Stroke in Young Adults

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Strokes in young adults are uncommon and often a diagnostic challenge. A retrospective study of strokes due to intracerebral hemorrhage, subarachnoid hemorrhage, or cerebral infarction was undertaken. We reviewed the medical records of 113 young patients aged 15-45 years who were admitted to the Medical Center Hospital of Vermont with a diagnosis of stroke between 1982 and 1987. This group comprised 8.5% of patients of all ages admitted for stroke, 2.3 times the proportion observed in the National Survey of Stroke. Nontraumatic intracerebral hemorrhage was diagnosed in 46 young patients (41%); the main causes included aneurysms, arteriovenous malformations, hypertension, and tumors. Subarachnoid hemorrhage was found in 19 young patients (17%); the majority were due to aneurysms. The remaining 48 young patients (42%) had cerebral infarction, the majority due to cardiogenic emboli and premature atherosclerosis. Mitral valve prolapse, the use of oral contraceptives, alcohol drinking, and migraine were infrequent sole causes of cerebral infarction in the absence of other risk factors. The case-fatality rate for this group of young patients with stroke was 20.4% compared with 23.9% for the National Survey of Stroke. Young adults with stroke deserve an extensive but tailored evaluation, which should include angiography and echocardiography. (Stroke 1990;21:382-386)

Strokes in young adults are relatively uncommon; the disorder usually occurs in the middle-aged and elderly. The National Survey of Stroke revealed that only 3.7% of all strokes occurred in patients aged 15-45 years.1 The etiologic and prognostic features that characterize strokes in older persons may not apply to young adults. Previous reports suggest that a cause can be found in 55-93% of young people with stroke,2-4 but there is considerable variation in causes among studies; therefore, further studies are needed. We have reviewed our experience in a regional referral hospital.

Subjects and Methods

We retrospectively reviewed the medical records of all patients aged 15-45 years with the diagnosis of hemorrhagic or nonhemorrhagic stroke admitted to the Medical Center Hospital of Vermont between January 1, 1982 and December 31, 1987. We included patients who suffered subarachnoid hemorrhage (SAH), intracerebral hemorrhage (ICH), or cerebral infarction before or during hospitalization. If a patient had more than one stroke during the study period, we included only the first one. Stroke was defined according to criteria of the World Health Organization.5 Stroke types were defined based on criteria of the Oxfordshire Community Stroke Project.6 Premature atherosclerosis was assumed if there were two or more risk factors for atherosclerotic disease in the absence of other identifiable causes of cerebral infarction. These risk factors for atherosclerosis included hypertension (sustained systolic blood pressure of >160 mm Hg and diastolic blood pressure of >90 mm Hg for at least 1 week after the stroke), diabetes mellitus (history of the disease requiring drug or dietary treatment before the stroke), transient ischemic attacks, coronary artery disease, hyperlipidemia (triglyceride concentration of >160 mg%, cholesterol concentration of >230 mg%, and/or high density lipoprotein concentration of <35 mg%), smoking, and peripheral vascular disease. Mitral valve prolapse (MVP) was diagnosed on the basis of published criteria for M-mode and two-dimensional echocardiographic images.7 A stroke was attributed to oral contraceptives if the woman was using them at the time of the cerebral infarction in the absence of other identifiable causes. A coagulation defect was defined as prolonged prothrombin, partial thromboplastin, or bleeding times. Criteria for migrainous stroke included a well-established history of migraine, a typical migraine headache at the time of the acute stroke, and the absence of other identifiable causes for the stroke. Alcohol was accepted as the cause for a stroke if the patient had a history of excessive alcohol use and had no other identifiable cause for the stroke. Available data from computed tomography (CT), cerebral angiography, autopsy, cerebrospinal fluid...
evaluation, 24-hour Holter monitoring, electrocardiography, chest roentgenography, echocardiography, electroencephalography, and laboratory tests were reviewed. The laboratory tests included complete blood count; prothrombin, partial thromboplastin, and bleeding times; erythrocyte sedimentation rate; syphilis serology; collagen-vascular disease profile; glucose concentration; lipid profiles; lupus anticoagulant assay; and others. Some clinical investigations were not available in every patient.

Results

A total of 113 young patients with stroke aged 15–45 years (63 males and 50 females) were admitted to the hospital during the 6 years. They comprised 8.5% of the 1,331 patients of all ages admitted for stroke. The sex ratio among all 1,331 patients was 1.29; 235 died. Most young patients (40%) were older than 40 years of age; their mean age was 35.0 years. Forty-six young patients (41%, 25 males and 21 females) sustained an ICH (Figure 1); these patients represented 22.5% of the 204 patients of all ages admitted with ICH. Table 1 shows the causes of ICH in these 46 young patients and the number who died. Among these 46 young patients, 13 were moderate to heavy drinkers of alcohol, six (one male and five females) had a history of migraine, less than four had the ICH during pregnancy and the puerperium, and two were known users of cocaine and illicit drugs. Most ICHs (63%) were lobar, and most resulted from a ruptured aneurysm, or less commonly an arteriovenous malformation.

Nineteen young patients (17%, nine males and 10 females) had an SAH (Figure 2); they comprised 15.8% of the 120 patients of all ages admitted with SAH. Most SAHs were the result of a ruptured aneurysm; three patients died (Table 2). Six SAH patients had a history of hypertension, and three were moderate to heavy drinkers of alcohol.

Forty-eight young patients (42%, 29 males and 19 females) had a cerebral infarction (Figure 3); these patients comprised 4.8% of the 1,007 patients of all ages admitted with cerebral infarction. Almost half of these young patients were >40 years of age. Among the 18 patients <35 years old, the sex ratio was 0.8; among the 30 who were ≥35 years old, it was 2.3. The causes of cerebral infarction in these young patients are summarized in Table 3; a cause was identified in all but two patients. Of the 17 patients with cardioembolic cerebral infarction, the underlying cardiac disease was demonstrated in 11 and presumed in the other six from analysis of the clinical presentation, history, and CT results. MVP was the probable cause of cerebral infarction in two patients, one of whom was an intravenous drug abuser. MVP was also found in another patient but was not thought to be the cause of the cerebral infarction. Echocardiography was performed in 25 of the 48 patients with cerebral infarction, and the results were normal in 10. Prolonged (24 hours) Holter monitoring was obtained in six patients and was normal in all six. Premature atherosclerosis was implicated as the cause of the cerebral infarction in 15 patients (11 males and four females, Table 3). Eight of the 15 had angiography;

| Table 1. Causes of Spontaneous Intracerebral Hemorrhage in 46 Young Patients |
|-----------------------------|------|---|
| Cause                        | No.  | %  |
| Ruptured aneurysm            | 21   | 45.6|
| Ruptured arteriovenous malformation | 9   | 19.6|
| Hypertension                 | 7    | 15.2|
| Tumor                        | 5    | 10.9|
| Coagulation abnormality      | 2    | 4.3 |
| Moyamoya disease             | 1    | 2.2 |
| Eclampsia                    | 1    | 2.2 |
| Total                        | 46   | 100.0|
| Deaths                       | 12   | 26.1|

| Table 2. Causes of Spontaneous Subarachnoid Hemorrhage in 19 Young Patients |
|-----------------------------|------|---|
| Cause                        | No.  | %  |
| Ruptured aneurysm            | 15   | 78.9|
| Ruptured arteriovenous malformation | 3   | 15.8|
| Venous angioma               | 1    | 5.3 |
| Total                        | 19   | 100.0|
| Deaths                       | 3    | 15.8|

Figure 1. Bar graph. Demographic characteristics of 46 young patients with intracerebral hemorrhage. Mean age was 33.1 years. Shaded bars, females; filled bars, males; x axis, age groups by years; y axis, number of patients.

Figure 2. Bar graph. Demographic characteristics of 19 young patients with subarachnoid hemorrhage. Mean age was 35.5 years. Shaded bars, females; filled bars, males; x axis, age groups by years; y axis, number of patients.
six angiograms were positive for carotid artery dissection, and the other two were normal. Risk factors for atherosclerotic cerebral infarction are summarized in Table 4. Nine of the 19 females with cerebral infarction were receiving oral contraceptives. Other causes for the cerebral infarction were found in seven, leaving two females with cerebral infarction presumed to be due solely to oral contraceptives. The lupus anticoagulant was the presumed cause of three embolic cerebral infarctions, all in females with systemic lupus erythematosus. Eight patients with cerebral infarction (16.7%) were moderate to heavy drinkers of alcohol. In seven of these eight patients, other causes for the cerebral infarction were found, leaving one patient with cerebral infarction presumed to be due solely to an alcoholic binge. Of the five patients with cerebral infarction due to nonatherosclerotic vascular disease, two had postoperative thromboemboli, one had thrombosis of the carotid artery after trauma to the neck and face, one had a carotid artery dissection, and another had vasculitis confirmed by angiography and autopsy. Eighteen patients with cerebral infarction had a history of migraine; in 17 there were other causes for the cerebral infarction, leaving only one patient diagnosed as having a migrainous stroke.

### Discussion

A cardiogenic cerebral embolus is one of the most common causes of stroke in the young, accounting for up to one third of the cases. In our series, 35% of the cases of cerebral infarction were of cardiac origin. The association between MVP and cerebral infarction is of special importance in patients who do not have other risk factors for stroke. MVP must be accepted as a cause of cerebral infarction since it is found in 29–40% of young people with ischemic stroke but in only 7% of matched controls. In our series, echocardiography was not done in all patients, which raises the possibility that even more patients might have had MVP.

Premature cerebral atherosclerosis is generally the result of risk factors for cerebrovascular disease such as hypertension, diabetes mellitus, hyperlipidemia, and cigarette smoking. We found that 31% of the young patients with cerebral infarction had an atherosclerotic cause; the majority of these were >35 years old. Our experience is similar to that in other surveys.

The use of oral contraceptives is associated with a ninefold increased risk of cerebral infarction in women. The Collaborative Group for the Study of Stroke in Young Women found that the risk of stroke with the use of oral contraceptives rose sharply in women with hypertension or migraine and those who were heavy smokers. Oral contraceptives alter platelet aggregation, enhance antithrombin III activity, decrease serum antithrombin levels, and increase the levels of certain coagulation factors, especially factor VII. In our series, 47.4% of the women with cerebral infarction were using oral contraceptives when their strokes occurred, but only two had strokes attributable solely to the oral contraceptives. It must be remembered that pregnancy increases the risk of ischemic events by approximately 13 times. The use of oral contraceptives, pregnancy, and the puerpe-
rium are often also implicated as causes of hemorrhagic strokes. Five women among our young patients experienced strokes (four hemorrhagic and one ischemic) during pregnancy or the puerperium.

Alcohol contributes to stroke in several ways, including induction of cardiac arrhythmias and cardiac wall abnormalities (which predispose to cerebral embolism), induction of hypertension, enhancement of platelet aggregation, activation of the clotting cascade, reduction of cerebral blood flow by stimulating cerebral vascular smooth muscle contraction, and alteration of cerebral metabolism. A Finnish study suggested that alcohol was a frequent contributing factor in the development of stroke; in a survey of patients with cerebral infarction, 40% had been intoxicated during the previous 24 hours. This rate of recent alcohol abuse was 4-7 times that for males of similar ages in the general population and 5-6 times that for females. The Honolulu Heart Program noted that the risk of hemorrhagic stroke doubled for light drinkers and tripled for heavy drinkers compared with nondrinkers, independent of their hypertensive status. In our series, 24 (21.2%) of the patients were moderate to heavy drinkers of alcohol: 13 had ICH, three had SAH, and eight had cerebral infarction. Alcohol was the sole cause of cerebral infarction in one patient.

Cerebral infarction is a potential complication of migraine headaches. The incidence of migraine among young patients with stroke varies little from that among the general population (approximately 15-30%). Spaccavento and Solomon found a 27% incidence of migraine among young adults with stroke and attributed all of the strokes to migraine. In another study, Adams et al. found that while 14% of their patients had a history of migraine, only 3% of the ischemic events were linked to migraine attacks. In our series, 18 patients (38% of those with cerebral infarction) had a history of migraine, but in only one (2.1% of those with cerebral infarction) were migraine the only cause of the stroke. Mechanisms by which migraine may produce stroke include vasospasm and/or arteriopathy, embolism, and platelet abnormalities.

Patients with migraine have evidence of vasomotor instability and platelet disturbances. CT and magnetic resonance imaging (MRI) will demonstrate an infarct, but often the angiogram is normal. Rothrock et al. prospectively evaluated 22 patients with acute migraine-associated stroke and demonstrated cerebral infarction or ICH by CT/MRI in 55% and abnormalities by cerebral angiography in 41% of the cases.

In our retrospective study, young patients comprised 8.5% of all patients admitted with stroke, both hemorrhagic and nonhemorrhagic, 2.3 times that in the National Survey of Stroke (3.7%). The proportion with ICH among our young stroke patients and stroke patients of all ages (41% and 15%, respectively) was higher than that calculated from Table 3.3 of the National Survey of Stroke (37% and 12%, respectively). This may reflect the fact that the Medical Center Hospital of Vermont is a regional neurologic and neurosurgical referral center. The ratio of ICH to primary SAH in our series was almost 2:1 for patients of all ages, while that in the National Survey of Stroke was 1:1. The National Survey of Stroke probably underestimated the frequency of ICH since many patients were collected before the availability of CT. The case-fatality rate in our overall series (17.7%) was less than that in the National Survey of Stroke (23.9%), which may be due to the higher proportion of young patients in our series.

Our study suggests that, although MVP, oral contraceptives, alcohol, and migraine need to be considered in patients with cerebral infarction and may be relatively frequent factors contributing to the development of a stroke, they are infrequent sole causes of stroke in the young.

References

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