Cerebral Infarction in Young Adults

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SUMMARY The etiologic and prognostic features which characterize cerebrovascular disease in the later decades of life are not applicable in younger patients. The records of 58 patients who had suffered cerebral infarction between the ages of 15 and 40 were reviewed in order to study these features.

Fifty-five percent of the patients were found to have had an identifiable etiology for their cerebral infarction, with nearly half of these suffering from embolic infarction of cardiac origin. In 45% no clear etiology could be established but hypertension was prevalent in those patients between 31 and 40 years of age. Follow up data were obtained on 68% of the hospital survivors; nearly 3% of them had completely recovered or had improved.

CEREBROVASCULAR DISEASE occurs predominately in the later decades of life. However, the occurrence of stroke in young adults is not an insignificant problem. The annual incidence of stroke in the 35 to 45 age group is estimated at 25 per 100,000.1 Aring and Merritt,2 in an age incidence tabulation of autopsied cases of cerebrovascular lesions, found that 5% of strokes occur in individuals under 40. It has been pointed out that this figure relates to necropsied cases, and that the actual incidence may be greater.3 Two large studies of cerebrovascular disease originating from India4 and Ceylon5 estimate that 27.2% and 32% respectively of all strokes occur in adults under 40. These findings may not be applicable to other world populations because of differences in culture, diet, genetics, or other unidentified factors.

The etiologic and prognostic features which characterize cerebral infarction among older patients may not be applicable to young adults. Because of the relatively low prevalence of degenerative arterial disease in the young, potentially treatable non-atheromatous conditions may exist in the young adult with stroke.6 Despite careful investigation, among young patients many cases of ischemic cerebrovascular disease emerge in which the etiology is unclear and the role of established risk factors is uncertain.7-12 In order to examine these factors, the records of young adults with cerebral infarction who had been hospitalized at the Medical College of Virginia hospitals were reviewed.

Methods

The Medical College of Virginia Hospital is a large urban teaching center with a population of referral as well as community care patients. The medical records of all inpatients age 15 to 40 with cerebrovascular disease admitted to the Medical College of Virginia Hospitals between August 1, 1970 and July 31, 1975 were reviewed retrospectively.

Patients included in the study had suffered cerebral infarction just prior to admission or while in the hospital. Patients with hemorrhagic strokes were not included. If a patient had more than one cerebral infarct during the period of the study, only the first was included.

Patient data collected included family history, predisposing factors, past diseases, history of present neurologic deficit, and outcome. When available, data were obtained in reference to brain scan, electroencephalogram, cerebral arteriogram, lumbar puncture, and autopsy findings. On the basis of available clinical and laboratory data, patients were placed into one of several etiologic categories.

Hypertension was defined as a diastolic pressure greater than 95 mm Hg, recorded on at least 3 separate occasions during hospitalization. Diabetes mellitus was defined as an abnormal glucose tolerance test or an abnormal fasting blood sugar (greater than 110 mg%). Hyperlipidemia was said to exist when serum cholesterol was greater than 270 mg% or serum triglyceride was greater than 140 mg%.

Follow up information regarding course of deficit, functional recovery and recurrence of cerebral infarction was obtained either by correspondence or telephone.

Results

A total of 58 patients fulfilled our criteria. Arteriography was performed on 35 patients (60.3%) and autopsy on 3 (5.2%).

Table 1 provides a summary of the sex, age, and racial characteristics of the 58 patients. The number of females was almost equal to the number of males. Over the age of 30, males were predominant whereas, between the ages of 21 and 30, females outnumbered the males 10 to 1. The incidence of cerebral infarction was greater in the older age groups, with nearly 3% of the patients being over 30 years of age. Fifty-seven percent of the patients were Negro and 43% were Caucasian.

The causes of cerebral infarction in these patients are summarized in table 2. Fifty-five percent of the patients had an identifiable etiology for their cerebral infarction, and of these, nearly one-half were embolic of cardiac origin. The majority of these latter patients suffered from rheumatic heart disease. Hematologic and inflammatory vascular disorders together accounted for 9 cases, and angiographically demonstrated extracranial vascular disease was present in 4 others. Post-partum hypercoagulability and cranial trauma were each thought to be responsible for 2 cases of cerebral infarction.

The characteristics of the group of patients in whom no clear etiology was determined are shown in table 3. Twenty-one of the 26 patients were over the age of 31. Ten of these 21 were hypertensive and 3 diabetic. None had hyperlipidemia. Of the 5 patients under 31, all were women and 3 of the 5 were taking oral contraceptives. Moreover, of...
the 8 females under 35 in this group, 5 were taking oral contraceptives and none of the 5 had any other predisposing factor for stroke.

Eight patients died during the initial hospitalization. Of the remaining 50 patients, follow-up information was obtained on 34 (table 4). Mean follow-up was 31 months with a range of 7 to 69 months. Thirteen (38%) of these patients were followed for more than 3 years and 4 (12%) for less than 1 year. Three patients died during the follow up period. All had a cardiac source for the initial cerebral infarct; 1 suffered a cardiac death and 2 died of recurrent cerebral infarction. Of the 31 survivors, 74% were recovered or improved and 71% were fully independent functionally. There did not appear to be any relationship between sex, age, race, or hypertension and prognosis in these patients.

Seven of the 34 hospital survivors with follow up information had subsequent cerebral ischemic events and 6 of them had a clear etiology for the initial event (3 cardiac, 1 inflammatory vascular, 1 hematologic and 1 extracranial atherothrombotic disease). Only 1 patient in the unknown category had a recurrent cerebral infarction.

Discussion

The incidence of cerebral infarction was noted to increase with age in our young adult population, a finding that has been observed by others. Although there is a male predominance in cerebral ischemia after age 40, the sex ratio is equal below this age both in our series, as well as in others. One explanation for this trend may be an increased risk of cerebrovascular disease among women of childbearing age associated with oral contraceptive use, pregnancy, and the puerperium. Among women in Ceylon age 15 to 45, the majority of ischemic strokes occur during pregnancy or the puerperium. Jolly et al. reported that a little over half of the young women with cerebral infarction in their series from India suffered from puerperal venous sinus thrombosis. Of our 16 female patients between the ages of 15 and 35, 2 suffered cerebral infarction in the puerperium and 5 were taking oral contraceptives. None, however, experienced venous sinus thrombosis.

Levine and Swanson emphasized the frequency of nonatheromatous potentially treatable conditions in young patients. Cerebral emboli of cardiac origin was the most common cause of cerebral ischemia in our study, as well as in Levine and Swanson's, with more than half the patients in this group having rheumatic heart disease. The search for a cardiac embolic source is important since the value of anticoagulation in decreasing mortality and preventing recurrent embolism has been established.

A number of hematologic abnormalities including polycythemia, sickle cell anemia, and coagulation abnormalities were found in this study. These disorders are well recognized causes of cerebral ischemia in the young adult. Recently, Kalendovsky et al. demonstrated that platelet hypercoagulability may underlie many of the strokes in young patients. Unfortunately, special coagulation studies were not performed on our cases.

Various vasculitides are known to produce focal ischemia. In Ford and Siekert's series of 114 patients with periarteritis nodosa, 13% experienced cerebral infarction or hemorrhage during the course of their illness. Systemic lupus erythematosus may involve the central nervous system in as many as 75% of the cases, although as in periarteritis, it is uncommon for neurologic signs to occur in isolation without other evidence of systemic disease. The diagnosis of collagen vascular disease was made prior to the episode of cerebral infarction in 2 of the 3 cases in this study. Other types of cerebral arteritis, such as granulomatous angiitis,
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and that which occurs with rheumatoid arthritis and scleroderma are rare and were not seen in this series.

Occlusive extracranial vascular disease was found in 4 of our patients in this study. All were over the age of 35 and, except for one, had either hypertension, diabetes or both. It appears that premature atheromatous disease was responsible for the occlusive process and ischemic symptoms in these patients. Two patients, aged 18 and 21, suffered internal carotid artery occlusion following head and neck trauma during automobile accidents. Humphrey and Newton, in their review of 117 patients under the age of 40 with internal carotid occlusion, reported that trauma was the most frequent contributing factor and that atherosclerotic involvement in these younger patients was uncommon.

The largest category of patients was that with no clear etiology for cerebral infarction. Louis and McDowell, reviewed 56 cases of non-embolic cerebral infarction occurring under the age of 50 and concluded that after the age of 30 cerebral infarction is most likely to be caused by atherosclerosis. Srofkin and Blakely with Berlin et al., also concluded that premature atherosclerosis constitutes an important pathogenic factor in the development of cerebral infarction among young adults. The frequency of known precursors of atherogenesis, such as hypertension and diabetes, were prominent in some studies but uncommon in others. The majority of our patients in an unknown category were hypertensive Negroes aged 31-40. Of the 21 patients over age 31, 10 were hypertensive and 3 diabetic. Moreover, if the 4 patients with extracranial vascular occlusive disease were added to this group, we would presume that atherosclerosis was the primary pathogenic factor for cerebral infarction in at least 17 patients.

The role of oral contraceptives as a cause of cerebral infarction in women is controversial. Some studies support the theory that there is an increased risk of thromboembolic cerebrovascular disease in young women taking birth control pills, while others feel that it is premature to incriminate these drugs. It is of interest that 5 of the 8 female patients under age 35 in the unknown category were taking oral contraceptives. None of these 5 had any other predisposing factors for stroke. These data, however, are not conclusive.

The initial hospital mortality of 14% among our patients was higher than expected and contrary to reports that acute stroke mortality is less with younger patients. These findings might be explained by the severity of deficit as evidenced by a disturbed level of consciousness in 7 of the 8 patients on admission, and the presence of serious concomitant disease in most cases. Of the 34 hospital survivors in whom follow up was obtained, 3 (9%) died during the 31 month mean follow up period. Studies on cerebral thrombosis in all age groups report mortality figures of 25-26% after 2 years among patients who survive the initial infarction. The better long term prognosis among younger patients with cerebral infarction has been also noted by others.

The quality of survival also appears to be better among younger patients. Of our hospital survivors who were followed up nearly 1/3 had completely recovered or improved and a similar proportion was functionally independent. All but 1 of Berlin’s 13 patients age 18 to 37 with cerebral infarction showed progressive improvement of their initial deficit. In David’s series of patients with cerebral infarction, in which the mean age was 55 years, only 38 of 67 had improved after 2 years and only one-half were able to take care of themselves.

Seven (21%) of the hospital survivors who were followed up suffered recurrent cerebral infarction during the follow up period. Three of these patients had underlying cardiac disease. The probability of recurrence of cerebral embolism associated with cardiac disease appears to be higher than for cerebral infarction of any other etiology and partly account for relatively high recurrence rate among our patients.

Conclusions

1) In our series 55% of young adults suffering cerebral infarction had an identifiable etiology for the event; cerebral embolism of cardiac origin appeared to be the most frequent cause.

2) Among our patients suffering cerebral infarction under the age of 30, the predominance of females may be partly explained by an increased risk of thromboembolic disease associated with the puerperal and oral contraceptive use.

3) Among our patients 31 to 40 years of age in whom no etiology could be established, hypertension was prevalent and cerebral infarction presumably resulted from premature atherosclerotic disease.

4) Our study indicated that the prognosis for recovery among young adults suffering cerebral infarction is favorable. Nearly 3/4 of hospital survivors improved and became functionally independent.

References

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A GREAT VARIETY of ocular signs have been described.

Ischemia, have been previously reported. The authors have recently encountered seven instances of internal carotid artery occlusion, presumably a sign of ocular ischemia. In addition to an ipsilateral internal carotid artery occlusion, arteriograms demonstrated that the major source of blood supply to the homolateral cerebral hemisphere was by retrograde flow through markedly enlarged ophthalmic arteries filled in retrograde fashion from dilated external carotid collateral channels in the orbit. This association of dilated episcleral arteries as a sign of increased orbital blood flow and the major source of collateral blood supply to the homolateral cerebral hemisphere has not been previously reported. We reemphasize the importance of a careful examination of the episcleral vessels in patients suspected of having internal carotid artery occlusions.

SUMMARY Dilated episcleral vessels associated with ipsilateral internal carotid artery occlusion have been previously reported though not widely appreciated. These ocular changes have been presumed to be manifestations of ocular ischemia. The authors have recently encountered this sign in seven patients and in none was there evidence of ocular ischemia. In addition to an ipsilateral internal carotid artery occlusion, arteriograms demonstrated that the major source of blood supply to the homolateral cerebral hemisphere was by retrograde flow through markedly enlarged ophthalmic arteries filled in retrograde fashion from dilated external carotid collateral channels in the orbit. This association of dilated episcleral arteries as a sign of increased orbital blood flow and the major source of collateral blood supply to the homolateral cerebral hemisphere has not been previously reported. We reemphasize the importance of a careful examination of the episcleral vessels in patients suspected of having internal carotid artery occlusions.

A GREAT VARIETY of ocular signs have been described in patients with cerebrovascular occlusive disease. Among these, dilated episcleral vessels associated with ipsilateral carotid artery occlusion, presumably a sign of ocular ischemia, have been previously reported. This association, however, has not been widely appreciated. The authors have recently encountered seven instances of internal carotid artery occlusion associated with ipsilateral dilated episcleral arteries in six patients in whom no signs of ocular ischemia were present. In addition, however, angiograms revealed that the major source of blood to the affected hemispheres was by way of markedly dilated ophthalmic arteries filling retrograde from external carotid orbital collateral channels. This ocular sign, we believe, may imply increased orbital blood flow and, therefore, carries additional physiological significance for the clinician in that it emphasizes the importance of maintaining a patent external carotid artery.

Two representative cases are described.

Case Reports

Case I (H.L.)

A 57 year old, right-handed, hypertensive, white male was admitted to the Neurology Service of the East Orange, New Jersey, Veterans Administration Hospital in January, 1977, with a history of several episodes of transient weakness of his left side for three months prior to his admission. Frequently the episodes were accompanied by fleeting sensations of giddiness and on one occasion with a complete loss of consciousness reported to have lasted 24 hours. The left-sided weakness on this occasion is said to have lasted about 48 hours. However, the subsequent attacks lasted no more than a "few minutes" to 2 to 3 hours. The patient was a known hypertensive who had had two previous admissions for uncontrolled blood pressure elevations.

Upon hospital admission he was found to be generally healthy but aesthetic with normal blood pressure, mild left-sided weakness, and a right carotid bruit. Ophthalmologic examination revealed markedly dilated and tortuous episcleral vessels in both eyes, which on slit lamp examination proved to be dilated arteries (fig. 1). Fundoscopic and formal field examinations were normal and vision was correctable to 20/20 bilaterally. Intraocular pressures were normal. Ophthalmodynamometry pressures were 40/20 in both eyes.

While in the hospital, the patient experienced several fleeting episodes of transient right upper extremity weakness which often seemed to be related to postural changes. However, he reported no frank syncope or giddiness. Aortic arch angiography with selective catheterization of both common carotids and the left vertebral arteries demonstrated complete occlusions of both internal carotid arteries and the right vertebral artery. There was modest stenosis at the origins of both external carotid arteries which were markedly dilated and filled in retrograde fashion the
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