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Stroke in young adults

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A prospective study of 100 consecutive cases of stroke (cerebrovascular accident, CVA) in the young was carried out during 1988 and 1989. Ischemic stroke and hemorrhagic stroke accounted for 51% and 49% of cases respectively. The mean age of onset of stroke in males and females were 32.6 ± 7.4 and 32.3 ± 9.2 respectively and there was no statistically significant difference between them. Rheumatic heart disease and vasculitis were important causes of ischemic stroke. Hypertension, aneurysm and arteriovenous malformations were common causes of hemorrhagic stroke. The overall mortality rate was 20%. The causes of death in this series were related to brain damage as well as underlying systemic diseases. Strategies for investigation of stroke in young adults are discussed briefly.

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กัมมันต์ พันธุมจินดา, เกียรติศักดิ์ ราชบริรักษ์. โรคหลอดเลือดสมองในคนอายุน้อย. จุฬาลงกรณ์เวชสาร 2533 พฤศจิกายน; 34(11): 835-842

ได้ทำการศึกษาหาสาเหตุของโรคหลอดเลือดในสมองในคนอายุน้อยจำนวน 100 ราย ในระหว่างปี 1988-1989 ในจำนวนนี้พบเป็นโรคสมองขาดเลือดและโรคหลอดเลือดสมองแตกจำนวน 51% และ 49% ตามลำดับ อายุเฉลี่ยในเพศชายและเพศหญิงเท่ากับ 32.6 ± 7.4 และ 32.3 ± 9.2 ซึ่งไม่มีความแตกต่างกันทางสถิติ โรคหัวใจ รูมาติก และหลอดเลือดอักเสบเป็นสาเหตุสำคัญของโรคสมองขาดเลือด ส่วนความดันโลหิตสูง หลอดเลือดโป่งพอง และหลอดเลือดผิดปกติแต่กำเนิด เป็นสาเหตุสำคัญของหลอดเลือดในสมองแตก อัตราตายในอนูกรรมมี 20% และสาเหตุการตายเกิดจากรอยโรคในสมอง และโรคทางกายที่เกิดขึ้นร่วมด้วย นอกจากนี้ ได้อภิปรายถึงแนวทางการตรวจค้นหาสาเหตุของโรคหลอดเลือดสมองในคนอายุน้อยพอเป็นสังเขป

The incidence of stroke (cerebrovascular accidents, CVA) in young adults varies geographically. According to the American National Stroke Survey⁽¹⁾, only 3% of cerebral infarctions occurred in young adult Americans. However, 30% of 850 stroke patients were under the age of 40 in India⁽²⁾. There has been no comparative study of the incidence of stroke in the young in Thailand. From unpublished data at the division of Neurology, Chulalongkorn Hospital, the incidence of stroke in the young is approximately 26% of all stroke patients.

Young stroke patients have a greater likelihood of underlying correctable or preventable lesions and should therefore be investigated more aggressively. In order to find base-line data in our institution, we have studied the causes of stroke in 100 cases admitted to Chulalongkorn Hospital.

Materials and Methods

During 1988 and 1989 one hundred consecutive stroke patients, aged 16 to 45 years were studied prospectively. The diagnosis of stroke was based on the clinical syndromes and neurological deficits of sudden or rapid onset, without apparent cause other than vascular disturbances. These included the following: 1) ischemic (thrombotic or embolic) occlusion of a cerebral vessel resulting in brain ischemia or infarction. 2) rupture of a vessel resulting in intracranial hemorrhage. This definition excluded traumatic processes which produced secondary vascular pathology. Embolic stroke was diagnosed by Cerebral Embolism Task Force's criteria⁽³⁾.

The basic evaluation of a young person with stroke was the same as that for older patients. A

complete history, physical and neurological examinations, were performed. Symptoms were classified into four groups: 1) TIA (Transient Ischemic Attack); 2) RIND (Reversible Ischemic Neurological Deficits); 3) progressive stroke and 4) complete stroke. CT-Scan of the head, chest x-ray, electrocardiogram (EKG), complete blood count, urinalysis, plasma glucose, serum lipid profile, erythrocyte sedimentation rate (ESR) and VDRL were performed in all cases. If the cause of the stroke could not be identified definitely, more sophisticated or invasive studies, e.g. complement level, SLE profile, echocardiogram, coagulogram, anticardiolipin antibodies and four vessel angiography were performed. Standard treatment for TIA and RIND were aspirin 300 mg. per day. For progressive stroke and cerebral embolism, anticoagulant therapy were given if there were no contraindication. In complete ischemic stroke, supportive measures and treatment of the underlying diseases were the mainstay of therapy. For hemorrhagic stroke from arteriovenous malformation (AVM) and aneurysm, surgical intervention was given if indicated. Other intracranial bleeding was treated symptomatically. Since the number of patients in each subgroup was small, analysis of the outcomes of treatment was not performed.

Results

Types of stroke. There were 51 ischemic strokes and 49 hemorrhagic strokes.

Age and Sex. The distribution of age, sex, mean and S.D. of ages in each type of stroke are shown in Table 1. The male to female ratio was 1.1 : 1. The mean age of males and females were 32.6 ± 7.4 and 32.3 ± 9.2 years. The difference was not statistically significant.

Table 1. Age & sex distribution of young stroke victims.

| Age | Ischemic stroke | | | Hemorrhagic stroke | | | |
|---------------|-----------------|----------------|----------------|--------------------|----------------|----------------|----------------|
| | M | F | T | M | F | T | T |
| 15-19 | 0 | 2 | 2 | 1 | 0 | 1 | 3 |
| 20-24 | 4 | 6 | 10 | 5 | 7 | 12 | 22 |
| 25-29 | 3 | 3 | 6 | 1 | 0 | 1 | 7 |
| 30-34 | 7 | 2 | 9 | 9 | 2 | 11 | 20 |
| 35-39 | 4 | 5 | 9 | 6 | 6 | 12 | 21 |
| 40-44 | 7 | 8 | 15 | 6 | 6 | 12 | 27 |
| Total | 25 | 26 | 51 | 28 | 21 | 49 | 100 |
| Mean \pm SD | 33.0 \pm 7.0 | 31.5 \pm 9.0 | 32.2 \pm 8.0 | 32.5 \pm 7.6 | 33.3 \pm 9.0 | 32.8 \pm 8.2 | 32.5 \pm 8.0 |

M = Male F = Female T = Total

Classification of clinical symptoms. In the ischemic strokes, there were 3/51 TIA, 4/51 RIND, 8/51 progressive strokes and 36/51 complete strokes. Most of the hemorrhagic strokes presented as complete strokes.

Types of lesions. Among ischemic strokes, the identified lesions were: 26/51 thrombotic, 18/51 embolic, and 7/51 undefined. Among hemorrhagic strokes, the locations were: 33/49 intracerebral, 12/49 subarachnoid, 3/49 intraventricular, and 1/49 multiple sites.

Locations of lesions. According to the clinical profiles and CT-Scans, the anatomical localization of both ischemic and hemorrhagic stroke in this study are presented in Tables 2 & 3. Ischemic stroke with negative CT-Scan and an ill-defined clinical syndrome was classified as "unknown vascular territory". All of the multiple ischemic lesions were caused by cardiogenic cerebral embolism. The vascular centrencephalon encompassed the major sites for hypertensive hemorrhage (8/15) and the minor site for non-hypertensive bleeding (6/34). One case of multiple hemorrhages was caused by leukemia.

Table 2. Distribution of the responsible vascular territory in ischemic stroke.

| Vascular territory | Male | Female | All |
|------------------------------------|-----------|-----------|-----------|
| Internal carotid artery | 3 | 0 | 3 |
| Anterior cerebral artery | 1 | 0 | 1 |
| Middle cerebral artery | 9 | 11 | 20 |
| Posterior cerebral artery | 1 | 0 | 1 |
| Vertebro-basilar artery | 4 | 3 | 7 |
| Multiple vessels | 0 | 3 | 3 |
| Lacunar infarction | 2 | 0 | 2 |
| Venous system (pills & puerperium) | 0 | 2 | 2 |
| Unknown | 5 | 7 | 12 |
| Total | 25 | 26 | 51 |

Table 3. Distribution of the location of hemorrhagic stroke.

| Location | Male | Female | All |
|------------------|-----------|-----------|-----------|
| Internal capsule | 4 | 5 | 9 |
| External capsule | 1 | 0 | 1 |
| Brainstem | 3 | 0 | 3 |
| Cerebellum | 1 | 0 | 1 |
| Lobar hemorrhage | 12 | 7 | 19 |
| Subarachnoid | 4 | 8 | 12 |
| Intraventricular | 2 | 1 | 3 |
| Multiple sites | 1 | 0 | 1 |
| Total | 28 | 21 | 49 |

Risk factors or causes of ischemic stroke. The most common cause of ischemic stroke in the young was cardiogenic embolism. Rheumatic valvular heart disease included 8 cases of mitral stenosis and 1 case

of mitral regurgitation. Other valvular lesions accompanied by mitral stenosis were: 1 case of mitral regurgitation, 1 case of tricuspid regurgitation, 1 case of mitral regurgitation with aortic regurgitation and 1

case of mitral regurgitation with tricuspid regurgitation. Atrial fibrillation was associated with mitral stenosis in 6 cases. Other valvular heart diseases, which were potential sources of cerebral embolism in this series were mitral valve prolapse (3 cases), prosthetic mitral valve (2 cases), and non bacterial thrombotic endocarditis (1 case). The non- bacterial thrombotic endocarditis was associated with Sjögren's syndrome and mucin-producing bronchiolo-alveolar carcinoma of the lung. Isolated cardiac arrhythmia was found in two cases. One was

atrial fibrillation and the other was the "sick sinus" syndrome. Vasculitis causing cerebral infarction included: 4 cases of systemic lupus erythematosus (SLE) and single cases of polyarteritis nodosa, herpes zoster ophthalmicus with contralateral hemiplegia, tuberculous meningitis, and purulent meningitis with arteritis and Sneddon's syndrome. No neurovascular complications from infective endocarditis or meningovascular syphilis were encountered in this series. Other risk factors for ischemic stroke are demonstrated Table 4.

Table 4. Risk factors in ischemic stroke.

| Risk factor | M | F | All |
|--|-----------|-----------|-----------|
| 1. Hypertension | | | |
| Alone | 3 | 0 | 3 |
| + Pills | 0 | 1 | 1 |
| + Diabetes mellitus | 1 | 0 | 1 |
| + Low HDL-cholesterol | 0 | 1 | 1 |
| + Smoking + Alcohol | 1 | 0 | 1 |
| 2. Hyperlipoproteinemia (Type IV, IIb) | 2 | 0 | 2 |
| 3. Smoking | 1 | 0 | 1 |
| + Alcohol | 2 | 0 | 2 |
| + Alcohol + Amphetamine | 1 | 0 | 1 |
| 4. Valvular heart disease | 6 | 9 | 15 |
| 5. Cardiac arrhythmia | 2 | 0 | 2 |
| 6. Cardiomyopathy | 0 | 1 | 1 |
| 7. Vasculitis | 2 | 7 | 9 |
| (one case was a contraceptive pill user) | | | |
| 8. Moya Moya disease | 0 | 1 | 1 |
| 9. Pills | 0 | 2 | 2 |
| 10. Polycythemia | 1 | 0 | 1 |
| 11. Anticardiolipin antibodies | 0 | 1 | 1 |
| 12. Unknown | 3 | 3 | 6 |
| Total | 25 | 26 | 51 |

M = Male
F = Female

Risk factors or causes of hemorrhagic stroke.

Hypertension, the most common risk factor in the elderly, was also the most prominent one in this series. Berry aneurysms and AVM were the second and third

most common causes of hemorrhagic stroke. Coagulopathies from anticoagulant therapy and liver cirrhosis were also found. Other potential risk factors in hemorrhagic stroke in this series are shown in Table 5.

Table 5. Risk factors in hemorrhagic stroke.

| Risk factor | M | F | All |
|--|-----------|-----------|-----------|
| Hypertension | | | |
| Alone | 5 | 7 | 12 |
| + Aortic regurgitation | 1 | 0 | 1 |
| + Alcohol | 1 | 0 | 1 |
| + SLE | 0 | 1 | 1 |
| Aneurysm | 3 | 8 | 11 |
| Arteriovenous malformation | 7 | 1 | 8 |
| Coagulation defect | 2 | 0 | 2 |
| Leukemia | 3 | 1 | 4 |
| Neurilemoma with subarachnoid hemorrhage | 1 | 0 | 1 |
| Pills | 0 | 3 | 3 |
| Alcohol | 1 | 0 | 1 |
| Unknown | 4 | 0 | 4 |
| Total | 28 | 21 | 49 |

M = Male

F = Female

Coagulation abnormalities. Apart from two cases of coagulation defects (cirrhosis and anticoagulant therapy) which caused hemorrhagic strokes, no abnormal coagulograms were detected in young stroke patients.

Contraceptive pills. There were 7 current contraceptive pill users (CPU), and the associated strokes were 2 cases of intracerebral hemorrhage, 3 cases of ischemic stroke (one with hemorrhagic infarction), 1 case of subarachnoid hemorrhage and 1 case of superior sagittal sinus thrombosis. Among these 7 cases, CPU was the possible single risk factor in 5 cases, and CPU associated with herpes zoster

vasculitis or hypertension were combined risk factors in two others.

Mortality rate. The overall mortality rate in this series was 20%. The mortality rate in ischemic stroke and hemorrhagic stroke was 8% and 12% respectively. Causes of death in ischemic stroke were related to massive infarction and cerebral edema as well as the underlying systemic diseases. Causes of death in hemorrhagic stroke were related to extensive hemorrhage and underlying blood dyscrasia i.e. leukemia. Details of underlying causes are shown in Table 6.

Table 6. Mechanisms of stroke in deceased patients.

| | Ischemic stroke | Hemorrhagic stroke |
|---------------|---------------------------------------|-----------------------------|
| Male | Cardiac embolism 2 (MCA occlusion) | Hypertension 2 |
| | Thrombosis 2 (VBA occlusion) | AVM (Post-operation) 1 |
| Female | Vasculitis 3 | Blood dyscrasia 4 |
| | SLE 1 | No risk factor 2 |
| | Sjogren syndrome* 1 | Hypertension 1 |
| | Polyarteritis nodosa 1 | Aneurysm 1 |
| | Cardiac embolism 1 (MCA occlusion) | Aneurysm (Post-operation) 1 |
| Total | 8 | 12 |

MCA = middle cerebral artery VBA = vertebrobasilar artery

associated with mucin-producing lung cancer and non bacterial thrombotic endocarditis

Discussion

In developing countries, stroke in young adults is not uncommon with 40% seen in India⁽²⁾, and 26% in our series. Only 3-4% were reported in developed countries⁽¹⁾. This probably reflects the population structure in developing countries where young adults predominate. Moreover, some risk factors e.g. rheumatic heart disease and infectious disease which can cause cerebral embolism and vasculitis are more common in developing countries.

We limited our study to strokes occurring in patient between 15-45 years old, the same age group used by Hachinski⁽⁴⁾ and in other studies⁽⁵⁻⁶⁾. We observed abrupt changes in the incidence of stroke after the age of 44, and we assume that risk factors may become different after that age.

The epidemiology of stroke in the young is most often studied in hospitals and be a selected group, since hospitals are referral centers⁽⁷⁾. A hospital study does nevertheless, allow us to identify definite causes of stroke and may give us valuable informations concerning their relative prevalence.

Stroke is the most common serious neurological problem in the world^(4,7-9) and the socio-economic impact is high. This is especially true in young adults. Most of our young stroke patients were in the third decade and the impact on the patient, their families, and society in general was tremendous. Stroke prevention should therefore be a national health objective of national importance. Some preventable etiologies accounting for the majority of cases in this series will be discussed briefly.

Cerebral embolism of cardiac origin accounted for almost 1/3 of all ischemic strokes in our series. Documented cardiac sources were valvular heart disease, cardiac arrhythmia, cardiomyopathy and non-bacterial thrombotic endocarditis. Other causes of cerebral embolism such as mural thrombus, bacterial endocarditis, atrial myxoma etc. were not encountered^(4,6,8,10,11).

Non-atherosclerotic cerebral vasculopathy causing ischemic stroke was identified in 10 cases. These included: SLE, infectious arteritis, drug abuse, polyarteritis nodosa, Sneddon's syndrome and Moyamoya disease. Cerebrovascular atherosclerotic risk factors (hypertension, abnormal lipid profiles, diabetes mellitus), which are common risk factors in the elderly⁽⁷⁾, did not play a prominent role in this series.

Intracranial hemorrhage from hypertension, aneurysm, and arteriovenous malformation, played major roles in our hemorrhagic strokes. This is compatible with data from other series^(4,5-8,12). However, bleeding from intracranial tumours such as glioma, choriocar-

cinoma, hypernephroma, malignant melanoma, which have been reported in other series as causes of intracranial hemorrhage, were not observed^(13,14). Instead, we had one case of bleeding from a neurilemmoma of the trigeminal nerve which was an extremely rare cause of tumour bleeding⁽¹⁵⁾.

Contraceptive pills^(16,17) and puerperium⁽¹⁷⁾, which may be causes of stroke in young females did play a role in this study. We found 7 cases of stroke possibly related to the contraceptive pills, these included subarachnoid hemorrhage, intracerebral hemorrhage, cerebral infarction, hemorrhagic infarction, and venous sinus thrombosis. Although many studies which associated oral contraceptives with stroke have been criticized for methodological defects, a review of this topic suggested that contraceptive usage might be associated with thrombotic stroke. The data concerning hemorrhagic stroke were less clear⁽⁷⁾. Cerebral venous and arterial thrombosis in the puerperium may be common in some developing countries such as India, according to Srinivasan⁽¹⁸⁾. We found only one case in our series.

Migraine is common in Thailand⁽¹⁹⁾. Migraine attacks may be associated with focal neurological deficits and can be the cause of stroke in the young⁽²⁰⁾. None of our 51 ischemic strokes had a history of migraine. Cigarette smoking and alcohol-consumption⁽²¹⁾, which may be related to stroke in the young, appeared to play a minor role in our study.

Based on the frequency of various causes of young stroke in our series, the diagnostic approach should begin with a clinical evaluation searching for systemic diseases such as rheumatic heart disease, hypertension, diabetes mellitus, contraceptive pill usage, systemic vasculitis, smoking, alcoholism, and drug abuse e.g. amphetamine. These data will uncover the underlying diseases causing strokes. According to our data on anatomical location of lesions and type of stroke detected by CT-Scan of the brain, further clues can be drawn. Deep seated hematoma or infarction are usually associated with hypertension. Multiple infarctions of cortical vessels suggest embolic phenomena. In a patient with suspected cardiogenic embolism but no obvious abnormal physical signs, chest x-rays, and EKG, echocardiograms may be useful for detection of mitral valve prolapse. In non-hypertensive intracranial hematoma and subarachnoid hemorrhage where no systemic disease such as vasculitis, anticoagulant therapy or blood dyscrasia are found, four vessel angiograms are needed for detection of AVM and aneurysm. Lumbar puncture is necessary for detection of stroke associated with meningitis. Cerebral biopsy, for

arteritis confined to the central nervous system, was not performed in this series and is rarely indicated. Serological studies for collagen vascular diseases should be performed in cases with no evidence of common causes of stroke, because stroke associated with collagen vascular disease is not uncommon. Other diagnostic

tests e.g. anticardiolipin antibodies should be further performed if the cause of stroke is still unknown.

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