RESEARCH PAPER

Mechanical Thrombectomy Using Retrievable Stents in Pediatric Acute Ischemic Stroke

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Objectives: To report efficacy and outcome of mechanical thrombectomy for treatment of pediatric acute ischemic stroke with large vessel occlusion using stent retrievers. **Methods**: Retrospective record review of institutional database for patients <18 years of age. **Results**: Five boys aged between 6 to 17 years received reperfusion therapy using mechanical thrombectomy for acute ischemic stroke with large vessel occlusion (2 basilar, 2 middle cerebral and 1 internal carotid artery). Pediatric National Institute of Health Stroke Scale (PedNIHSS) at onset ranged from 12 to 21. Complete recanalization as defined by the modified Treatment In Cerebral Infarction scale (mTICI 3 or 2b) was achieved in all, using stent retreivers. Favorable outcome as per the modified Rankin scale (mRS 0-1) was achieved in all with no peri-procedural complications. **Conclusions**: Mechanical thrombectomy using retrievable stents is a safe and effective therapy for pediatric ischemic stroke due to large vessel occlusion, and may be offered in carefully selected patients.

Keywords: *Hemiparesis, infarction, Large vessel occlusion, Treatment*.

Ischemic stroke is largely an adult entity and rare in pediatric population but owing to the developing nature of brain, survivors of childhood strokes may develop severe physical and cognitive disabilities requiring lifelong support, which leads to higher and sustained financial and societal burden [1]. Pediatric strokes differ from adults in terms of presentation, risk factors, pathophysiology and response to reperfusion and preventive strategies [2,3]. The current decade has witnessed a revolution in the management of adult strokes due to large vessel occlusion (LVO) using mechanical thrombectomy (MT) with many large randomized control trials showing favorable outcomes [4]. However the same has not been validated in children. We present our experience of endovascular therapy (EVT) using next generation MT devices in pediatric acute ischemic stroke (AIS) with LVO.

METHODS

Institutional database was analyzed retrospectively from January 2013 to April 2018 for patients less than 18 years of age who underwent MT for AIS with LVO. The demographic and clinical features like pattern and severity of weakness as per PedNIHSS [5] were studied. The extent of infarct on imaging was quantified using the Alberta Stroke program Early CT score (ASPECTS). The angiographic findings, procedural details, post-procedural care, angiographic and clinical outcome were analyzed. The radiological outcome was quantified using the modified Treatment In Cerebral Infarction (mTICI) score [6]. The clinical outcome was graded using the Modified Rankin Scale score (mRS) at three months follow-up [7].

Case 1 (*Fig.* 1 panels a-e)

A six-year-old boy was diagnosed with recurrent posterior circulation stroke. He had developed three non-disabling strokes despite being treated with aspirin, over a span of 2 months, after which he worsened rapidly. His initial intracranial magnetic resonance (MR) time-of-flight angiogram was unrevealing. His new MR angiogram showed basilar artery (BA) occlusion (***Table* I**). A digital subtraction angiography (DSA), showed a dissection involving the left vertebral artery (VA) with filling defect suggestive of thrombus and complete occlusion of the distal BA. The clot was retrieved by stent-retriever with complete recanalization of the BA.

Case 2 (*Fig.* 1 f-j)

A six-year-old boy came with history of giddiness and irritability for 24 hours with difficulty breathing and quadriparesis soon after waking up. MRI brain with MR angiogram showed multiple infarcts in right hemi-pons with occluded BA. DSA showed complete occlusion of the distal BA (***Table* I**). The clot was retrieved with

complete recanalization of the BA. Extensive workup for etiology including 2D Echo and hemoglobin electrophoresis did not reveal any cause.

Case 3 (*Fig*. 1 k-o)

A 17-year-old boy presented with sudden onset of loss of speech and right hemiplegia for two hours. A contrast enhanced CT (CECT) scan of brain showed ill-defined hypodensities in left fronto-temporo-parietal lobes and ganglio-capsular region with occlusion of M1 segment of middle cerebral artery (MCA). DSA showed complete occlusion of left M1 (***Table* I**). The clot was retrieved using stent retriever. Detailed evaluation for etiology revealed iron deficiency anemia, a normal 2D Echo & antiphospholipid antibody and ANA (anti neutrophillic antibody) panel.

Case 4

A 13-year-old boy, known case of severe rheumatic mitral valve stenosis with severe pulmonary hypertension (PH), underwent mitral valve replacement at our center. On post-operative day three, he developed acute onset of left hemiplegia with gaze deviation to right side. A CECT scan of brain with angiogram showed subtle loss of grey white differentiation in right frontal lobe with complete occlusion right internal carotid artery (ICA) (table 1). DSA showed complete occlusion of right ICA. The clot was retrieved by stent retriever (**Fig. 2**). Twenty four hours later he was started on conventional heparin, and was later switched to oral acenocoumarol (Acitrom).

Case 5

A 13-year-old boy, known case of Ebstein's anomaly with tricuspid regurgitation with severe PH, underwent Blalock-Taussig shunt at our center. On post-operative day two, he developed acute onset of right hemiplegia with gaze deviation to left with profound drowsiness (***Table* I**). A CECT scan of brain with angiogram showed subtle focus of hypodensity in left corona radiata and lentiform nucleus with left MCA occlusion. DSA showed occlusion of left M1 segment of MCA. The clot was retrieved using stent retriever.

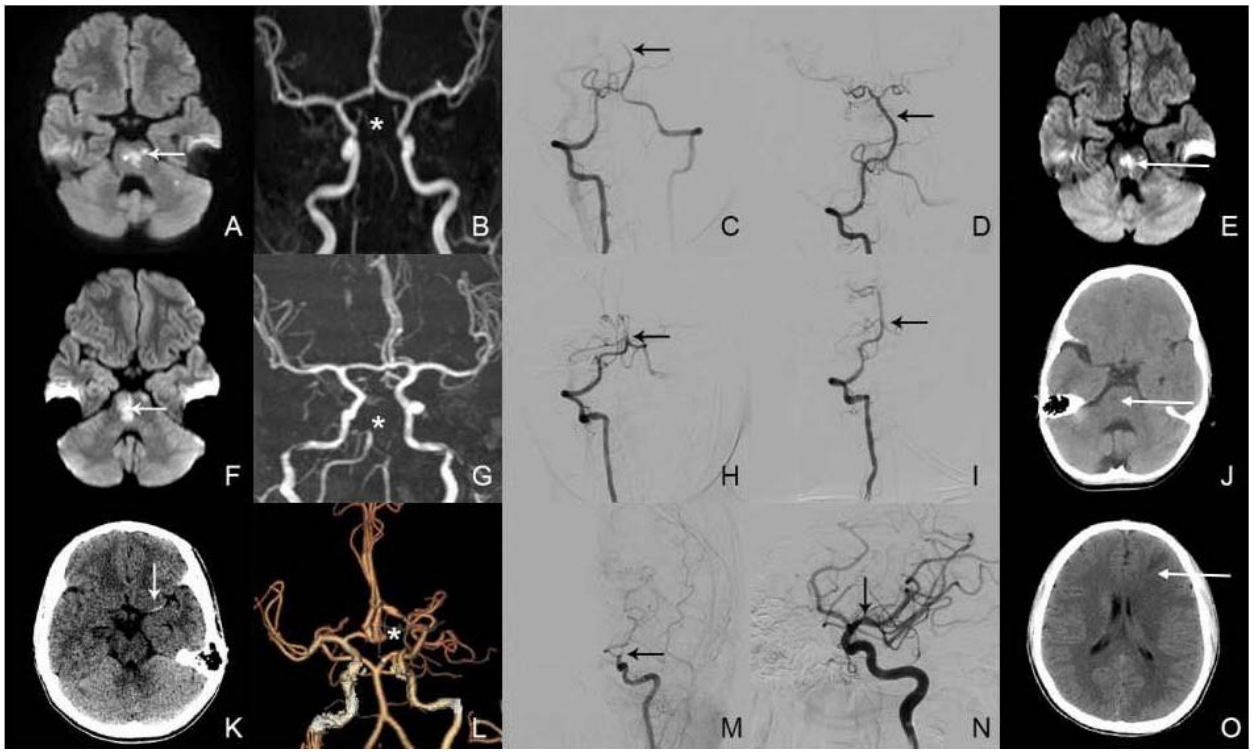

FIG. 1 *Case 1: MRI at admission showing pontine infarcts [arrow] (A) with basilar occlusion on MRA* (B) and DSA [arrow] (C). Post thrombectomy DSA [arrow] (D) showing complete recanalization and MRI [arrow] (E) showing no evolution of infarcts; Case 2: MRI at presentation showing right pontine infarcts [arrow] (F) with basilar occlusion on MRA* (G) and DSA [arrow] (H). Post thrombectomy DSA [arrow] (I) showing complete recanalisation and CT scan after 24 hours showing small right pontine infarct [arrow] (J); Case 3: CT at admission showing dense MCA sign on left [arrow] (K) with left MCA occlusion on CTA* (L) and DSA [arrow] (M). Post thrombectomy DSA [arrow] (N) showing complete recanalisation and CT scan after 24 hours showing small left frontal infract [arrow] (O).*

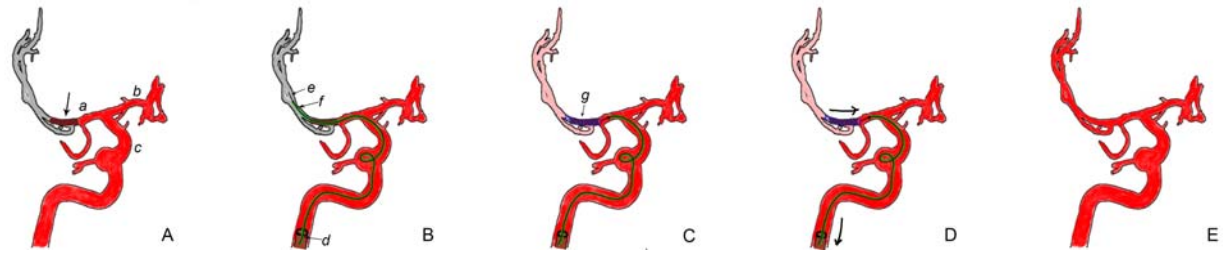

FIG. 2 *Schematic representation of procedure of Mechanical Thrombectomy using Retrievable stent, (A) Internal carotid artery (c) and its branches Middle cerebral artery (a) and anterior cerebral artery (b). There is occlusion of the proximal MCA (arrow) with clot shown in brown color with absence of flow (shown as grey color) distal to the clot; B. A guide catheter is shown in the ICA (d) through which a microcatheter, shown in green color (f), over a microwire (e), has been negotiated across the clot into distal MCA; C. The microwire has been removed and the stent retriever (g), shown in blue color, has been negotiated through the microcatheter and deployed across the clot and flow re-established (shown as pink color); D. After keeping the stent open into the clot for 3-5 minutes, it is slowly withdrawn back into the guiding catheter; E. Normal flow (shown in red color) and complete recanalization achieved.*

RESULTS

Five boys aged between six to seventeen years (median 13 y) underwent MT. Common femoral artery was used for vascular access in all cases. None of the patient received intravenous (IVT) or intra-arterial thrombolysis (IAT). Case 1 and 2 were out of the window period while case 4 and 5 had undergone cardiac surgery and hence IVT was contraindicated in them. Only one patient (Case 3) was eligible for IVT however the guardians opted to skip IVT and go for MT directly. All patients received injection heparin 60 units per kilogram of bodyweight through the sheath at the beginning of the procedure. Case 1, 4 and 5 received oral anticoagulation following the procedure. Case 3 received conventional heparin initially (7 days) followed by dual antiplatelets while case 2 was discharged on single antiplatelet drug only. The mRS at approximately 90 days ranged from 0 to 1 with no death or dependency. Angiographically, mTICI 3 grade reperfusion was achieved in 4 patients while 2b was achieved in one. There were no periprocedural complications.

DISCUSSION

The 2012 Thrombolysis in Pediatric Stroke trial [8] to which the medical fraternity was looking forward to for answers was stopped in 2014 due to failure to recruit patients. It is thus less likely to have more trials for intravenous thrombolysis and even more so for intrarterial thrombolysis or MT in the near future. Hence careful extrapolation of adult treatment protocols seems the only plausible alternative at present. For adult AIS, IVT within 4.5 hours of symptom onset and MT till 6 hours [9] (in select few cases upto 24 hours if there is significant deficit-to-infarct mismatch [10]) are the two major treatment options available. However, owing to developmentally immature nature of the hemostatic and fibrinolytic system in children, there is low endogenous plasminogen level and higher plasminogen activator inhibitor-1 (PAI-1) level which makes the dose and response of tissue plasminogen activator (tPA) unpredictable [3,11].

Similarly MT may not be as straightforward as it may seem in adults as LVO in children may be because of cerebral arteriopathy wherein the vessels are inflamed and friable. Along with this the disparity in size of vessels makes MT challenging in pediatric population [12]. Hence careful selection of patients and devices is of utmost importance to avoid any therapeutic misadventure. In our series two patients had cardioembolic stroke and one had dissection, such patients may be the ideal candidates in whom adult recommendations can be applied safely. Most of the current data on EVT in pediatric stroke comprise of small case series or individual case reports. As per the 2017 review on EVT for AIS in children, till 2016, only 68 cases using EVT have been reported out of which 24 were using IAT while 44 used MT with or without IAT [13]. The patients who underwent IA mechanical thrombectomy *had significantly better clinical (79.5% versus 20.5%; P*=0.001) and radiographic outcomes (complete recanalisation, 79.1% versus 38.9%; P=0.002) with fewer complications (13.6% versus 37.5%; P=0.006) than those who underwent IA fibrinolysis only [13]. These findings are also reflected in our series where there were no complications with clinical and radiological outcomes (table no. 1) comparable to previously reported series. The major limitation of this study is its retrospective nature, based on review of case records. Small sample size and lack of any control group are the other major limitations.

TABLE I DETAILS OF CLINICAL AND RADIOLOGICAL FEATURES, TREATMENT AND OUTCOME OF CHILDREN WHO UNDERWENT MECHANICAL THROMBECTOMY

	Case 1	*Case 2*	*Case 3*	*Case 4*	*Case 5*
Age (y)	6	6	17	13	13
Sex	male	male	male	male	male
Risk factor / etiology	Vertebral artery dissection	-	-	Rheumatic heart disease Severe mitral valve stenosis post mitral valve replacement	Ebstein's anomaly with severe tricuspid regurgitation post Blalock taussig shunt
Major clinical deficits	right hemiparesis with ataxia and anarthria	quadriparesis with ataxia and bulbar dysfunction	right hemiparesis with global aphasia and hemisensory loss	left hemiplegia with left hemianopia and hemi neglect	right hemiplegia with gaze deviation to left, drowsiness
Time of symptom onset (onset to door time)	24 hours	24 hours	2 hours	30 mins	60 mins
Imaging parameters					
ASPECTS (CT /MRI) on initial imaging	6 (MRI)	8 (MRI)	7 (CT)	9 (CT)	7 (CT)
ASPECTS (CT/MRI) 24 hours after procedure	8 (MRI)	8 (CT)	7 (CT)	9 (CT)	8 (CT)
Vessel involved on CT/ MR angiogram	basilar	basilar	left M1	right ICA	left M1
Procedure details					
Device used for mechanical thrombectomy (size)	Solitaire (4 × 20 mm)	Solitaire (4 × 20 mm)	pREset (4× 20 mm)	Solitaire (4 × 20 mm)	pREset (6 × 30 mm)
Number of passes	1	2	1	2	2
Recanalization as per mTICI scoring	TICI 3	TICI 3	TICI 3	TICI 3	TICI 2b
Type of anesthesia	General anesthesia	General anesthesia	Conscious sedation	General anesthesia	General anesthesia
Puncture to recanalisation time	60 minutes	45 minutes	20 minutes	30 minutes	45 minutes
Onset to recanalization time	26 hours	26 hours 45 minutes	180 minutes	100 minutes	165 minutes
Outcome measures					
PedNIHSS on admission	15	12	19	15	21
PedNIHSS at 24 hours	4	4	19	0	18
PedNIHSS on discharge	0	4	10	0	5
MRS score on admission	5	5	5	5	5
MRS at 3 months	0	0	1	0	1

ASPECTS: Alberta Stroke Program Early CT Score (extent of infarction); CT: Computed Tomography ; MRI: Magnetic Resonance Imaging ; mTICI: modified Treatment In cerebral Infarction; PedNIHSS: Pediatric National Institutes of Health Stroke Scale; MRS: Modified Rankin scale.

WHAT THIS STUDY ADDS?

- Mechanical thrombectomy appears to be a safe and effective tool for pediatric acute ischemic with large vessel occlusion in carefully selected patients.

Stroke in children, though infrequent, is disabling and hence there is need to sensitize caregivers and physicians to the necessity of timely intervention. Our series suggests that MT may be a safe and effective procedure for pediatric AIS with LVO. MT may be strongly considered for severe pediatric strokes with LVO on a case to case basis, as it is life saving and decreases long-term morbidity.

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