*Case Report*

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# Right Middle Cerebral Artery Infarct after Minor Head Trauma in an Infant

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**Abstract**

Ischemic stroke (IS) in the pediatric population is extremely rare. In this age group, the occurrence of IS often concurs with underlying congenital heart disease, haematological, metabolic or immunological conditions. In contrast, the association between IS and minor head injury in children has been sparse. The authors report a case of a healthy 10 yrs 8 months old male who was found to have a right middle cerebral artery territory infarct. An extensive medical workup was performed, and it was negative for any previously undiagnosed co-morbidities. Given the paucity of such cases, the condition and its management are discussed in corroboration with current literature.

***Keywords:*** Stroke in Children; Ischemic CVA; Hemiparesis; Ischemic Stroke.

## INTRODUCTION

The incidence of ischemic stroke (IS) in pediatrics is rare. Conversely, in the aging population, strokes are common with well established risk factors associated with IS include nutrition, hypertension, coagulopathy disorders, carotid stenosis, and patent foramen ovale.[1] However, in young adults, the list of potential stroke causes is extensive. According to the *Toast* (Trial of Org 10172 in Acute Stroke Treatment) criteria, both strokes of unde termined and of other determined etiology are the most common types among them.[2] Broadly speaking, causative factors in children can be similar to young adults where by the diagnosis is often linked to a background of congenital heart disease, haematological and, or immunological conditions. Interestingly, there have been reports of IS associated with head injury in patients less than 12 months of age.[3] The authors describe the case of a 10 year 8 months - old child who developed progressive unilateral hemiparesis secondary to a left middle cerebral artery (MCA) territory infarct, etiology unknown. Given the in frequency of such cases, the condition is discussed in corroboration with current literature.

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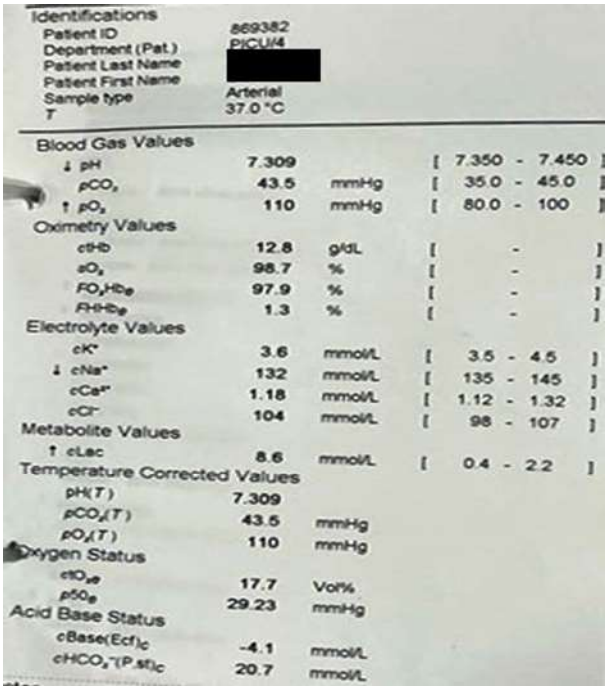
## CASE REPORT

A previously well 10 year 8 months male of non-consanguineous parents presented to the

Emergency Department. According to the history, there was sudden on set of headache more on right side of head since 2 days, associated with vomiting, left upper limb of weakness, gradually involving left lower limb. Complaint of slurring of speech with deviation of mouth on right side with dribbling of saliva. No loss of consciousness was observed. Physical examination demonstrated that he had a full Glasgow Coma Scale with bilaterally equal and reactive pupils, child was able to understand what we talk as well able to talk but in slurred speech. There was normal extraocular movement. No scalp hematoma, significant skin swelling or bruise was noted. However, his left upper limb demonstrated motor power 2 out of 5 and lower limb 3 out of 5. Muscle tone in right limbs was normal but was reduced in left upper and lower limb. He was admitted for close neuromonitoring. On the following day, he was found to have progressed left lower limb weakness (power 2 out of 5) associated with hypertonia and hyper reflexia. In addition, there was no clinical improvement of his previously documented left upper limb weakness. No neurological deficit observed on his right side. Child had a facial deviation on right side. The remainder of his cranial nerves was intact.



| Identifications | | | |
|---|---|---|---|
| Patient ID | 869382 | | |
| Department (Pat.) | PICU/4 | | |
| Patient Last Name | [redacted] | | |
| Patient First Name | | | |
| Sample type | Arterial | | |
| T | 37.0 °C | | |
| **Blood Gas Values** | | | |
| ↓ pH | 7.309 | | [ 7.350 - 7.450 ] |
| $pCO_2$ | 43.5 | mmHg | [ 35.0 - 45.0 ] |
| ↑ $pO_2$ | 110 | mmHg | [ 80.0 - 100 ] |
| **Oximetry Values** | | | |
| ctHb | 12.8 | g/dL | [ - ] |
| $sO_2$ | 98.7 | % | [ - ] |
| $FO_2Hb_c$ | 97.9 | % | [ - ] |
| $FHHb_c$ | 1.3 | % | [ - ] |
| **Electrolyte Values** | | | |
| cK+ | 3.6 | mmol/L | [ 3.5 - 4.5 ] |
| ↓ cNa+ | 132 | mmol/L | [ 135 - 145 ] |
| cCa++ | 1.18 | mmol/L | [ 1.12 - 1.32 ] |
| cCl- | 104 | mmol/L | [ 98 - 107 ] |
| **Metabolite Values** | | | |
| ↑ cLac | 8.6 | mmol/L | [ 0.4 - 2.2 ] |
| **Temperature Corrected Values** | | | |
| pH(T) | 7.309 | | |
| $pCO_2(T)$ | 43.5 | mmHg | |
| $pO_2(T)$ | 110 | mmHg | |
| **Oxygen Status** | | | |
| $ctO_{2c}$ | 17.7 | Vol% | |
| $p50_c$ | 29.23 | mmHg | |
| **Acid Base Status** | | | |
| $cBase(Ecf)_c$ | -4.1 | mmol/L | |
| $cHCO_3^-(P,st)_c$ | 20.7 | mmol/L | |

An ABG (Fig. 1) was done upon arrival to ED.

| | |
|---|---|
| pH | 7.309 |
| PCO2 | 43.5 |
| PO2 | 110 |
| K+ | 3.6 |
| Na+ | 132 |
| Cl- | 104 |
| Lactate | 8.6 |
| HCO3- | 20.7 |

A CT Scan (Fig. 2, 3) was done which showed a wedge shaped hypodensity involving right fronto-temporo-parietal region suggestive of acute infarct in right MCA artery, there was no hemorrhage seen.

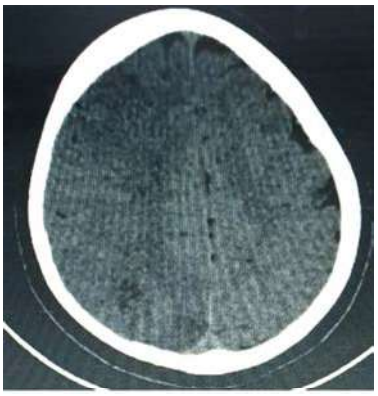


**Fig. 2**

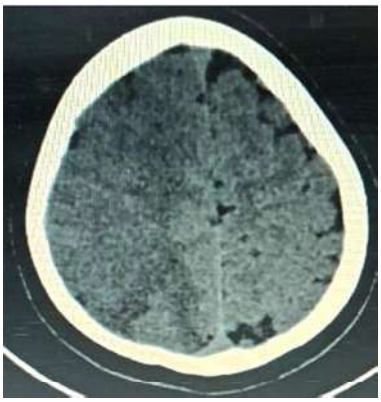


**Fig. 3**

An Magnetic Resonance Imaging (MRI) brain (Fig. 4, 5) reported restricted diffusion in the right fronto-temporo-parietal regions, in keeping with a right MCA territory infarct. Diffuse thinning of right MCA and intracranial segments of right ICA suggested Vasculitis/Moya disease. No midline shift, hydrocephalus or effacement of the basal

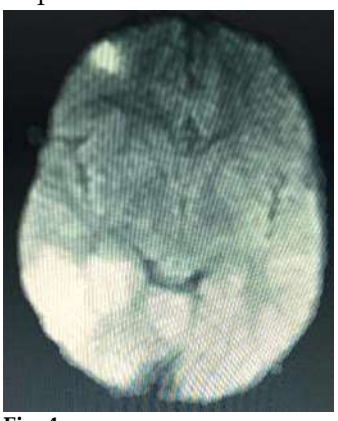


**Fig. 4**

cisterns was seen.

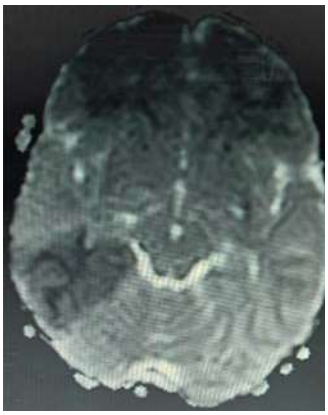


**Fig. 5**

MR angiography demonstrated no flow-limiting stenosis of the anterior or posterior cerebral circulation. No arteriovenous malformation was seen. On the next day after admission, the patient had an unfortunate event of convulsions followed by cardiac arrest and was revived with the need of dopamine and dobutamine infusion post ROSC, the patient was intubated and put on a ventilator. The patient had a cardiac arrest at night the day after admission and ROSC was not achieved.

As part of the stroke workup, a comprehensive list of relevant cardiac, hematological, immunological and metabolic investigations was performed to exclude the possibility of underlying medical conditions for the cause of his IS.

| Investigation | Results | Reference Values |
|---|---|---|
| Hb | 12.9 gm/dL | 12.5 – 16.1 gm/dL |
| Platelet | 3.25 lakhs /µL | 1.5 – 4.5 /µL |
| Neutrophils | 86% | 40 – 80% |
| Lymphocytes | 12% | 20 – 40% |
| PCV | 38.7% | 36 – 37% |
| MCV | 89.0 fL | 78 – 95 fL |
| MCH | 29.8 pg | 26 – 32 pg |
| MCHC | 33.3 gm/dL | 32 – 36 gm/dL |
| RDW | 16.0% | 11 – 17% |
| RBC Count | 4.34 X 106 /µL | 4.2 – 5.6 /µL |
| WBC Count | 11460 cells /µL | 4000 - 10500 cells /µL |
| Serum Urea | 11.0 mg/dL | 10 – 50 mg/dL |
| Serum Creatinine | 0.43 mg/dL | 0.7 – 1.5 mg/dL |
| Prothrombin Time | 15.8 sec | 11 – 15 sec |
| INR | 1.22 | < = 1 |
| APTT | 30.2 sec | 30 – 40 sec |

His collective results were also reviewed by a hematologist who was of the opinion that the latter values were likely reactive to the intracranial event and hence, deemed equivocal at this stage. A detailed family history was also taken to exclude any hereditary causes for stroke, and this was negative. The patient was started on aspirin for his IS from the day of admission.

## DISCUSSION

In comparison to adults, children with strokes present different layers often have unique risk factors that are less common. In Addition, presumptive risk factors for paediatric stroke often differ in children compared with adults.[7,8] Despite an increased incidence of paediatric stroke, there is often a delay in diagnosis, and patients may remain under and, or misdiagnosed.[5,7] A key contributing factor is the limited expressive and interpretive skills of symptoms presented by young children.[9] Further more, patients may present with subtle symptoms that mimic other diseases, leading to a low level suspicion by the attending clinician.[5] With the benefit of recent in sights, we are now aware that studies show that the risk of stroke is higher for 2 weeks after trauma. On set is frequently delayed, providing an opportunity for stroke prevention during this period.[10] However, various studies report that the majority of children admitted for minor head injury generally have a good outcome.[11,16] Presumably, this may cause potential patients to have their diagnosis of IS to be delayed. Therefore, the current challenge is to identify specific children who are at higher risk of developing IS in cohort of children diagnosed with minor head injury.

Pediatric ischemic stroke may be caused

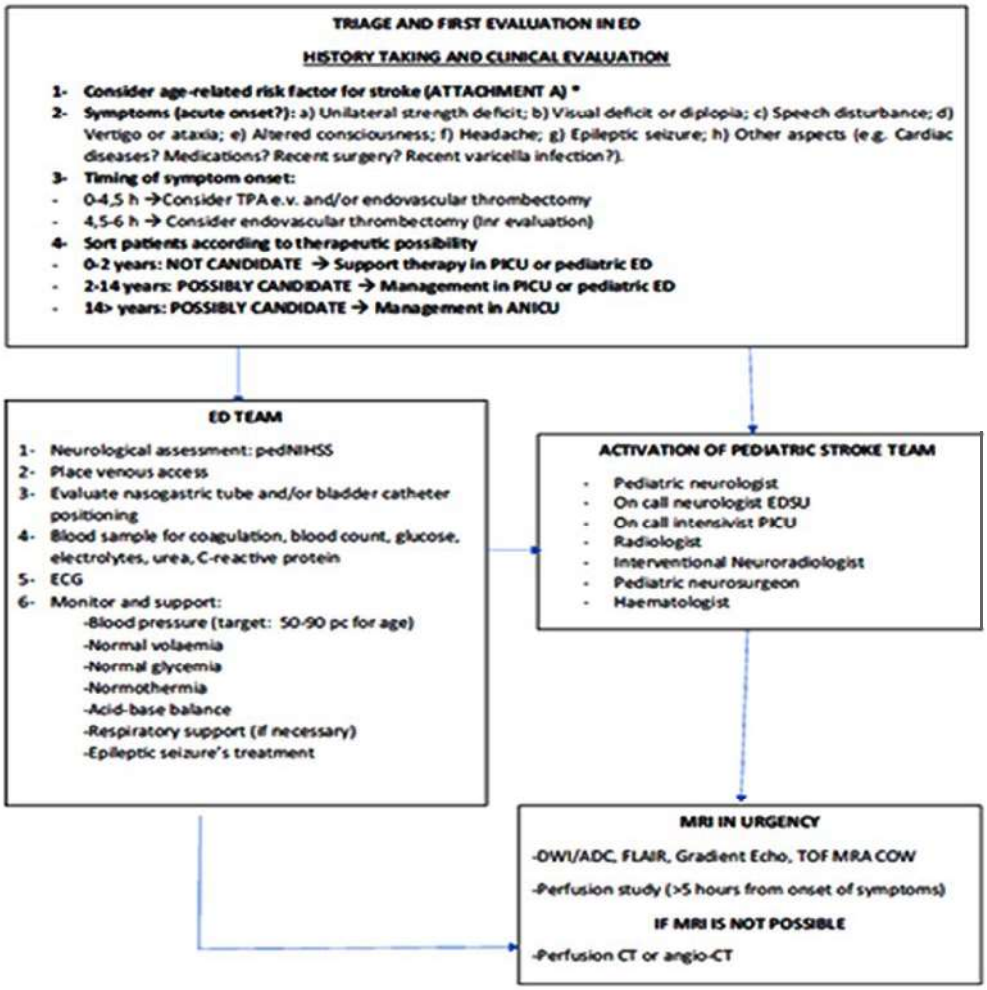
by several factors inducing thrombo-embolic occlusions of cerebral blood vessels and the activation of a complex cascade of events resulting in a permanent brain damage.[7,8,11–15] The main risk factors in children older than 28 days and their respective frequencies are summarized in

**Attachment A*:** Risk Factors For Childhood Arterial Stroke (28 days - 18 years)

| | |
|---|---|
| Arteriopathies (intra and extracranial) 21-53% | Moya Moya |
| | Sickle cell arteriopathy |
| | Post-varicella arteriopathy |
| | Arterial dissection |
| | Primary CNS vasculitis |
| | Para/post infectious vasculitis |
| | Fibro muscular dysplasia |
| Cardiac 24-31% | Congenital/acquired heart diseases |
| | Patent foramen ovale(PFO) |
| | Arrythmia |
| | Previous cardiac surgery/catheterization |
| | Endocarditis |
| | Other |
| Hypercoagulable State 28-13% | Protein C deficiency |
| | Protein S deficiency |
| | Factor V Leiden mutation (G1691A) |
| | Prothrombin mutation (PTG20210A) |
| | MTHFR (C677T polymorphism) |
| | Antithrombin III deficiency |
| | Increased factor VIII |
| | Hyperlipo proteinemia (alpha) |
| | Lupus anticoagulant |
| Acute Systemic Conditions 22-9% | Infectious diseases |
| | Sepsis |
| | Shock |
| | Acidosis/Anoxia |
| | Other |
| Haemato Oncological 9-19% | Sickle cell disease |
| | Haemolytic/iron deficiency anemia |
| | Haematological malignancy |
| | Solid extracranial tumors |
| | Other |
| Chronic head and neck disorders 9-10% | Brain tumors |
| | Aneurysm/arterio-venous malformations |
| | Other cranial/neck tumors |
| | Migraine |
| | Other |
| Genetic/metabolic 1% | Mitochondrio pathy (e.g.MELAS, POLG1 mutation) |
| | Fabry disease |
| | PHACE syndrome |
| | ACTA2/COL4A1 mutation |
| | Trisomy 21 |
| | Deficiencyof Adenosine Deaminase 2 |
| | Connective tissue disorders (e.g. Ehlers Danlos-/ Marfan/Loeys Dietz syndrome) |
| Other 10% | Previous brain surgery |
| | Trauma |

Non atherosclerotic arteriopathies, cardiac disorders, and prothrombotic states account for most of the cases, with a variable distribution of their frequency in different geographical areas or age range.

Data collected from the International Pediatric



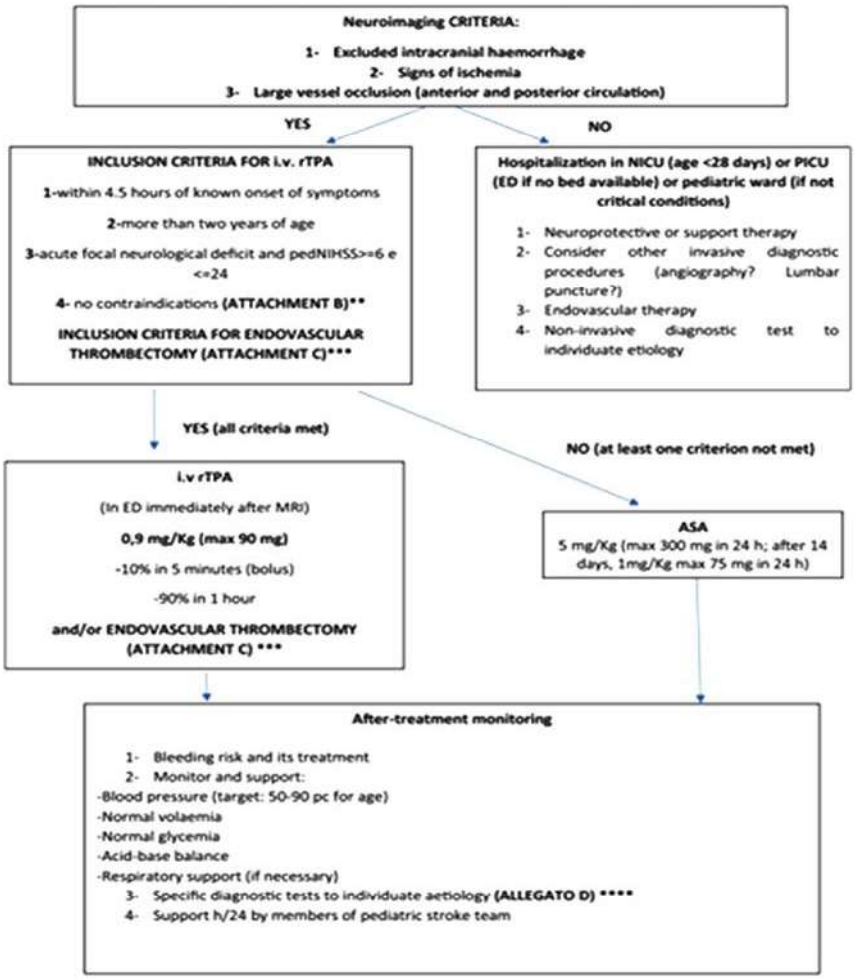

Stroke Study, a worldwide prospective study on 676 pediatric patients between 0 and 18 years, evidenced a higher prevalence of acute systemic conditions (including dehydration, sepsis, fever, acidosis, shock, anoxia/asphyxia, viral gastroenteritis) in Asia and South America and a lower prevalence of arteriopathies in Asia and chronic systemic conditions (haematological, oncological, and genetic disorders) in Europe and Australia.[15] Non atherosclerotic arteriopathies were the predominant aetiology in all the age ranges, with the highest prevalence in children between 5 and 9 years old, while the highest prevalence of cardiac disorders and acute conditions were reported in patients under the age of 5.[14,16] The term "non-atherosclerotic arteriopathies" included a group of heterogeneous disorders resulting in lesions or structural abnormalities involving the cerebral blood vessels' wall as a consequence of infectious, parainfectious or inflammatory mechanisms but also genetic predisposition or vascular malformation (e.g., focal cerebral arteriopathy, PHACE, sickle cell disease, post-varicella arteriopathy, fibromuscular dysplasia).[17] The VIPS (Vascular Effect of Infection In Pediatric Stroke Study) study identified viral infections in the prior week, recent vaccination, black ethnicity, and rural residence as risk factors for a higher occurrence of arterial ischemic stroke in children.[18,19] Serological evidence of recent, and mostly asymptomatic, herpes virus infections were detected in 45% of the enrolled patients with a predominance of HSV1 and HSV2 over VZV (respectively 24.5% versus 11.3% of the cases).[20] A large prospective cohort study by De Veber *et al.* that recruited 894 children with stroke in Germany, Canada, and UK, aiming to determine the association between prothrombotic conditions and risk of recurrent episodes of stroke, evidenced

a recurrence rate of 17.9% between 1 day and 136 months after the first stroke.[21] The following conditions were identified as independent risk factors for recurrence: antithrombin deficiency (hazard ratio 3.9; 95% confidence interval 1.4 – 10.9), increased Lipoprotein (a) (hazard ratio 2.3; 95% confidence interval 1.3–4.1) and more than one prothrombotic marker (hazard ratio 1.9; 95% confidence interval 1.1–3.2).[21]

Cardiac conditions associated with stroke encompass a wide spectrum of either acquired or congenital diseases. A study by Rodan *et al.*, that recruited 135 patients with congenital heart diseases and a diagnosis of acute ischemic stroke from Canadian Pediatric Ischemic Stroke Registry, reported a 10 years recurrence rate of 27%.[22] The most common associated risk factors included mechanical heart valve (hazard ratio = 8.8), systemic infection (hazard ratio = 5.7), and prothrombotic state (hazard ratio = 2.9).[22] Asaki *et al.* identif ied two additional risk factors in a retrospective case control study on 52 cardiopathic children who developed an arterial ischemic stroke after invasive procedures: length of ICU hospitalization and post-procedural infections.[23]

The most updated pediatric stroke guidelines

For neuro imaging the criteria is described in Attachment B.




state that it is feasible to apply r TPA in children from 2 years of age, with persistent disabling neurological deficits (e.g., Pediatric NIH Stroke Scale score ≥ 6 at the time of intervention) and radio graphically confirmed cerebral large artery occlusion, within 4.5 h of known onset of symptoms.[2,35,36] The suggested drug dosage is the same used for adults, although according to known agerelated differences in the fibrinolytic system with children having higher levels of tissue plasminogen inhibitor than adults, it would be reasonable to consider that children might benefit of higher dosages of r TPA.[2,13] The lacking initiation of an anti-thrombotic treatment for stroke prevention is associated with a 1.5–2.5 fold increased risk of recurrences after a first episode.[2] Anti-thrombotic

therapies are contraindicated in the acute setting when haemorrhagic stroke has not been excluded and in other cases including Moya Moya disease, surgery within the previous 24th, methotrexate toxicity, thrombocytopenia with platelet count less than 50,000/mm3, or history of heparin induced thrombocytopenia.[2]

**ATTACHMENT B**: CONTRAINDICATIONS TO THROMBOLYSIS**

-Unknown time of symptoms onset
-Pregnancy (adolescents)
-Clinical presentation suggestive of subarachnoid haemorrhage (SAH), even if brain imaging is negative for blood
-Patient who would decline blood transfusion if indicated
-History of prior intracranial haemorrhage
-Known cerebral arterial venous malformation, aneurysm, or neoplasm
-Persistent systolic blood pressure more than 15% above the 95th percentile for age while sitting or supine
-Glucose less than 2.78mmol/L or more than 22.22mmol/L
-Bleeding diathesis including platelets less than 100 000, prothrombin time (PT) more than15s (international normalised ratio (INR) more than 1.4), or elevated activated partial thromboplastin time (aPTT) more than upper limits of the normal range
-Clinical presentation consistent with acute myocardial infarction (MI) or post-MI pericarditis that requires evaluation by cardiology before treatment
-Prior stroke, major head trauma, or intracranial surgery within the past three months
-Major surgery within 10 days
-Parenchymal biopsy within 10 days (relative contraindication)
-Gastrointestinal or urinary bleeding within 21 days (relative contraindication)
-Arterial puncture at non-compressible site or LP within seven days (relative contraindication). Patients who have had a cardiac catheterization via a compressible artery are not excluded
-Patient with malignancy or within one month of completion of treatment for cancer
-Patients with an underlying significant bleeding disorder. Patients with a mild platelet dysfunction, mild von Willebrand disease, or other mild bleeding disorders are not excluded
**Stroke related exclusion criteria:**
-Mild deficit (Paediatric National Institute of Health Stroke Scale (PedNIHSS) less than 4) at start of tPA infusion or at time of sedation for neuroimaging, if applicable
-Severe deficit suggesting large territory stroke, with pre-tPA PedNIHSS more than 24, regardless of the infarct volume seen on neuroimaging
-Stroke suspected to be due to subacute bacterial endocarditis, Moya Moya, sickle cell disease, meningitis, bone marrow, air, or fat embolism
-Previously diagnosed primary angiitis of the central nervous system (PACNS) or secondary central nervous system (CNS) vasculitis. Focal cerebral arteriopathy of childhood is not a contraindication
**Neuroimaging related exclusion criteria:**
-Intracranial haemorrhage on pre-treatment head CT and MRI
-Intracranial dissection (defined as at or distal to the ophthalmic artery)
-Large infarct volume, defined by the finding of acute infarct on MRI involving one-third or more of the complete middle cerebral artery (MCA) territory involvement
**Drug-related exclusion criteria:**
-Known allergy to recombinant tissue plasminogen activator
-Patient who received heparin within four hours must have activated partial thromboplastin time (aPTT) in normal range
-Low molecular-weight heparin (LMWH) within past 24 hours (aPTT and INR will not reflect LMWH effect)

Specific prevention the rapies may be considered for selected aetiologies (e.g., transfusions or hydroxyurea for sickle cell disease, L-arginine for MELAS, agalsidase or migalast at for Fabry disease, pyridoxine in combination with folic acid and vitamin B12, methionine restricted, cystine supplemented diet and betaine, for homocystinuria) even if adequate supporting evidences are often not available because of their rare occurrence.[2,42] The usefulness of other specific strategies (e.g Anticoagulation for pediatric arterial dissection, patent foramen ovale closure, steroids for focal cerebral arteriopathies, or surgical strategies for moyamoya) remain controversial.[2]

The most recent protocols have all been similarly developed from multidisciplinary working groups involving paediatric and adult specialists (emergency physicians, stroke unit fellows, neurologists, interventional and diagnostic neuroradiologists, anaesthesiologists).[43–46] All the protocols were organized in three diagnostic steps based on (a) the quick assessment of the patient at the point of care (either emergency departments, intensive care units, or in-hospital wards), (b) the transfer to the MRI suite where pre-determined hyperacute MRI stroke protocols are being performed, and (c) the determination of eligibility for recanalization therapy, according to the presence/absence of inclusion/exclusion criteria (see Attachment C).

**A) INCLUSION CRITERIA FOR THROMBECTOMY**

1. Persistent neurological deficit (PedNIHSS ≥6)
2. Onset of symptoms < 6 hours
3. Radiologically confirmed large vessel occlusion (anterior or posterior circulation)
4. Age ≥ 2 years

**B) AFTER-THROMBECTOMY MANAGEMENT**

1. Clinical monitoring of femoral artery access
2. Forced supine decubitus for at least 8 hours
3. Blood count control after 6 hours
4. Brain MRI after24 hours
5. Removal of the compression bondage after 12 hours
6. Inr available for emergencies

**ATTACHMENT D****: DIAGNOSTIC TESTS TO INDIVIDUATE ETIOLOGY (AFTER ACUTE PHASE OR AFTER TREATMENT)**

**Blood second-level tests:**

- Antibodies: aCL, β2GPI, LAC, ANA, dsDNA, ANCA, ENA
- C3, C4
- Total cholesterol, triglycerides, ApoA1 e B, Lipoprotein A
- Homocysteine and other specific metabolic tests (MTHFR, folate, B12, lactate, sialo transferrin isoelectrofocusing, enzymatic test for Fabry disease)
- Pathological haemoglobin
- Serology for varicella
- Ammonium
- Screening for Thrombophilia
- Pregnancy test
- Anti Xa (if monitoring EBPM)
- Urine tox screen

**Medical consultations:**

- Cardiological (ECG, transthoracic echocardiogram and, if necessary, transoesophageal echocardiogram)
- Infectious disease specialist (consider LP if meningoencephalitis is suspected)

**Others (if indicated):**

- EEG
- VEP

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