormal hyperdense or hypodense lesion on the brain parenchyma. Both pupils were isochor, with a diameter of 3 mm. No hematoma or bleeding on her groin puncture site was reported. By hospitalization Day 2, her initial left hemiplegia had improved markedly and her Ped NIHSS score had decreased to 7. A cardiologist consultation was advised, and echocardiography revealed no intracardiac thrombus. During hospitalization from Day 1 to Day 6, she was started on dopamine at 3 μg/kg/min (Indop, Fahrenheit, Jakarta, Indonesia) to achieve a systolic blood pressure of 120–140 mmHg. On hospitalization Day 4, a follow-up arterial spin labeling (ASL) magnetic resonance imaging (MRI) (Fig. 3) showed increased cerebral blood flow (CBF) around the infarcted area, suggestive of luxury perfusion. As part of her stroke treatment, she was started on oral acetylsalicylic acid 80 mg (Aspilets, Darya-Varia, Jakarta, Indonesia) once a day and oral atorvastatin calcium 20 mg (Truvas, Kalbe Farma, Jakarta, Indonesia) once a day. By hospitalization Day 9, the patient still had weakness in her left arm but showed modest improvement in the left facial droop. She was discharged the following day for outpatient rehabilitation with a Ped NIHSS score of 1. Good neurological recovery was observed with a Modified Rankin Scale (mRS) score of 1 at the second- and six-month follow-up, with no evidence of recurrent stroke.

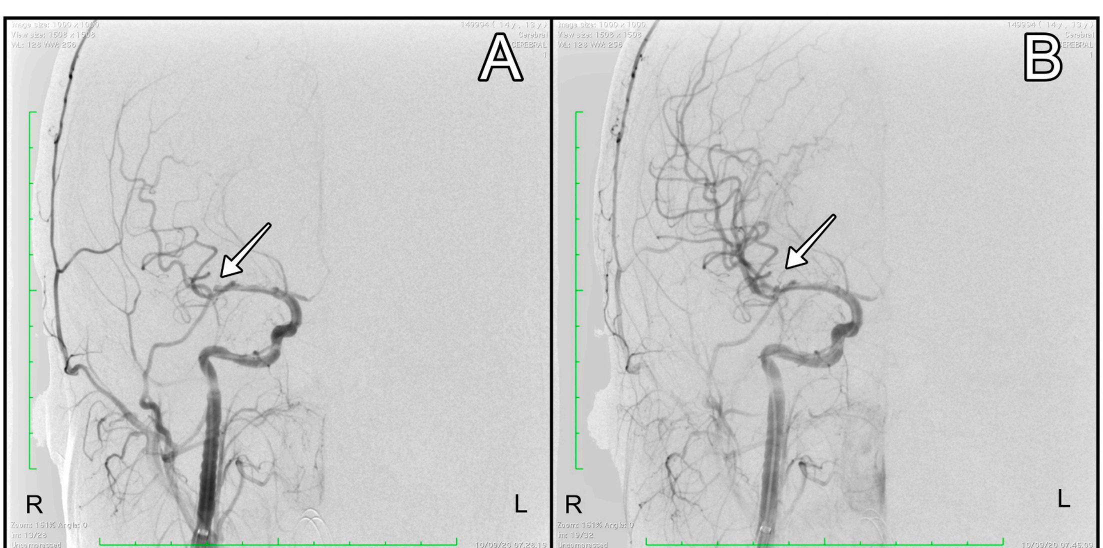

Fig. 2. (A) Pre-thrombectomy angiogram and (B) post-thrombectomy angiogram.

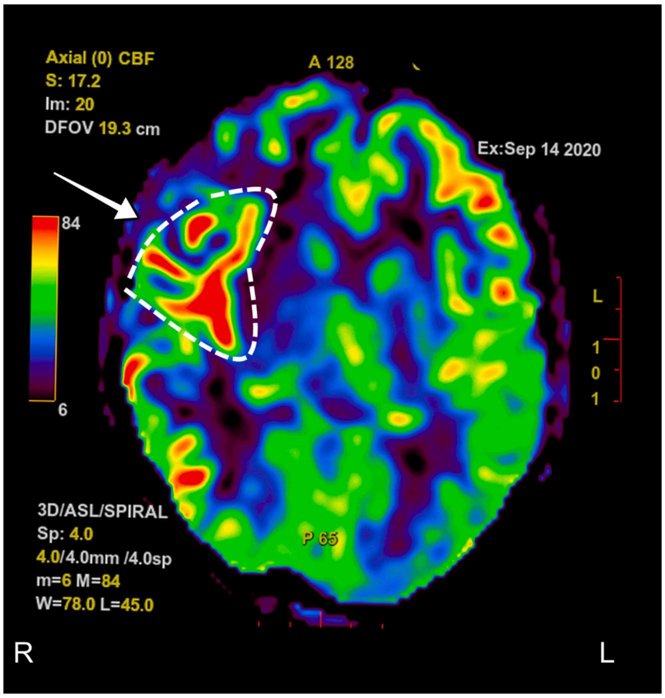

Fig. 3. ASL MRI post thrombectomy showed increased CBF around the infarcted area (dashed lines), suggestive of luxury perfusion.

2.2. Case 2

An eight-year-old Asian girl without significant past medical history was referred from a community primary hospital to Dr. Soetomo General Academic Hospital on April 2021, with severe face drooping and left hemiplegia following sudden vomiting. The patient was initially rushed to the previous hospital by her parents 2 h after her last known well (LNW) incident. On further anamnesis with her parents, six days prior, she had slipped and fallen to the ground and then complained of a continuous headache. Her initial trauma had involved a transient loss of consciousness, but her parents had not brought her to the ED since she had shown no focal neurological deficit. At the ED at a previous hospital, a head CT scan without contrast had revealed a hyperdense right MCA sign (yellow arrow, Fig. 4A).

The patient had then been referred to our hospital for further treatment, and she arrived 8 h after LNW. Her weight was 25 kg, her blood pressure was 115/60 mmHg, her pulse was 84 beats/min, her respiratory rate was 18 breaths/min, and she was afebrile. Her initial Ped NIHSS score on admission was 14. Diffusion weight imaging (DWI) without contrast (Fig. 4B) revealed a restricted diffusion area on the right fronto-temporo-parietal and right corona radiata suggestive of a hyperacute thromboembolic infarction on the right MCA territory. Time-of-Flight (TOF) MR angiography of the brain (yellow arrow, Fig. 4C) showed occlusion on the M1 division of the right MCA.

She was taken for emergent mechanical thrombectomy 10 h after LNW. An angiogram of the right internal carotid artery confirmed occlusion of the right M1 of the MCA (white arrow, Fig. 5A and C). Mechanical thrombectomy was performed and passed in the M2. Successful recanalization (mTICI 2B) was achieved in 62 min (white arrow, Fig. 5B and D).

Within 12 h after thrombectomy, the patient underwent a head CT scan evaluation and demonstrated post-interventional cerebral hyper density (PCHD) on the right temporoparietal without a space-occupying effect (Fig. 6), suggestive of post-contrast staining. The patient was admitted to the PICU of Dr. Soetomo General Academic Hospital for three days. Her groin puncture site showed no hematoma or bleeding. By hospitalization day 7, the patient showed significant improvement of the left extremity weakness and facial weakness. Her Ped NIHSS score decreased to 6. The patient was discharged on day 10. Her mRS score on the second- and six-month follow-up was 1, with residual left arm spasticity and left drop foot.

3. Discussion

Childhood stroke with LVO is a rare but serious condition with substantial rates of morbidity and mortality [2]. It affects an estimated two to six per 100,000 children every year [1]. Most children who survive a stroke will experience long-term neurological, motor, and cognitive impairments [1,2]. Given its low incidence, evidence is lacking that can guide treatment decisions for childhood stroke. Endovascular treatment is a standard acute revascularization therapy for AIS in

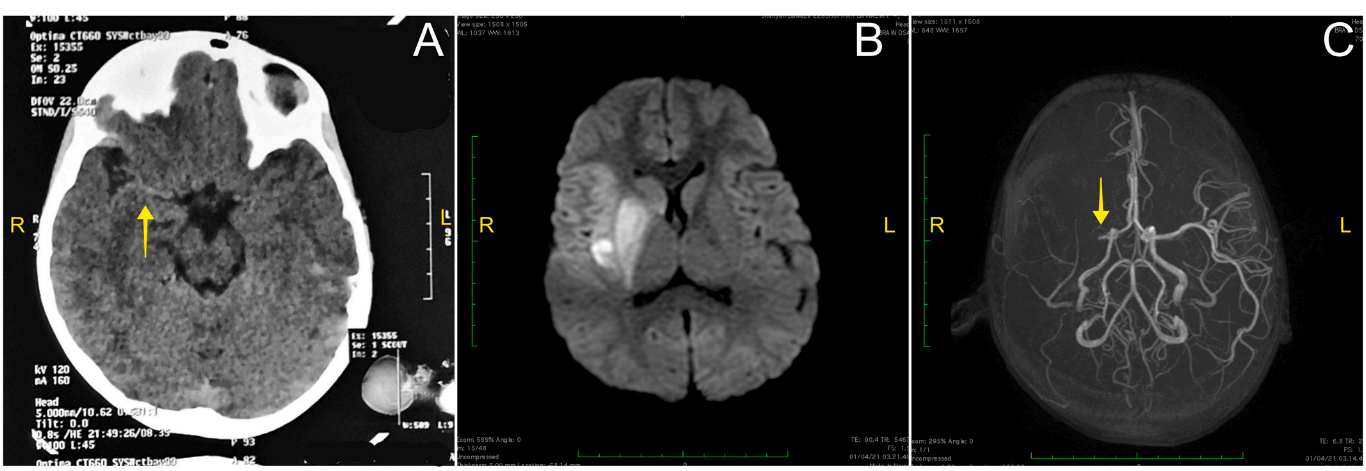

Fig. 4. (A) Head CT scan (non-contrast) showed hyperdensity (yellow arrow) of the right MCA.
(B) DWI MRI showed hyperacute infarction on the right MCA territory and (C) TOF MRA showed occlusion on M1.

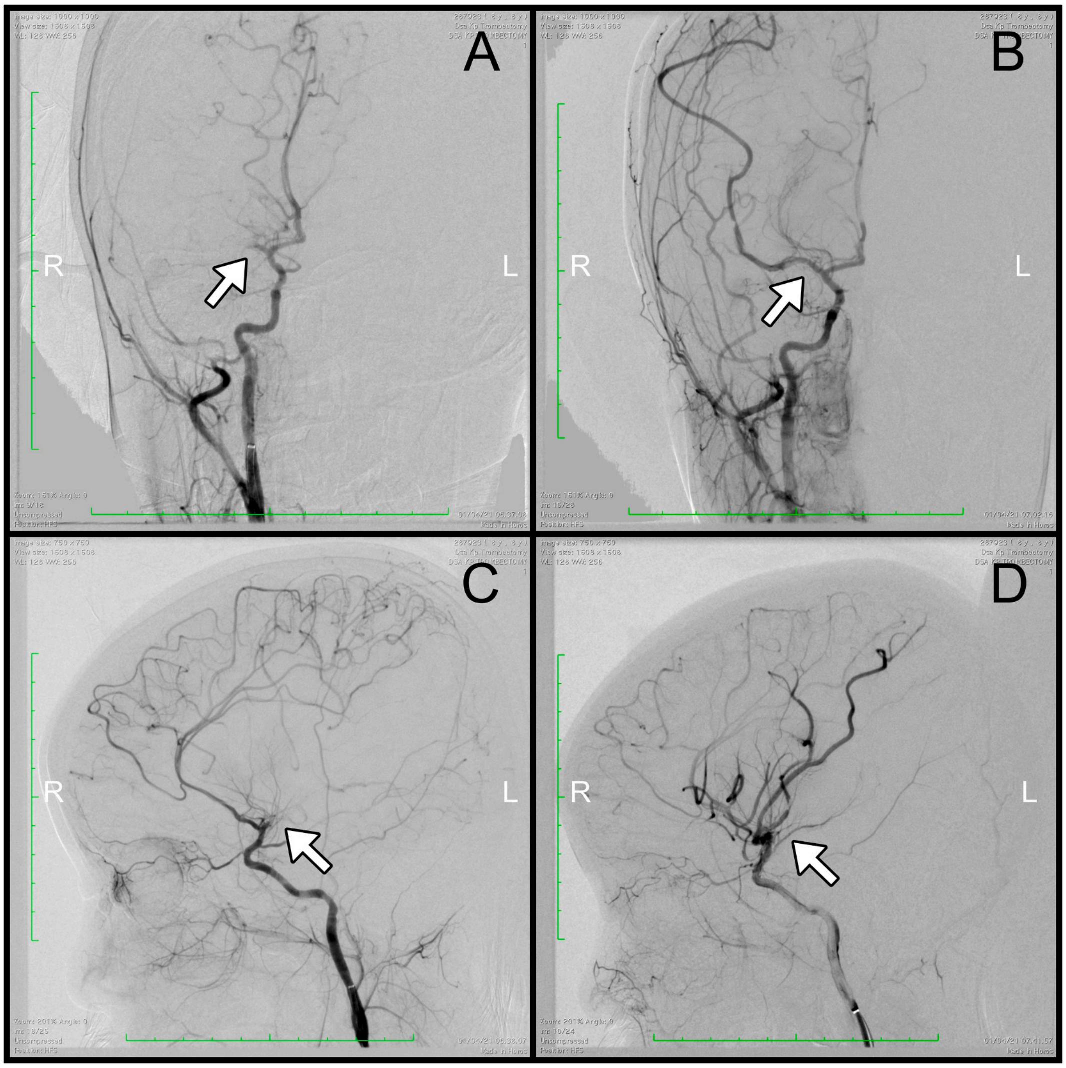

Fig. 5. (A) (C) Pre-thrombectomy angiogram and (B) (D) post-thrombectomy angiogram.

adult patients [5], but its role in the pediatric population is uncertain because of a lack of randomized trials that address its efficacy and safety in children.

We searched for related journals and articles about primary thrombectomy for pediatric stroke by conducting a literature review from 2016 to 2021, using the PubMed, Google Scholar, and Science Direct databases. Searches were implemented using the keywords "pediatric stroke", "childhood stroke", "mechanical thrombectomy", "endovascular treatment", and "primary thrombectomy", in all possible combinations, for articles published in the last 5 years (Table 1). Posterior circulation data were separated from the anterior circulation data. The patient and intervention characteristics are summarized in Table 1. A total of 14 case reports with 21 cases (including the current report) were included in the review [6–17].

Thrombectomy has potential appeal for childhood AIS due to its longer post-stroke time window for intervention, although the actual duration of the interval from LNW to groin puncture has not been established for pediatric cases [3]. Our literature review included present cases, 21 cases of pediatric stroke with a mean age of 12.8 years (SD 2.77) (Table 2). The mean LNW to puncture is 299 min (SD 147.1) in 19 cases. The American Heart Association/American Stroke Association (AHA/ASA) Guideline for AIS in 2015 [18] stated a new recommendation that endovascular therapy may be reasonable for some patients <18 years of age with LVO, in whom treatment can be initiated within 6 h of symptom onset. However, the benefits and risks remain unestablished in this age group [3,18].

Thus, in 2019, the AHA/ASA limited the consideration of this intervention to children who meet some criteria. The criteria include persistent disabling neurological deficits (e.g., Ped NIHSS score $\geq$ 6 at the time of intervention), radiographically confirmed cerebral large artery occlusion, larger children, treatment decision made in conjunction with a pediatric neurologist, and intervention performed by an experienced endovascular surgeon [3]. This literature review demonstrated that the mean initial Ped NIHSS of 13.21 (SD 6.18) with MCA (61%) is the most common occlusion (Table 2). In our cases, the children were large, at 40 kg and 25 kg in case 1 and case 2, respectively. Both had LVO on initial head CT scans, and the thrombectomy was performed by an endovascular surgeon who was experienced in treating both children and adult stroke.

All patients in this literature review achieved mTICI $\geq$ 2B recanalization, with a remarkable neurological outcome during follow-up. This result is in line with previous studies in which successful recanalization was accomplished in >80% of pediatric stroke cases who underwent thrombectomy [19–21]. Reduction in the Ped NIHSS score (Table 2.), as

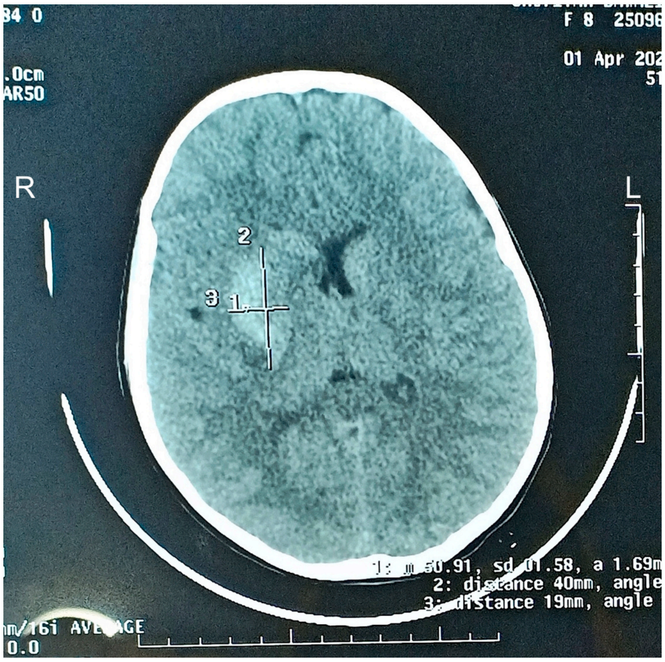

Fig. 6. Head CT scan without contrast 12 h after thrombectomy showed right temporo-parietal cerebral hyperdensity.

a short-term outcome of MT, varied between 0 and 15, with a mean of 8.07 (SD 5.47). This finding is compelling, as previous studies in pediatric stroke in cases who underwent EVT reported mean reductions of Ped NIHSS of 10.2 [19] and 11.5 [20]. In our review, the lower mean reduction probably reflects the fewer data points obtained, since only 14 cases provided the pre- and post-thrombectomy Ped NIHSS.

One major consideration when utilizing EVT in children relates to its safety. The Save ChildS Study demonstrated that the safety profile of thrombectomy in childhood stroke does not differ from the safety profile in randomized clinical trials for adults [21]. Complication rates were low in that study, including only a single case (1%) of symptomatic intracerebral hemorrhage (ICH) and malignant infarction in three patients (4%) [21]. The Save ChildS Study also showed no vascular complications, such as arterial dissection, periprocedural thrombosis, or puncture site complication [21]. Our patients also showed none of these complications. In addition, a systematic review of individual patient data by Bhatia et al. [22] also revealed only one patient (8.8%), from 113 yielded cases, who experienced symptomatic ICH after MT. Another study by Cappelari et al. [23] discovered no significant differences in efficacy and safety between primary and secondary MT for anterior circulation stroke in children. In that study, the proportions of asymptomatic ICH were similar in both MT groups, but the proportions of favorable neurological outcomes were higher in the primary MT group [23].

In our case 2, the CT scan evaluation conducted at 12 h revealed post-interventional cerebral hyper density (PCHD) in the infarcted area. Post-interventional cerebral hyper densities (PCHD) are common CT findings and have been described in 23% to 84% of patients after MT [24]. However, no density thresholds allow for a reliable differentiation between hemorrhage and contrast staining on immediate CT evaluation [24,25]. The only reliable method for distinguishing between the two is a CT scan performed at least 19–24 h after endovascular therapy. Alternative imaging methods, such as dual-energy CT or MRI, should be considered for patients who require a more rapid differentiation [25].

Rates of recurrent AIS in childhood range from 6% to 35% [2]. More than one of every ten children will suffer another stroke within a year [26]. Neither of our cases experienced recurrent stroke, but one case by Buompadre et al. [6] in our literature review demonstrated recurrent stroke within four days after the first thrombectomy. The etiology was cardiac emboly in that case [6]. As in adult stroke, antithrombotic agents are a mainstay treatment in preventing stroke. The 2008 AHA scientific statement [27] substantially supported either initial aspirin or low-dose low-molecular-weight heparin (LMWH) for initial therapy in pediatric AIS. However, the circumstances in which antiplatelet or anticoagulant agents are the best initial and long-term secondary prevention treatment are unclear in children. In addition, a prospective multicenter follow-up study [28] has provided evidence that aspirin is not superior to low-dose LMWH, and vice versa, in preventing recurrent stroke in children. Our patient (Case 1) was on oral acetylsalicylic acid 80 mg (Aspilets, Darya-Varia, Jakarta, Indonesia) once a day and showed no evidence of recurrent stroke in the sixth-month follow-up visit.

Cardiac etiology is the most common etiology for this study (47%). This finding is in line with a study by Bhatia et al. [22], who found that cardio-embolic comprised 40.7% of the presumed etiology in 108 cases of pediatric stroke. Six of 14 cases (43%), including our cases, demonstrated good neurological outcomes, with mRS scores of 1. Only one case by Appavu et al. [17] had a poor long-term outcome, with an mRS score of 4. Interestingly, the presumed etiology of this case was inflammatory arteriopathy due to COVID 19 infection [17].

4. Conclusion

Pediatric stroke is uncommon but carries significant morbidities and mortalities. The etiologies of AIS in this population differ significantly from stroke in adults. In our report, the presumed etiology in case no. 1 was viral infection-induced arteriopathy, since she had a history of chicken pox. The presumed etiology in case 2 was arterial dissection, since the patient had a history of trauma that had caused headache and had undergone a transient loss of consciousness. The limitation of this article is that we only conducted our literature review with similar case reports. However, given the remarkable short-term and long-term neurological outcomes, our cases and review of the literature demonstrate the success of primary mechanical thrombectomy for AIS treatment in children.

Abbreviations

Ped NIHSS	Pediatric National Institute of Health Stroke Scale
CT	computed tomography
AIS	acute ischemic stroke
mRS	modified Rankin Scale
EVT	endovascular treatment
LVO	large vessel occlusion
ED	emergency department
HU	Hounsfield unit
MCA	middle cerebral artery
DSA	digital subtraction angiography
MT	mechanical thrombectomy
mTICI	modified thrombolysis in cerebral infarction
PICU	pediatric intensive care unit
ASL	arterial spin labeling
MRI	magnetic resonance imaging
CBF	cerebral blood flow
LNW	last known well
DWI	Diffusion Weighted Imaging
TOF	Time-Of-Flight
MR	magnetic resonance
PCHD	Post Contrast Hyper Density
AHA/ASA	American Heart Association/American Stroke Association
SD	Standard Deviation
ICH	intracerebral hemorrhage
LMWH	Low Molecular Weight Heparin

Table 1
Summary of the published primary mechanical thrombectomy performed in childhood stroke affecting anterior circulation.

Authors	Age	Sex	Baseline Ped NIHSS	LNW to puncture	Occlusion location	Recanalization	Etiology	Post MT Ped NIHSS (time)	mRS score (time)	Reduced Ped NIHSS* (time)
Buompadre et al., 2016 [6]	8 yrs	Female	7	5 h (300 min)	Left ACA (A1) + Left MCA (M1)	NA	Cardiac	2 (8 h)	NA	5 (8 h)
	8 yrs	Female	12 (4 days after 1st thrombectomy)	315 min	Left MCA (M1 + M2)	NA	Cardiac (recurrent)	7 (12 h) 4 (2 months)	NA	5 (12 h)
Madaelil et al., 2016 [7]	17 yrs	Male	13	4 h (240 min)	Right ICA + Right MCA (M2)	mTICI 3	Gunshot wound	NA	0 (3 months)	NA
Weiner et al., 2016 [8]	15 yrs	Male	9	8 h (480 min)	Right ICA Terminus + Right MCA (M1)	mTICI 2c	Cardiac	1 (8 h)	NA	8 (8 h)
Bhogal et al., 2018 [9]	11 yrs	Female	2	317 min	Left MCA (M1)	mTICI 3	NA	0 (at discharged)	0 (3 months)	2 (NA)
	16 yrs	Male	15	138 min	Left MCA (M1)	mTICI 2b	Vasculitis	2 (at discharged)	2 (3 months)	13 (NA)
	15 yrs	Female	23	269 min	Left carotid T	TICI 3	Cardiac	NA	0 (3 months)	NA
Kim et al., 2018 [10]	14 yrs	Male	2	7 h 37 min (457 min)	Right ICA + Right MCA	NA (improved distal filling)	NA	NA	NA (decreased fine movement dexterity of left fingers)	NA
Stowe et al., 2018 [11]	9 yrs	Male	23	4.5 h (270 min)	Left MCA (M1)	mTICI 2b	Cardiac	7 (24 h) 3 (72 h)	NA	16 (24 h) 20 (72 h)
Adeeb et al., 2020 [12]	11 yrs	Female	NA	8.5 h	Right MCA	mTICI 2b	Dissection	NA	NA	NA
Bhatti et al., 2019 [13]	17 yrs	Male	19	160 min	Left MCA (M1)	mTICI 3	Idiopathic	19 (24 h)	1 (3 months)	0 (24 h)
	13 yrs	Male	15	70 min	Right ICA	mTICI 3	Cardiac	0 (24 h)	0 (3 months)	15 (24 h)
	13 yrs	Male	21	120 min	Left MCA (M1)	mTICI 2b	Cardiac	18 (24 h)	1 (3 months)	3 (24 h)
Huang et al., 2020 [14]	12 yrs	Male	12	3 h (180 min)	Right ICA + Right ACA (A1) + Right MCA	NA	Idiopathic	NA	2 (5 months)	NA
Parra-Farinas et al., 2020 [15]	14 yrs	Female	19	NA	Left MCA (M1)	mTICI 2b	Idiopathic	4 (24 h)	1 (3 months)	15 (24 h)
	16 yrs	Female	8	NA	Left MCA (M2)	mTICI 3	Idiopathic	0 (24 h)	0 (3 months)	8 (24 h)
	13 yrs	Female	18	NA	Right ICA + Left MCA (M1)	mTICI 2b	Cardiac	4 (24 h)	1 (3 months)	14 (24 h)
Tona et al., 2020 [16]	12 yrs	Female	NA	NA	Left MCA (M1)	mTICI 2b	Cardiac myxoma	NA	NA	NA
Appavu et al., 2021 [17]	8 yrs	Female	15	NA	Left MCA (M1)	NA	Inflammatory arteriopathy due to COVID 19	15 (7 days)	4 (NA)	0 (7 days)
Current case no. 1	13 yrs	Female	10	6 h (360 min)	Right MCA (M2)	mTICI 2b	Arteriopathy	7 (48 h)	1 (6 months)	3 (48 h)
Current case no. 2	8 yrs	Female	14	10 h (600 min)	Right MCA (M1)	mTICI 2b	Dissection	6 (7 days)	1 (2 months)	8 (7 days)

Abbreviations: ACA = anterior cerebral artery; ICA = internal carotid artery; LNW = last known well; MCA = middle cerebral artery; mTICI = modified thrombolysis in cerebral infarction; mRS = modified Rankin Scale; NA = not available; Ped NIHSS = pediatric national institute health stroke scale;
* Reduced NIHSS = Baseline NIHSS - Post MT NIH.

CRediT authorship contribution statement

Ayu Yoniko Christi: Conceptualization, Data curation, Writing – original draft. **Nur Setiawan Suroto:** Conceptualization, Data curation, Writing – review & editing. **Zaky Bajamal:** Conceptualization, Data curation. **Asra Al Fauzi:** Data curation, Writing – review & editing.

Declaration of competing interest

The authors report no conflicts of interest.

Table 2
Cases characteristic demography.

Sex		
Male	n (%)	9 (42%)
Female	n (%)	12 (57%)
Age (year)	Mean ± SD	12.8 ± 2.77
Baseline NIHSS	Mean ± SD	13.21 ± 6.18
LNW to puncture (minute)	Mean ± SD	299 ± 147.1
Occlusion location		
ICA	n (%)	1 (4%)
MCA	n (%)	13 (61%)
Carotid	n (%)	1 (4%)
ACA + MCA	n (%)	1 (4%)
ICA + MCA	n (%)	4 (19%)
ICA + ACA + MCA	n (%)	1 (4%)
Recanalization		
mTICI 2b	n (%)	9 (56%)
mTICI 2c	n (%)	1 (6%)
mTICI 3	n (%)	6 (37%)
Etiology		
Cardiac	n (%)	9 (47%)
Vascular	n (%)	5 (26%)
Idiopathic	n (%)	4 (21%)
Trauma	n (%)	1 (5%)
Post thrombectomy NIHSS	Mean ± SD	6.13 ± 6.16
mRS score		
mRS 0	n (%)	5 (36%)
mRS 1	n (%)	6 (43%)
mRS 2	n (%)	2 (14%)
mRS 4	n (%)	1 (7%)
Reduced NIHSS	Mean ± SD	8.07 ± 5.47

Abbreviations: ACA = anterior cerebral artery; ICA = internal carotid artery; LNW = last known well; MCA = middle cerebral artery; mTICI = modified thrombolysis in cerebral infarction; mRS = modified Rankin Scale; NA = not available; NIHSS = national institute health stroke scale;

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Ethical approval

This is a case report; therefore, it did not require ethical approval from the ethics committee. However, we obtained permission from each patient's parents to publish their data.

Consent

Written informed consent was obtained from each patient's family for publication of this case report and accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal on request.

Research registration

This case report is not eligible for obtaining a research registry since it only contains a report of a known entity with no new surgical or medical interventions.

Provenance and peer review

Not commissioned, externally peer-reviewed.

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