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TRANSIENT ISCHEMIC ATTACK IN PEDIATRIC PATIENTS WITH MOYAMOYA DISEASE: CLINICAL FEATURES, NATURAL HISTORY AND PREDICTORS OF STROKE

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INTRODUCTION

Transient Ischemic Attack in children has been poorly described. It is the most common presentation in children with Moyamoya Disease. Revascularisation might be effective in stroke prophylaxis but timing is not clear.

The aim of this study was to describe the clinical characteristics of TIAs in children with Moyamoya and explore the risk factors for stroke after TIA.

METHODS

The study was conducted according to the Declaration of Helsinki and approved by the Beijing Tiantan Hospital Research Ethics Committee. Consent was obtained from all parents or legal guardians of patients in this study. Of the 696 patients with Moyamoya vasculopathy admitted to Beijing Tiantan Hospital from 2009 to 2015, 155 were children. Patients who presented with TIA as the first presentation were identified, a diagnosis of Moyamoya and TIA was made by the neurologists or neurosurgeons based on clinical assessment and with use of computed tomography angiography (CTA) or digital subtraction angiography (DSA). Inclusion criteria was children with Moyamoya who presented with TIA as their first presentation. Patients whose initial presentation was not TIA, had no DSA data, and had quasi-Moyamoya disease were excluded from the study.

The following terminology were defined

TIA - as neurological dysfunction caused by a focal brain ischemia with symptoms lasting less than 24 hours, irrespective of ischemic lesions detected by brain imaging

Recurrent TIA – involving more types of symptoms or symptom extensions as symptom progression.

TIA fluctuations – as the complete remitting and relapsing of TIA for two times or more within the first 24 hours of the initial TIA

Symptom progression – included new types of symptoms e.g previously involving motor symptoms recurrent involving language symptoms

Symptom extension – in recurrent TIAs first TIA e.g involved arms, recurrent involved arms and legs

Stroke – new symptomatic neurological deterioration lasting at least 24 hours or causing death that could not be attributed to a nonvascular cause.

Cerebral hypo-perfusion - when the patient had at least one of the following – prolonged mean transit time, time to peak or decreased cerebral blood flow.

Follow up period – the time between the initial clinical presentation and the last clinical follow-up or revascularization, whichever occurred first

Previous clinical records from other hospitals were obtained, clinical data was reviewed and information that included demographic data, vascular risk factors and TIA symptoms was recorded on admission. Two intervention neurologists reviewed the imaging that included DSA MRI CTA and CT perfusion images

RESULTS

There were 60 patients that were included in the study. TIA was more common among the early school going age and there were no patients identified in infancy. The majority of patients with triggering events were in the school going age. The commonest clinical presentation was motor weakness (n = 53 [88.3%]) and the largest number of patients had TIA for less than 10min with a mean duration of episodes of 15.0 minutes (ranging from 20 seconds to 300 minutes). Sixty percent of patients in this cohort showed progression of disease, as per DSA, to development of external carotid artery collaterals and beyond. Almost 97% of the patients that underwent CT perfusion examination demonstrated hypoperfusion, with 71% with decreased cerebral blood flow. Nearly all patients (n = 55 [91.7%]) had recurrent TIAs during follow-up, thirty (50%) within 30 days of follow up. Nineteen children [31,6%] had more than 5 recurrent TIAs. Stroke events occurred in 23% of children with TIA.

DISCUSSION

The current study had strengths and limitations. It was the first and the largest, prospective cohort but it was a single centre and selection bias could not be avoided. There is not adequate data on characteristics of TIA. It has been identified that risk factors for stroke are different in children than those in adults

CONCLUSION

In conclusion, in this study female gender, TIA progression and grade 3 Suzuki grading were identified as risk factors. There was, however, no statistical

significance for longer duration of initial TIA episode as a risk factor for stroke in multivariate analysis.

FEASIBILITY, SAFETY, AND OUTCOME OF RECANALIZATION TREATMENT IN CHILDHOOD STROKE

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Sandra Big et al

INTRODUCTION

Recanalization treatment in adult patients with Acute Ischemic Stroke (AIS) is well documented. Studies have shown that it is highly effective in reducing disability without increasing mortality if done within 4.5hrs of with the onset of symptoms. The data on outcomes with recanalization is however lacking in the pediatric population.

This study aimed to describe the feasibility, safety and outcome of IVT/EVT in children with AIS.

METHODS

This was a cohort of patients included in the Swiss NeuroPediatric Stroke Registry (SNPSR). They included children who were between1 month and 16 years of age diagnosed between 2000 and 2015 with AIS with a pediatric National Institute of Health Stroke Score (pedNIHSS) of ≥ 4. PedNIHSS is a stroke scale that has 11 items, each with instructions for the patient. A point is awarded according to the response from the patient per item assessed, where 0 indicates normal functioning and a higher point indicates worsening degree of dysfunction. The scale was adapted from adults and modified for children, the items assessed include level of consciousness (response to noxious stimulus, response to questions and response to commands), best gaze, visual, facial palsy, motor arm, motor leg, limb ataxia, sensory and best language. The diagnosis of AIS was made with Computed Tomography (CT) or Magnetic Resonance Imaging (MRI) They recorded baseline characteristics, treatment modalities, time of onset of symptoms to diagnosis and treatment and the stroke severity. Recanalization therapy was adapted based on international and institutional adult stroke guidelines. They then compared recanalization therapy with standard care.

Recanalization therapy included patients that received IVT, endovascular pharmacological and/or mechanical treatment. IVT was performed within 4,5 hours of symptom onset, extended time windows were applied in selected cases and in patients with basilar artery occlusion.

EVT was performed if

(1) the diagnosis of ischemic stroke was established,

(2) baseline pedNIHSS score was ≥ 4 points,

(3) haemorrhage on cranial CT or MRI was excluded,

(4) vessel occlusion correlated with neurological deficit, and

(5) no individual clinical or premorbid conditions or laboratory findings contraindicated thrombolysis

The discretion of the neuropediatrician, neurologist or interventional neurologist determined the final decision.

RESULTS

Of the 216 children diagnosed with AIS, 150 had a pedNIHSS score ≥ 4 and 16 received recanalization therapy. The mean duration of delay to diagnosis was 8 hrs with 4 patients receiving treatment at > 6 hours after symptom onset. In 56% of patients who received recanalization therapy; aetiology of AIS, using a cascade classification, was unknown. There were however risk factors for 1/3 of the unknown aetiology group. The occlusion was found in internal carotid artery, basilar artery and in middle cerebral artery.

DISCUSSION

The comparison of patients treated with thrombolysis and endovascular thrombectomy did not reveal any statistical difference. There were however statistically significant differences between those patients who received recanalization and those who got standard therapy, patients who received recanalization therapy had a higher pedNIHSS than those with standard care and this was the only significant predictor of outcome.

CONCLUSION

In summary, in this study, recanalization therapy is feasible and safe but benefit after 4,5 hours from symptom onset is questionable. There weren't more frequent complications, including treatment-related mortality, compared to the group that received standard therapy. No firm conclusion could be made regarding bleeding related to the arteriopathy as a risk of bleeding as there were inadequate numbers to make that conclusion. More evidence from randomised control trials in the paediatric population is still needed.

Paediatric Stroke Imaging

Alexander Khakaf, Michael Iv, Heather Fullerton, Max Wintermark. Paediatric Neurology 86 (May 2018) 5-18.

Introduction

Paediatric stroke is a distinct clinical entity with unique aetiologies, diagnostic considerations, and other challenges compared with stroke in adults. It is classified as either ischemic or haemorrhagic, with each category accounting for approximately half of paediatric strokes.

Diffusion weighted imaging (DWI) is highly sensitive for hyperacute and acute stroke. Apparent diffusion coefficient (ADC) maps confirmation that DWI hyper-intense lesion is related to restricted diffusion rather than intrinsic tissue T2 signal. Susceptibility Weighted Imaging (SWI) has increased sensitivity for blood products and calcifications as compared with Gradient Recall Echo and utilizing specific techniques can be used to differentiate between them.

ARTERIAL ISCHAEMIC STROKE

AIS Is defined as a presentation including a focal neurological deficit which corresponds to an identified region of ischemic brain. The two most common risk factors for AIS include cerebral arteriopathy and congenital cardiac disorders (i.e. thrombo-embolic disease).

Computed tomography (CT) is an efficient multi diagnosis but has significant drawbacks, including exposure of the developing brain to ionizing radiation and low sensitivity for acute infarctions. Magnetic resonance imaging (MRI) is the preferred modality for diagnosis, but in hospitals without readily available MRI or in unstable patients, CT maybe necessary. Diffuse Weighted Imaging demonstrates increased signal in an area of infarction and corresponding signal loss in the same region on Apparent Diffusion Coefficient maps. Susceptibility Weighting Imaging can demonstrate blooming (i.e. hypo-intensity) at the site of a thrombosis, which is referred to as the “susceptibility vessel sign,”

MRAs of the head and neck are favoured over CTAs and can facilitate the identification of conditions such as transient cerebral arteriopathy (TCA), arterial dissection, Moya-Moya disease, and fibromuscular dysplasia (FMD).

Transient Cerebral Arteriopathy (TCA)

Is a unilateral inflammatory arterial process which typically manifests initially as an occlusion or irregular stenosis in the distal internal carotid artery (ICA), proximal middle cerebral artery, and/or proximal anterior cerebral artery. The pathophysiology of TCA is thought to be mediated in part by a post infectious inflammatory process e.g Varicella infections. Other associated infections which have been observed in a smaller number of patients include unspecified upper respiratory infections, Epstein-Barr virus, herpes simplex virus, and enterovirus.

Other forms of Arteriopathy

Moya-Moya Disease

It is defined as a progressive occlusive cerebrovascular disorder with bilateral narrowing of distal ICAs or their proximal branches, with subsequent growth of collaterals. This condition can develop in isolation (primary) or in association with known risk factors (secondary), including sickle cell disease, radiation therapy, and Down

Arteriopathy in Sickle Cell Disease

It manifests as unilateral or bilateral stenosis and/or occlusion of the ICA and its branches. Vascular imaging demonstrated variable appearances of such filling defects, including stenosis and/or occlusions with smooth tapering, beading, and other irregular vessel contours.

HAEMORRHAGIC STROKE

It is defined as non-traumatic intra-parenchymal and/or subarachnoid haemorrhage. Most haemorrhagic strokes in children are related to arteriovenous malformations (AVM), cavernous malformations (CM) or aneurysms. Less common risk factors include brain tumours and hematologic conditions, such as acute leukaemia, thrombocytopenia, and other coagulopathies.

In the context of MRI's higher sensitivity for hyperacute and/or acute ischemic infarcts, MRI remains the preferred first-line modality in patients with haemorrhagic stroke.

The classic appearance for AVMs on T1-weighted imaging (T1WI) and T2-weighted imaging (T2WI) is a conglomeration of flow voids forming a “honeycomb” pattern with possible adjacent gliosis manifesting as increased T2 signal. In contrast, Cavernous Malformation's appearance on T1W1 and T2WI is that of a “popcorn ball” with areas of low and high signal for blood products at varying stages of evolution and associated gradient recall ECHO (GRE) and/or SWI blooming.

Intracranial aneurysms in paediatric patients include saccular, fusiform, and giant aneurysms (i.e. greater than 2.5cm in diameter). Flow voids on T1W1and/or T2WI will outline a focally dilated intracranial artery with a morphology corresponding to the aneurysm type.

MRA and CTA are first-line modalities, but have decreased sensitivity for smaller AVMs and aneurysms. Therefore, conventional angiography is indicated in children with haemorrhagic stroke, negative CTA and/or MRA, and absence of other risk factors that would account for intracranial haemorrhage. Again, in the setting of acute intracranial haemorrhage, vascular abnormalities maybe obscured by blood products, which will necessitate follow-up vascular imaging if initial studies are negative. No consensus guidelines exist for the timing of follow-up vascular imaging in paediatric patients post AVM resection.

Cerebral sinovenous thrombosis

Paediatric ischemic and/or haemorrhagic strokes related to sinovenous thrombo-occlusive disease have risk factors that overlap significantly with Acute Ischemic Stroke, and broadly include infection, trauma, and hematologic disorders such as anaemia, polycythaemia, and hypercoagulable states. Thrombosis may involve the dural sinuses, cortical and/or deep cerebral veins, and can often span both systems. Ischemia related to sinus or venous thrombosis results from backup of arterial blood flow secondary to venous congestion and/or arterial compression.

It is important to note that haemorrhage is a common finding in intracranial venous thrombosis and is related to diapedesis of blood from venous congestion.

Non-enhanced CT may demonstrate hyperattenuating thrombus within a cortical vein as the “cord sign”. Sinovenous thrombus’ appearance T1W will be isointense (relative to brain) acutely, hyperintense sub-acutely, and isointense again chronically. OnT2WI the thrombus will be hypointense acutely, and hyperintense in the subacute and chronic phases. Sinovenous thrombosis often presents as the classic “empty delta sign” where the thrombus manifests as a hypoattenuating triangle within the peripherally opacified straight or transverse sinus.

Conclusion

MRI is the initial modality of choice, including shortened stroke protocols (e.g.DWI, ADC, and SWI and/or GRE), followed by vascular imaging to detect abnormalities which may underlie an identified stroke. These patients require follow-up vascular imaging at institution-specific intervals to identify previously occult vascular abnormalities, recurrence and/or progression of known lesions, and/or new infarcts. Evolving MR perfusion techniques are making progress in identifying salvageable brain parenchyma, and vascular imaging methods (e.g.vessel wall imaging and black blood MRI) are helping to recognize vascular abnormalities that so often under lie these cases.