RESEARCH BRIEF

Cerebral Infarction after Mild Head Trauma in Children

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We conducted this retrospective, case record review to determine the risk factors and clinical features associated with cerebral infarction after mild head trauma in children. The median age of the cohort was 2.18 years (range, 6 mo-8 y). Most (26/29) of the patients developed the neurological symptoms and signs within 72 hours after trauma, 51.7% within 30 minutes. The first symptoms included hemiparesis (20), facial paresis (7), and convulsion (7). 86.21% of the lesions lay in basal ganglia region. Pre-existing basal ganglia calcification was identified in 13 as a risk factor.

Keywords: *China, Etiology, Head injury, Outcome, Stroke.*

Stroke is one of the top ten causes of childhood death and there is a high risk of serious morbidity for the survivors [1]. The causes of childhood stroke are numerous. Head trauma is reported to be a possible cause of childhood stroke [2]. While minor injuries to the head are a very common occurrence in childhood, cerebral infarction is an exceedingly rare sequelae. Posttraumatic cerebral infarction has been reported in children [3-10]. We retrospectively studied children with cerebral infarction after mild head trauma to identify risk factors and describe the presenting clinical features in children.

METHODS

Children between 1 month and 14 years old with cerebral infarction after mild head trauma were recruited from the electronic database of the pediatric neurologic ward of Shengjing Hospital of China Medical University between August 2008 and September 2011. Patients who had been diagnosed with ischemic or hemorrhagic stroke, epilepsy and other central nervous system disease before enrollment; patients who had vascular malformation, Moyamoya syndrome, cerebral arteritis, congenital hemiplegia and coagulation disorder; and patients who had signs of infection (fever, cough, nasal discharge, diarrhea, urinary tract infection etc.) were excluded. Children with cerebral infarction due to other reasons were chosen as controls, including 19 cases with cerebral infarction associated with *Mycoplasma pneumoniae* infection, 10 cases with moyamoya disease, 4 cases with cerebral infarction related to viral encephalitis, 3 cases with bacterial meningitis complicated by cerebral infarction, 2 cases with cerebral infarction due to intracranial hemorrhage, 1 case with tubercular meningitis complicated by cerebral infarction, and 5 cases with unexplained factor.

The following data were extracted: age, gender, mode of injury, neurological manifestation, neuroimaging (CT scan, MRI, and magnetic resonance angiography), laboratory examination (complete blood count, hematocrit level, platelet level, electrolytes, blood gas analysis, routine coagulation study, including prothrombin time, activated partial thromboplastin time, fibrinogen levels, plasminogen levels, hemoglobinopathy study, erythrocyte sedimentation rate, C-reactive protein, liver and renal function test, blood lactate level, blood ammonia level, immunoglobulin quantitative determination, T cell subgroup assay, thyroid gland function levels, including FT3, FT4, TSH, anti-thyroglobulin antibodies, anti-thyroid peroxidase antibodies, parathormone, anticardiolipin, antinuclear antibody, rheumatoid factor, complement levels, lupus, anticoagulant assay, lipid profile, creatine phosphokinase, cytomegalovirus DNA in plasma or urine, pathogen examination (including *Mycoplasma pneumoniae*, respiratory syncytial viruses, adenovirus, influenza viruses, parainfluenza virus, Echo virus, Coxsackie virus, Epstein-Barr Virus, toxoplasma, rubella virus, measles virus), clinical outcome, and recurrence.

Statistical analysis: SPSS V.16.0 (SPSS, Chicago, Illinois, USA) was used for data analysis. Fisher's exact test or γ^2 test was used to assess the frequency of risk factors and clinical features. Univariate relationships

between risk factors were analyzed using logistic regression. Results were calculated as odds ratios and 95% confidence intervals with probability value (2-tailed). *P* values<0.05 were considered statistically significant.

RESULTS

A total of 73 children with cerebral infarction were seen during the study period. Twenty-nine patients (6 month to 8 year) presented with acute cerebral infarction due to mild head trauma. The mode of injury was a fall in 14 (from bed in 10) children and fall down steps in 15. The first clinical presentations appeared within 30 minutes in 15 children (51.7%), between 30 minutes and 24 hours in 8 (27.6%), between 24 hours and 72 hours in 3 (10.3%), between 3 days and 7 days in 1 (3.4%), and after 7 days in 2 (6.9%). There was no loss of consciousness in any child. Clinical manifestation was hemiparesis (with facial paresis in 7, aphasia in 2); seizures (generalized in 5, focal in 2); gait disturbance with aphasia in 1; and aphasia in 1. Six of 22 patients whose first clinical presentation was not seizure had recurrent convulsion onset after the injury (***Table* I**). Basal ganglia calcification was identified in 13 cases (44.8%). The median age at time of stroke was 3.5 years (range, 6 months to 5 years). We compared the frequency of risk factors between patients with cerebral infarction due to mild head trauma and due to other reasons. Basal ganglia calcification was not identified in any of the cases with other reasons. There were no significant differences for the rest of risk factors in our cohort (***Table* II)**.

No child had evidence of fracture and intracranial hemorrhage on CT scanning (done between 2 hours to 48 hours). On magnetic resonance imaging the lesion was located in basal ganglia in 25, dorsal thalamus in 2, multi lesion in 1, and parietal lobe in 1. The lesion was unilateral in 24 children and bilateral in the rest. Repeat MRI was done 1 week after the first MRI in 5, 2 weeks in 4. This showed decreased size in the original lesion. Magnetic resonance angiography was performed in 18 children (62.1%), and 3 were abnormal, including few branch of middle cerebral artery in 1, stenosis of vertebral artery in 1, tenuous internal carotid and stenosis of arteria cerebri anterior in 1. Compared to the children with cerebral infarction due to other reasons, basal ganglia were more likely to be affected, and most of head MRA were normal in our cohort (***Table* I**).

Bilateral basal ganglia calcification was confirmed by head CT scan in 9 children with cytomegalovirus infection. The results of other laboratory examinations were all normal.

All cases were managed on conservative treatment, and without antiplatelet agents and anticoagulant agents. After a median follow-up of 13.5 months (range, 3 -39 months), all patients had a good outcome, except one still had mild facial paralysis after 18 months. There were 3

TABLE I CHARACTERISTICS OF THE STUDY SUBJECTS

Characteristics	*Mild head trauma(n=29)*	*Controls (n=44)*
Male	18 (62.1)	23 (52.3)
Age (median, y)	2.18	5.26
Initial symptom		
Hemiparesis	20 (69)	30 (68.2)
Seizure	7 (24.1)	10 (22.7)
Facial paresis	7 (24.1)	20 (45.4)
Basal ganglia lesion*	25 (86.2)	20 (45.4)
Abnormal MRA*	3/18 (16.7)	30/42 (71.4)
Recurrence[#]	3 (10.3)	14 (31.8)

***P<0.001,* [#]<0.05; *values are in no. (%).*

TABLE II RISK FACTORS IN CHILDREN WITH CEREBRAL INFARCTION DUE TO MILD HEAD TRAUMA AND CONTROLS

Risk factors	*Mild head trauma (n=29)*	*Controls (n=44)*	*Odds ratio (95%CI)*
Basal ganglia calcification*	13 (44.8%)	0	
Cytomegalovirus	11 (37.9%)	8 (18.2%)	2.75 (0.941, 8.035)
Mycoplasma pneumoniae	12 (41.4%)	26 (5 9.1%)	0.49 (0.189, 1.267)
Epstein-Barr virus	2 (6.9%)	0	
Echo virus	1 (3.4%)	1 (2.3%)	1.54 (0.092, 25.569)
Coxsackie virus	1 (3.4%)	1 (2.3%)	1.54 (0.092, 25.569)
Influenza viruses	1 (3.4%)	1 (2.3%)	1.54 (0.092, 25.569)
Parainfluenza virus	1 (3.4%)	1 (2.3%)	1.54 (0.092, 25.569)

**P<0.001.*

patients recurrently diagnosed with ischemic stroke, including one 15-month-old boy due to mild head trauma after 8 months, one 4-year-old girl and 2-year-old boy due to *M. pneumoniae* infection after 1 year, and 1.5 years, respectively. Compared to the children with cerebral infarction due to other reasons, recurrence was negligible.

DISCUSSION

The cases described here did not present with loss of consciousness after mild head trauma [11]. It is possible that the fall leading to the head injury could have been the first presenting symptom of a neurological event. It is difficult to definitively rule this out; however, the head injury was witnessed in all the patients and their parents clearly observed the emergence of the neurological signs following a brief interval.

The pathogenesis of ischemic stroke after minor head trauma in children is still being elucidated. The anatomical characteristics of the growing brain in infancy, motion of the brain due to the trauma, and vasospasm or stretch and a shearing injury of the vessel with an intimal lesion and subsequent thrombosis, may all play a part [6]. The MRA changes in previous reported cases and our cohort were almost normal, without vascular occlusion or stenosis. Other causes may be: traumatic dissection of the common carotid, internal carotid arteries or of the vessels of circle of Willis, congenital predisposition to rupture of cervical or intracranial arteries, and prothrombotic status or cardiac disease may be possible causes for cerebral ischemic lesions in children [5,12]. Thus, before classifying a cerebral infarction in children as idiopathic, it is imperative to exclude all possible causes.

Basal ganglia calcification is the major risk factor identified in our study. Pathological basal ganglia calcification is due to various causes likes metabolic disorders, infectious and genetic diseases and others [13]. Hypoparathyroidism and pseudohypoparathyroidism are the most common causes of pathological basal ganglia calcification. However, the results of thyroid gland function and parathormone were all normal in the children with basal ganglia calcification in our study. Infections including toxoplasmosis, rubella, cytomegalovirus, cysticercosis, and AIDS cause multiple and asymmetric intracranial calcification. In our study, there were 11 children with cytomegalovirus infection. 9 of the 11 children were confirmed to present with basal ganglia calcification by brain CT scan. However, it was symmetric basal ganglia calcification, not asymmetric one. Inherited and neurodegenerative diseases *e.g.* Cockayne syndrome, tuberous sclerosis, Fahr's syndrome, and Down syndrome cause symmetrical, bilateral basal ganglia calcification which is not related to metabolic disorders. As neuroimaging after head tauma was normal except for the infarction, concluded that basal ganglia calcification had existed before head trauma. However, the cause leading to basal ganglia calcification was not clear. Children are particularly vulnerable to transforming, stretching, and distorting forces, which can be imposed by even minor head injuries. When calcification existed, it is easier to develop vasospasm and/or thrombosis. However, authors have concluded that basal ganglia calcification cannot be considered as a clinically relevant neuroradiological finding in the majority of cases and that it should not be used as an explanation for frequently observed neurological disturbances [14,15].

One of the main limitations of retrospective studies is that medical records are not always detailed and negative responses to questions in the history may not always be recorded, and there are considerable errors, such as confounding and bias. Details of blood results and radiological imaging were sometimes missing. In order to clarify the risk factors and the clinical features of children with cerebral infarction after mild head trauma, future multricentric, prospective studies are recommended.

Contributors: FHY: study design; clinical and radiographic data collection; analysis and interpretation of clinical and radiographic data; statistical analysis; writing-up of manuscript; intellectual content of manuscript. HW: study design; analysis and interpretation of clinical and radiographic data, writing-up of manuscript; intellectual content and critical revision of manuscript; mentorship of the project. JMZ: clinical outcome data collection; intellectual content and critical revision of manuscript. HYL: study design; analysis and interpretation of radiographic data.
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