Histological structural abnormalities of superficial temporal arteries used for extracranial-intracranial anastomosis

FERNANDO G. DIAZ, M.D., PH.D., JACOB CHASON, M.D., CARL SHRONTZ, M.D., JAMES I. AUSMAN, M.D., PH.D., AND MANUEL DUJOVNY, M.D.

Departments of Neurosurgery and Pathology, Henry Ford Hospital, Detroit, Michigan

Histological evaluation of the superficial temporal artery resected at the time of extracranial-intracranial anastomosis was performed in 64 consecutive patients. A neuropathologist who was not aware of the medical condition of these patients studied all specimens under light microscopy with hemotoxylin and eosin, Verhoff, and Mallory stains. Intimal proliferation was observed in 62 samples, intimal fibrosis in 56, fragmentation of the internal elastic lamina in 45, splitting of the internal elastic lamina in 41, fragmentation of the media in 38, and fragmentation of the minimal external elastic tissue in 17. Stenosis of the vessel was observed, and graded from 0% to 50%, with a mean of 20%. The development of intraluminal stenosis was considered to be secondary to the development of intimal fibrosis and hyperplasia. The changes observed were progressive and conformed with those previously described; there was no evidence of correlation with sex, diabetes, or hypertension. The implications for the development of occlusion of the anastomosis or stroke, and for patient survival are discussed.

KEY WORDS: superficial temporal artery, middle cerebral artery, STA-MCA anastomosis, intimal hyperplasia, vascular stenosis, extracranial-intracranial bypass, artery bypass

The treatment of cerebrovascular disease has recently included extracranial-intracranial anastomosis for the revascularization of lesions previously inaccessible to surgery. While the superficial temporal artery (STA) has been considered a "normal artery," some histological arterial changes have been described. This paper deals with the histological characteristics of a cumulative series of these vessels used for cerebral revascularization. Various factors that may have an ultimate effect on the long-term patency, patient survival, and the potential for infarction will be discussed.

Clinical Material and Methods

The STA was obtained from 64 patients at the time of cerebral revascularization. The patients consisted of 42 men and 22 women; there were 46 white patients, 17 black, and one Asiatic. They ranged in age from 18 to 84 years, with a mean of 56 years. The lesions undergoing surgical treatment included occlusions of 41 internal carotid arteries, six middle cerebral arteries (MCA's), six basilar arteries, and one MCA stenosis. Thirty-six patients were hypertensive, and 21 were diabetic. An STA-MCA anastomosis was completed in 58 patients, and an STA to superior cerebellar bypass was completed in six.

The STA was dissected in the conventional manner under the microscope, and extreme care was taken to leave a 3- to 4-mm cuff of galea and connective tissue on either side of the vessel. The amount of manipulation of the vessel was kept to a minimum. Arterial branches were dissected under the microscope and carefully cauterized or ligated with 4-0 silk sutures. The STA was clamped proximally and the distal end transected. The distal 8 mm of the artery was then excised and sent for histological analysis.

The specimens were studied under light microscopy utilizing the routine hematoxylin and eosin (H & E) stain, Verhoff elastic stain, and Mallory trichrome stain. The histological evaluation was carried out without knowledge of possible contributing or associated risk factors. The following parameters were...
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Fig. 1. Photomicrographs of different specimens of superficial temporal artery. Upper Left: This sample shows evidence of mild to moderate intimal fibrosis which has resulted in the development of endothelial hyperplasia. Notice the widespread fibrosis throughout the thickness of the endothelial layer, which also has focal minimal reduplication of the internal elastic lamina. The amount of endothelial hyperplasia observed in this section produced 25% stenosis of the vessel lumen. Verhoff, × 45. Upper Right: This section shows moderate intimal fibrosis with the formation of endothelial hyperplasia. There are several areas of destruction of the internal elastic lamina with loss of continuity of this layer. There is also the deposition of calcium into areas of the vessel wall which are darkly stained. Fragments of the elastic tissue in the adventitia are also seen. The endothelial hyperplasia resulted in approximately 25% reduction of the vessel lumen in this specimen. Verhoff, × 45. Lower: A moderate amount of intimal fibrosis and endothelial hyperplasia is shown in this specimen. The internal elastic lamina appears intact in the entire periphery of the vessel wall, and there is only artifactual separation from the media. The endothelial hyperplasia contributed to the development of 50% reduction of the vessel lumen in this specimen. Verhoff, × 36.

studied in all cases: The amount of intimal fibroblastic proliferation, the characteristics of the internal elastic lamina including fragmentation and splitting, the characteristics and thickness of the media, and the presence of fragments of elastic tissue at the junction with the adventitia. The degrees of stenosis or luminal occlusion were determined by estimating the degree of luminal narrowing.

The histological and clinical results were then submitted to statistical analysis using the Michigan Interactive Data Analysis System (MIDAS) of the Statistical Research Laboratory of the University of Michigan. The different variables were submitted to analysis of variance and polynomial regression analysis. The level of significance was set at p < 0.05.

Results

In 62 patients, the STA showed evidence of fibrous hyperplasia (Fig. 1 upper left). Intimal proliferation was the single most important factor in the development of stenosis of the vessel lumen in 56 of the patients (Fig. 2). The internal elastic lamina was

Fig. 2. Intimal proliferation histogram showing degrees of intimal hyperplasia. One = no involvement (two cases); two = mild involvement (35 cases); three = moderate involvement (22 cases); four = marked involvement (five cases).
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TABLE 1
Percent obstruction in 64 superficial temporal artery specimens*

<table>
<thead>
<tr>
<th>Group</th>
<th>% Obstruction</th>
<th>Cases</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No.</td>
<td>Percent</td>
</tr>
<tr>
<td>A</td>
<td>&lt;5</td>
<td>33</td>
</tr>
<tr>
<td>B</td>
<td>5–15</td>
<td>12</td>
</tr>
<tr>
<td>C</td>
<td>16–25</td>
<td>8</td>
</tr>
<tr>
<td>D</td>
<td>26–50</td>
<td>8</td>
</tr>
<tr>
<td>E</td>
<td>none</td>
<td>3</td>
</tr>
</tbody>
</table>

* See also Fig. 3.

Discussion

Because the purpose of the bypass procedure is to increase cerebral circulation to previously ischemic areas, it would be ideal if the arteries used were reasonably normal and if these vessels, once applied to the ischemic area, had the potential for long-lasting patency. Limited studies have evaluated the histological characteristics of the STA; most have been done in cadavers of patients who died from unrelated causes, and a variety of lesions have been described for different age groups.

The STA is a small muscular artery located in the scalp below the dermis and above the galea. In children under 5 years old, this artery has been described as “having no tunica intima, a single layer of endothelial cells appearing directly on a scalloped, thick and unblemished internal elastic lamina. An imperfect and ill-defined internal elastic lamina separates the media from the collagenous adventitia. The media is composed of less than 10 layers of circularly arranged smooth muscle cells, among which there is little demonstrable collagen and only a few fine twigs of elastic fibers.”

In autopsy studies, it has been noted that various alterations do occur in the STA with increasing age. Most agree that children have a normal artery with the characteristics as described, some with intimal cushions. These cushions are boat-like structures composed of a smooth-muscle cell stroma, with ramifications of internal elastic lamina, and are covered with endothelium. These cushions are seen in most children, usually at a bifurcation, and are thought to represent areas of stress in which future atherosclerotic changes will take place or to represent arterial growth points which will eventually disappear.

The first histological abnormalities appear in the young adult, including the development of intimal hyperplasia, and, in some, intimal duplication usually without significant stenosis. The internal elastic lamina has been reported as split and/or fragmented and, in some, smooth-muscle cells have been incorporated into the intima. In the middle-aged adult, the changes observed in the intima are more severe. These are generally associated with a small drop in the caliber of the vessel, with minor amounts of stenosis. The internal elastic lamina is usually split, with obvious fragmentation.

In the elderly, these changes are marked. The hyperplasia of the intima is often severe and, in some, contains smooth-muscle cells with duplication of the intima associated with considerable narrowing of the lumen. The internal elastic lamina is fragmented and split, with fibrosis of the media. Some investigators believe that the smooth-muscle cells found in the
intima travel through gaps in the internal elastic lamina and become localized in the intima;\(^1,3,17-19\) others consider that with the reduplication of the internal elastic lamina, some of the smooth-muscle cells are actually incorporated within the intima by the outward movement of the internal elastic lamina.\(^1,5,10,22,23\)

In some specimens, the development of intimal hyperplasia has been thought secondary to the increment of ground substance, predominantly phospholipid.\(^2,22,23\) It should be noted that in none of our STA specimens or in those previously described was there any intimal lipid or cholesterol deposition.\(^1,9-11,13,23\) It is believed that all of the changes observed are those associated with increasing age and are not related to hypertension or diabetes.\(^1,9-11,17,21,23,24\)

Most investigators believe that the mechanisms by which atherosclerosis develops are generally the result of local stress,\(^7,14,17,20,22,24\) The factors include progressive vessel tapering,\(^20\) frequent curves,\(^1,4,20\) bifurcations,\(^7,17,20\) fixation points,\(^20\) and pulsatile flow.\(^20\) The importance of some of these factors in generating atherosclerotic plaques has been demonstrated experimentally.\(^20\) A series of grafts were placed in femoral arteries of dogs to increase their length and tortuosity; when the anastomosis had remained patent, all developed local atherosclerotic changes in spite of having a normal diet. These atherosclerotic changes were greater at the points of fixation. The development of intraluminal shear forces produces a local vacuum or suction effect\(^14,20\) on the intima which in turn tears the endothelial cells of the vessel. This action leads to the local deposition of platelets with the activation of the local reparative process, the migration of smooth-muscle cells, and formation of collagen.\(^5,8,10,17\)

Atherosclerosis of the larger arteries is usually associated with the local deposition of low-density lipoproteins. The smooth-muscle cell acts as a phagocyte ingesting these low-density lipoproteins.\(^22,24\)

When there is a lysosomal deficiency in the smooth-muscle cells, phagocytosis is not completely effective and increasingly larger amounts of low-density lipoproteins are deposited in the vessel wall.\(^22,24\) However, in those patients in whom there is an abnormal amount of high-density lipoprotein, these depositions do not occur,\(^24\) because the high-density lipoproteins have a protective effect in decreasing the ultimate development of lipid deposition on the vessel wall. In some instances, it has been felt that diastolic hypertension tends to increase the local deposition of lipids in the cerebral arteries.\(^5,15\) The systemic arteries are more influenced by the systolic hypertension and, in some cases, by systemic hyperlipidosis.\(^10,52-24\)

The histological changes observed in the STA segments in our patients conform to the findings reported previously.\(^1,3,10,13\) In 62 patients, we observed the development of endothelial hyperplasia with intimal proliferation, which was the result of widespread fibrosis. The intimal proliferation contributed to stenosis of the vessel lumen, which varied from 0% to 50%, with a mean of 20%. The internal elastic lamina was fragmented in 45 patients and was split in 41. During the course of STA-MCA anastomosis, we have observed that the vessel layers separate. Extreme caution must therefore be taken not to lose sight of this separation, because it may result in vessel occlusion, vessel dissection, or pseudoaneurysmatic formation at the anastomotic site.\(^12\)

Thirty-eight of our patients had medial fibrosis which did not contribute significantly to the development of stenosis. In those with fragmentation of an incomplete and relatively insignificant external elastic lamina, the luminal narrowing or dilatation was not significant.

The development of fibrosis of the intima and of the media has been considered a favorable condition for the use of the STA in anastomosis.\(^9-11\) The increased rigidity of the vessel wall that results from the fibrosis could favor the dilatation of the vessel and prevent the disruption of the vessel wall, which could potentially occur because of the increased pressure head carried by this vessel.\(^9\)

There was a definite correlation between the degree of intimal hyperplasia and luminal stenosis, which was most marked in white patients. This predilection for whites must reflect a sampling error in our patient population, since the number of nonwhite patients was too small.

No definite correlation with age, sex, blood pressure, or diabetes was found for any of the histological changes. Because our population was composed mostly of patients older than 50 years, a bias was created that prevents a clear correlation with the histological changes as described previously (Fig. 4).

Considering the factors involved in the generation of atherosclerosis, the anastomosis of the STA to an
intracranial vessel could permit these changes to progress more rapidly. The anastomosis puts new demands on the STA by increasing the amount of blood and the pressure at which the blood travels through the vessel. Since the vessel carries more blood, it frequently tends to hypertrophy and develop new curvatures. The operative procedure produces the local development of fibrosis which fixes the vessel in position. The fixation of the vessel associated with the development of curvatures and the increased local intraluminal pressure should increase the stress exerted on the vessel wall. By increasing the local stress, there is a potential for local development and progression of the atherosclerotic changes previously outlined. By creating a new bifurcation or confluence as the STA is anastomosed to the MCA, the potential for development of new areas of atherosclerosis would also be increased at this point and in nearby regions of the MCA on either side of the anastomosis.

It is interesting to speculate that this operation that has been intended to increase the circulation to the brain may have only a temporary effect on the cerebral circulation. Since the local stress factors and shear forces are increased on the STA, it is possible that with time these changes may become accentuated and eventually occlude the vessel.

If these changes were actually to develop and progress at the same rate as those that occur in the systemic circulation, it is also interesting to propose that the changes may not develop as rapidly as other systemic changes. Most of these patients generally succumb to their systemic disease; they die from atherosclerotic changes in other circulatory areas, such as the coronary circulation, the systemic, or renal circulation. Myocardial infarction is the most predominant cause of death in all of these patients.

Since the progression of the systemic changes is not affected by the anastomosis, it is quite possible that the local vessel changes may not develop quickly enough to cause eventual cerebral problems. If the anastomosis had the potential to decrease the incidence of stroke and augment the circulation to relatively ischemic areas of the brain, it is quite likely that the changes described would constitute only a histological curiosity. However, it is important to be keenly aware of the potential development of occlusion of the vessel with all of the associated sequelae that may follow, which could include episodes of transient cerebral ischemia, or a cerebral infarction and death.

References
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Address reprint requests to: Fernando G. Diaz, M.D., Ph.D., Department of Neurosurgery, Henry Ford Hospital, 2799 West Grand Boulevard, Detroit, Michigan 48202.