The Etiology and Outcome of Cerebrovascular Diseases in Northeastern Thai Children

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Objective: *To review the etiology and outcome of cerebrovascular diseases among children in Northeastern Thailand.*
Study design: *Retrospective, descriptive study.*
Setting: *Srinagarind Hospital, Khon Kaen, Thailand.*
Material and Method: *The authors studied 109 pediatric patients admitted between April 1995 and 2006.*
Results: *The mean age was 11.6 years and the male-to-female ratio was 1.06:1. The ages at onset ranged from 6 months to 15 years, while the most commonly affected age group were children between 10 and 15 years. The authors identified 74 hemorrhagic strokes (65%) and 35 ischemic strokes (31%). The most common etiologic factor in hemorrhagic and ischemic strokes was arteriovenous malformations and cardiac diseases respectively. The five most common presenting symptoms were headache, alteration of consciousness, hemiparesis, vomiting, and seizures. The mortality rate was 22%.*
Conclusion: *Knowledge of the etiologies and outcomes of cerebrovascular disease in children should improve diagnosis and management.*

Keywords: *Cerebrovascular disease, Hemorrhagic stroke, Ischemic stroke, Children, Etiology, Outcome*

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Cerebrovascular diseases are rare in children as the reported incidence of stroke in children (birth to 14 years) is 2.5 to 2.7 cases per 100,000 children[1,2]. Cerebrovascular diseases usually presented with acute focal neurological deficit but not always, as some patients presented with migrainous-like headache or epilepsy. The causes of pediatric stroke are diverse, unlike for adults in whom hypertention and artherosclerosis predominate[3]. The diagnosis is usually delayed because of a lack of awareness of childhood stroke in the general public and the healthcare community[4]. The delay results in the high morbidity and mortality rates.

Stroke is among the top ten causes of death in children in the United States. In 1998, the estimated mortality rate from stroke, in children below one year of age, was 7.8 cases per 100,000[5]. According to Lanthier et al, death occurs in ~20% of patients[6]. Apart from death, 45% of pediatric stroke patients have a persistent neurological deficit or seizure disorder after the acute event[4].

Despite its being rare, cerebrovascular disease is not uncommon in Srinagarind Hospital, the main tertiary care center in Northeast Thailand. Thus, the purpose of the present study was to review the etiology and outcome of cerebrovascular diseases among children in Northeast Thailand.

Material and Method

The authors retrospectively reviewed the medical records (for the 12-year period April 1995 to 2006) of pediatric patients with cerebrovascular diseases admitted to Srinagarind Hospital, Division of Pediatric Neurology, Department of Pediatrics, the main referral center in northeast Thailand.

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Definition

Stroke is defined as a focal neurological deficit of sudden onset, not solely related to seizure, resulting from irreversible, focal ischemic (ischemic stroke) or hemorrhagic (hemorrhagic stroke) damage to the brain parenchyma secondary to a cerebrovascular disorder[6].

Inclusion criteria

1. Patients diagnosed with a cerebrovascular disease;

2. Between 1 month and 15 years of age; and,

3. Having undergone at least one neuro-imaging study (viz., cranial computed tomography (CT), cranial magnetic resonance imaging (MRI) or cerebral angiography).

Exclusion criteria

1. Incomplete medical records; or,

2. Post-traumatic stroke.

The data collected includes age, sex, age at onset of symptom, clinical features, etiology, and outcome of cerebrovascular disease.

Statistical analysis

The continuous data were assessed by mean, standard deviation (SD) and range. The category data were expressed as number and percent.

Results

General characteristics

Of the 109 patients fulfilled the criteria, 56 were male (51%) and 53 female (49%). The male-to-female ratio was 1.06:1. The age at onset ranged between 6 months and 15 years (mean, 11.6 $\pm$ 9.4 years). The most commonly affected age group was between 10 and 15 years (Table 1).

Etiologic factors

In the presented group of patients, 74 had had hemorrhagic (68%) and 35 ischemic strokes (32%). The ratio of hemorrhagic stroke to ischemic stroke was 2:1. The most common etiology among the hemorrhagic strokes was arteriovenous malformation (AVM) (32%), followed by hematologic disease (31%) and idiopathic hemorrhagic strokes (19%). By comparison, the most common etiologic factor in ischemic strokes was cardiac disease (17%), while 43% were idiopathic ischemic strokes. All of the etiologic factors for hemorrhagic strokes and ischemic strokes are presented in Table 2 and Table 3, respectively. The causes of cerebrovascular diseases in 12 leukemic patients were thrombocytopenia, hyperviscosity and CNS involvement with subarachnoid hemorrhage (9, 3, and 1 cases, respectively).

Table 1. Age at onset of 109 patients with cerebrovascular diseases

Age at onset	No. of patients (%)
1 month – 5 years	24 (22)
> 5 years – 10 years	28 (26)
> 10 years – 15 years	57 (52)
Total	109 (100)

Table 2. The etiologic factors of 74 patients with hemorrhagic strokes

Etiologic factors	No. of patients (%)
Vascular diseases	31 (42)
Arteriovenous malformations (AVM)	24 (32)
Aneurysm	4 (5)
Angioma	1 (1)
Carvernous hemangioma	1 (1)
Venous hemangioma	1 (1)
Hematologic diseases	23 (31)
Acute leukemia	12 (16)
Hemophilia	2 (3)
Anticoagulant usage	2 (3)
Disseminated intravascular coagulation (DIC)	2 (3)
Aplastic anemia	1 (1)
Acquired prothrombin complex deficiency (APCD)	1 (1)
Wilson disease with liver failure and coagulopathy	1 (1)
Post-hemodialytic coagulopathy	1 (1)
Congenital cyanotic heart disease	1 (1)
Cardiac diseases	1 (1)
Rheumatic heart disease	1 (1)
Infectious disease	2 (3)
Dengue hemorrhagic fever	2 (3)
Miscellaneous	4 (5)
Brain tumor	2 (3)
Wilms tumor with brain metastasis	1 (1)
Idiopathic	14 (19)
Total	74 (100)

Clinical features

The five most common features of stroke

Table 3. The etiologic factors of 35 patients with ischemic strokes

Etiologic factors	No. of patients (%)
Cardiac diseases	6 (17)
Rheumatic heart disease	2 (6)
Ventricular septal defect (VSD) (post-operative VSD closure)	1 (3)
Atrial stenosis	1 (3)
Atrial myxoma	1 (3)
Hypertrophic obstructive cardiomyopathy	1 (3)
Hematologic diseases	6 (17)
Congenital cyanotic heart disease	3 (9)
Acute leukemia	1 (3)
Protein C deficiency	1 (3)
Protein C and protein S deficiency	1 (3)
Vascular diseases	4 (11)
Moyamoya disease	4 (11)
Miscellaneous	4 (11)
Neuropsychiatric SLE with vasculitis	2 (6)
Hypovolemic shock	1 (3)
Dyslipidemia	1 (3)
Idiopathic	15 (43)
Total	35 (100)

patients were headache, alteration of consciousness, hemiparesis, vomiting, and seizures (52, 46, 44, 43, and 34%, respectively). Other features are presented in Table 4.

The five most common features in hemorrhagic strokes were headache, vomiting, alteration of consciousness, hemiparesis, and seizures (66, 60, 39, 35, and 30%, respectively). The five most common features in ischemic strokes were hemiparesis, alteration of consciousness, seizures, headache, and cranial nerve palsy (69, 54, 43, 23, and 20% respectively).

The range of duration of symptoms before admission was 1 hour to 11 years (median, 1 day). The patient with the 11-year duration had arteriovenous malformations and presented with congenital mass at the occipital area. In 26 patients, symptoms developed during hospital admission.

Neuro-imaging studies

The most common neuro-imaging study used was CT scan, angiography and MRI (67, 34, and 25 cases, respectively) and some underwent more than one study. Positive results for each study were 94, 79, and 84%, respectively (Table 5).

Table 4. Clinical features of 109 patients with cerebrovascular diseases*

Clinical Features	Hemorrhagic stroke in 74 patients No. (%)	Ischemic stroke in 35 patients No. (%)	Total No. (%)
Headache	49 (66)	8 (23)	57 (52)
Alteration of consciousness	29 (39)	19 (54)	50 (46)
Hemiparesis	26 (35)	24 (69)	48 (44)
Vomiting	44 (60)	4 (11)	48 (43)
Seizures	22 (30)	15 (43)	37 (34)
Cranial nerve palsy	2 (3)	7 (20)	9 (8)
Visual disturbance	5 (7)	1 (3)	6 (5)
Dysphasia/aphasia	3 (4)	3 (9)	6 (5)
Fever	1 (1)	1 (3)	2 (2)

* Some patients had more than one manifestation

Table 5. Neuroimaging studies in 109 patients*

Neuroimaging	No. of patients	Result	
		Positive, No. (%)	Negative, No. (%)
CT scan	67	63 (94)	4 (6)
Angiography	34	27 (79)	7 (20)
MRI (± MRA or MRV)	25	21 (84)	4 (16)

* Some patients performed more than one studies

Table 6. Outcomes of treatments in 109 patients

Outcomes	Hemorrhagic No. (%)	Ischemic No. (%)	Total No. (%)
Complete recovery	26 (35)	9 (26)	35 (31)
Sequalae	13 (18)	19 (54)	32 (28)
Death	20 (27)	4 (11)	24 (22)
Recurrence	1 (1)	0 (0)	1 (1)
Loss follow-up	3 (4)	3 (9)	6 (6)
Refer	11 (15)	0 (0)	11 (10)
Total	74	35	109

Outcomes of treatments

Craniotomy and clot removal were performed in 30 patients suffering hemorrhagic strokes, while anticoagulants (low molecular weight heparin, heparin or warfarin sodium) were given in 12 cases of ischemic

stroke. All patients received full supportive treatments. The overall mortality rate was 22%; in hemorrhagic *vs.* ischemic strokes were 27 *vs.* 11%, respectively. Complete recovery overall, in hemorrhagic, and in ischemic strokes was 31, 35, and 26%, respectively. Sequalae were found in 28, 18, and 54% of overall, hemorrhagic, and ischemic strokes, respectively. Overall outcomes are described in Table 6. The common sequelae were hemiparesis with spasticity, seizures, and dysphasia (45, 7, and 6 cases, respectively).

Discussion

Despite the rarity of cerebrovascular diseases, there were 109 patients in the present study. CT scanning was the first neuro-imaging study used in most of the presented patients since it is available for emergency case and it is easy to perform in younger children. MRI or angiography will be performed if CT scan was negative or for further study. Angiography is limited in young children in the authors' setting because of the small size of their arteries.

All together, the authors identified 74 hemorrhagic and 35 ischemic strokes, in contrast to other studies in which ischemic strokes were usually higher than hemorrhagic strokes[2,7-10]. The two most common etiologies of hemorrhagic strokes were vascular and hematologic diseases (42 and 31 percent). The authors found no sickle cell disease which was the most common cause of ischemic stroke in the Baltimore-Washington Cooperative Young Stroke Study[11] since sickle cell disease has not been diagnosed in Thais (Medline database and Thai Index Medicus). The mortality rate in the present study was high (22%) because of late presentation, the limited availability of neuro-imaging instruments outside the authors' tertiary care facility, and the paucity of neurosurgeons.

Srinagarind Hospital is the main tertiary center for Northeast Thailand; thus, the authors have seen the cerebrovascular and hematological diseases as well as their complications (especially hemorrhage). Nineteen percent of the presented cases were idiopathic hemorrhagic strokes, perhaps due to the ruptured small AVM or aneurysm, which cannot be found in the neuro-imaging studies. Cardiac emboli were the most common cause of ischemic stroke as in other studies[7,9]. The reasons for the high ratio of ischemic stroke in cardiac diseases were the hyperviscosity in congenital cyanotic heart diseases and the emboli in other heart diseases. The authors saw idiopathic ischemic strokes in 43% of cases; the high ratio probably due to the limitation of the hematologic laboratory, which only recently (2004) began assessing protein C, protein S and antithrombin III.

The predominant age at onset of cerebrovascular diseases in the present study was among 10-15 year-olds, the age when AVMs usually rupture[12]. The clinical features of ischemic and hemorrhagic strokes were similar; therefore, the authors cannot use clinical features to differentiate between the two. Consequently, neuro-imaging studies must play an important role in diagnosis. The highest positive result of CT scan is probably due to the high ratio of hemorrhagic stroke, which can be diagnosed by CT scan, but CT scanning provides limited detail on etiology, size, and location. Thus, cerebral angiography and MRI ($\pm$ MRA) have an important role for diagnosing cerebrovascular diseases in children. MRI is recommended as the preliminary investigation of choice, but where this is not available, CT scan to exclude hemorrhage is mandatory[13,14]. In Srinagarind Hospital MRI is not available in the emergency setting, so the authors use CT scan as the first investigation.

Conclusion

The authors retrospectively reviewed the etiology and outcome of cerebrovascular diseases of children presenting at the main tertiary medical centre in Northeast Thailand and found a higher ratio of hemorrhagic stroke in contrast to other studies. The respective etiologic factors were diverse as in other studies; the most common in hemorrhagic *vs.* ischemic stroke being vascular diseases (especially AVM) *vs.* cardiac diseases. Headache, alteration of consciousness, hemiparesis, vomiting, and seizure were the five most common features for both types. The appropriate use of CT scan, MRI and angiography together will help in making the diagnosis. The mortality rate of the presented patients remains high (22%). Therefore, knowledge of the etiology and outcomes of cerebrovascular disease in children should improve diagnosis and management.

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สาเหตุและผลการรักษาโรคหลอดเลือดสมองในเด็กภาคตะวันออกเฉียงเหนือของไทย

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วัตถุประสงค์*: เพื่อทบทวนสาเหตุและผลการรักษาโรคหลอดเลือดสมองในเด็กภาคตะวันออกเฉียงเหนือของไทย*
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วัสดุและวิธีการ*: ทบทวนเวชระเบียนของผู้ป่วยเด็กที่เป็นโรคหลอดเลือดสมอง 109 ราย*
ผลการศึกษา*: อายุเฉลี่ย 11.6 ปี สัดส่วนเพศชายต่อหญิง 1.06:1 อายุที่มีอาการ 6 เดือนถึง 15 ปี พบผู้ป่วยหลอดเลือดสมองแตก 74 ราย หลอดเลือดสมองตีบหรืออุดตัน 35 ราย สาเหตุที่พบบ่อยที่สุดในกลุ่มหลอดเลือดสมองแตก และกลุ่มหลอดเลือดสมองตีบหรืออุดตัน คือ arteriovenous malformation และโรคหัวใจ ตามลำดับ อาการที่พบบ่อยที่สุดคือ ปวดศีรษะ ความรู้สึกตัวเปลี่ยนแปลง อ่อนแรงครึ่งซีก อาเจียน และชักตามลำดับ พบอัตราตายร้อยละ 22*
สรุป*: ความรู้เกี่ยวกับสาเหตุและผลการรักษาโรคหลอดเลือดสมองในเด็กจะช่วยให้การวินิจฉัยโรคและการรักษาดีขึ้น*