Pathogenesis of Cerebral Infarction Secondary to Mechanical Carotid Artery Occlusion

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Abstract:
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- The immediate postoperative cerebral complications of 65 carotid occlusions were evaluated. The occlusions were done in all but one case for intracranial saccular aneurysms and were performed by either direct ligation (quick type) or slow turning down of a Silverstone clamp or similar device (slow occlusion). Cerebral complications occurred in 21 patients. The quick type of occlusion of the artery resulted in a complication rate of 24% whereas the slow type had a rate of 38%. A total of 123 cases involving cerebral complications after carotid ligation were collected from the literature and evaluated. The combined total of 81 cases of transient complications that were collected from the literature and from our series showed that such deficits occur frequently from 10 minutes to six hours after the occlusion of the vessel.

ADDITIONAL KEY WORDS
aneurysm, thrombosis, embolism, neurosurgery, complication, subarachnoid hemorrhage

Watson and Silverstone (1) claimed, in 1939, that the first carotid ligature was performed by Paré (2) in 1585 and involved a patient with a cerebral complication, who presented with hemiplegia and aphasia. It is not clear whether Paré actually ligated a carotid trunk or only a branch. At any rate, the observed symptoms in Paré’s case did not actually consist of aphasia and hemiplegia but rather of aphony and homolateral upper monoplegia that are more readily explained by a local peripheral-nerve injury from the sword stab that caused hemorrhaging from the neck.

Lynn (3) claimed to have performed the first ligature of a common carotid artery in a patient with severe hemorrhage after tumor extirpation as early as 1792; there were no complications in this case. Mettauer (4) and Pilcher and Thuss (5) stated that Abernethy (6) had performed his famous operation in 1798 or 1799. This patient was gored in the neck by a cow horn and was treated with ligation of the left internal and common carotid arteries. About 14 hours after surgery, he became delirious and convulsive and began to move his right extremities less and less. The next carotid artery ligation without complications probably was performed by Fleming about 1803 (7). The first ligature because of an extracranial aneurysm was done by Cooper (8) in 1805. The patient suffered sudden hemiparesis and a sensation of numbness in the arm and leg 8½ days after the ligation of the common carotid artery; the symptoms cleared slowly during a four-day period. Many cases were reported after this, and Norris (9) had collected 149 cases by 1847, Le Fort (10) 435 cases by 1868, and Pilz (11) 520 cases by 1868. By 1957 Arnulf (12) had noted 5,243 reported ligations. The first study concerning ligatures for intracranial aneurysm...
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Rysms, however, was done by Schorstein (13) in 1940.

Ligations have been done for many conditions, including neck injuries with severe hemorrhages and hemorrhage associated with surgical treatment of neoplasms or infection, as well as in epilepsy, hysteria, tic douloureux, and even paralysis due to "brain congestion." At the present time, however, the ligation of a carotid artery is done mainly because of arterial or arteriovenous aneurysms that cannot be attacked directly and is only rarely used for control of hemorrhages.

The purpose of this study was to develop a group of possible mechanisms that are important factors in the pathogenesis of cerebral infarction from carotid artery occlusion. The data were gathered from an analysis of postoperative complications in a series of 62 cases and of data collected from 123 cases in the literature.

**Methods**

**OUR SERIES**

The histories of all patients who underwent ligation or clamping of the common or the internal carotid artery at the Mayo Clinic from 1955 through 1964 were evaluated. Of the 62 patients involved, 61 had surgery because of intracranial arterial aneurysms filling from the carotid artery, and one patient suffered from a posttraumatic arterial aneurysm of the internal carotid artery at the base of the skull. Three of the 62 patients first had occlusion of the common carotid and later also had occlusion of the internal carotid. There were nearly twice as many females as males affected, and the highest incidence occurred in the two age groups from 40 through 59 years (table 1). The distribution of the 65 occlusions according to age of patient and site of occlusion is shown in table 2.

Not all occlusions were carried out in the same way. In 43 patients, the artery was clamped temporarily for 15 to 30 minutes, the patients being watched for changes in their neurological status. Afterward, the artery was ligated or was clamped with a Silverstone or similar-type clamp immediately; this is termed the "quick" type of occlusion. This procedure made it possible for the occlusion to be opened later on if necessary without requiring a second surgical intervention. Twenty-two occlusions were done with a clamp, which was turned down within one to six days; this was the "slow" type of occlusion. The "quick" type was performed nearly twice as many times as the "slow" type.

Sixty of the 65 occlusions were done while the patient was under the influence of local anesthetic or, in the case of the "slow" type of occlusion, no anesthetic at all. The remaining five occlusions were performed with the patient under general anesthesia.

The postoperative complications considered in the study were only those of neurological change that occurred while the patient was hospitalized after surgery and which originated from the central nervous system. Changes that might have been caused by local-pressure phenomena of the aneurysms on cranial nerves were not included in the study. There were no reports of late complications (except recurrence of subarachnoid bleeding) that occurred after hospital dismissal. Long-term follow-up studies concerned with the efficiency of ligation in cerebral aneurysms were not done.

**CASES FROM THE LITERATURE**

A total of 123 detailed cases involving complica-
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TABLE 3
Distribution of 65 Occlusions in 62 Patients According to Age of Patient and Presence or Absence of Complications

<table>
<thead>
<tr>
<th>Age, yr</th>
<th>Complications</th>
<th>Without</th>
<th>With</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>10-19</td>
<td>4</td>
<td>0</td>
<td>4</td>
<td></td>
</tr>
<tr>
<td>20-29</td>
<td>2</td>
<td>1</td>
<td>3</td>
<td></td>
</tr>
<tr>
<td>30-39</td>
<td>5</td>
<td>3</td>
<td>8</td>
<td></td>
</tr>
<tr>
<td>40-49</td>
<td>15</td>
<td>4</td>
<td>19</td>
<td></td>
</tr>
<tr>
<td>50-59</td>
<td>13</td>
<td>7</td>
<td>20</td>
<td></td>
</tr>
<tr>
<td>60-69</td>
<td>2</td>
<td>6</td>
<td>8</td>
<td></td>
</tr>
<tr>
<td>70-79</td>
<td>3</td>
<td>0</td>
<td>3</td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>44</td>
<td>21</td>
<td>65</td>
<td></td>
</tr>
</tbody>
</table>

occlusions in 115 patients after ligation of the carotid arteries were analyzed. Eight of the 115 patients had suffered two separate incidents after a single ligation. In 25 of these 123 complications, the symptoms disappeared completely, or nearly so, within 24 hours of the operation ("transient type"). In the remaining 98 complications, the symptoms "persisted," meaning that they cleared within several days, weeks, months or years, or that they never cleared.

Findings

Our Series

There was no difference in the incidences of complication between males (seven complications in 22 occlusions) and females (14 complications in 43 occlusions). The combined complication rate for both sexes was high (32%). This is in part due to the inclusion of minor and transitory changes. Except for the age group 60 through 69 years, there were always fewer occlusions with complications than without (table 3).

The number of complications occurring

TABLE 4
Presence or Absence of Complications in the Different Age Groups and Their Relationship to the Speed of Occlusion

<table>
<thead>
<tr>
<th>Age, yr</th>
<th>Without complications</th>
<th>With complications</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Quick*</td>
<td>Slow*</td>
<td>Quick</td>
</tr>
<tr>
<td>10-19</td>
<td>2</td>
<td>2</td>
<td>0</td>
</tr>
<tr>
<td>20-29</td>
<td>2</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>30-39</td>
<td>3</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td>40-49</td>
<td>14</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>50-59</td>
<td>10</td>
<td>4</td>
<td>3</td>
</tr>
<tr>
<td>60-69</td>
<td>0</td>
<td>1</td>
<td>3</td>
</tr>
<tr>
<td>70-79</td>
<td>1</td>
<td>2</td>
<td>0</td>
</tr>
<tr>
<td>Total</td>
<td>32</td>
<td>12</td>
<td>10</td>
</tr>
</tbody>
</table>

* "Quick" means occlusion within 30 minutes; "slow," occlusion after 30 minutes, usually one to six days.

TABLE 5
Relationship Between Presence or Absence of Complications and Location and Speed of Occlusion

<table>
<thead>
<tr>
<th>Carotid</th>
<th>Without complications</th>
<th>With complications</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Quick*</td>
<td>Slow*</td>
<td>Total</td>
</tr>
<tr>
<td>Common</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Left</td>
<td>8</td>
<td>3</td>
<td>11</td>
</tr>
<tr>
<td>Right</td>
<td>13</td>
<td>4</td>
<td>17</td>
</tr>
<tr>
<td>Internal</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Left</td>
<td>7</td>
<td>4</td>
<td>11</td>
</tr>
<tr>
<td>Right</td>
<td>4</td>
<td>1</td>
<td>5</td>
</tr>
<tr>
<td>Total</td>
<td>32</td>
<td>12</td>
<td>44</td>
</tr>
</tbody>
</table>

* "Quick" means occlusion within 30 minutes; "slow," occlusion after 30 minutes, usually one to six days.
after the "slow" and the "quick" procedure is listed in tables 4 and 5. A comparison of the totals shows that only 24% of the "quick" occlusions showed complications, compared with 48% of the "slow" ones. Only three of the 11 patients who had complications after "slow" closure had transitory neurological defects during a previous temporary clamping; one patient tolerated this well. For six patients there was no report of such a trial available. Three of these six patients underwent the clamp application under general anesthesia. Interestingly, complications occurred in 11 of the 39 occlusions of the common carotid artery (28%) and in ten of the 26 occlusions of the internal carotid artery (38%).

Most complications in our series occurred from several hours to as much as days after the occlusion of one of the carotid vessels in the neck, the average interval being 17 hours. There was no observable relationship between the interval and the type of occlusion ("quick" or "slow"), the site of occlusion (common or internal carotid artery in the neck), or the severity of the observed symptoms. Five of the 21 patients died: two because of rebleedings, one after intracranial surgery, and two because of the cerebral infarction that was caused by the carotid ligation. This gives an immediate mortality rate of the carotid ligature of about 3%.

Nine of the 21 complications were "transient," which means that the symptoms disappeared completely or almost completely within 24 hours. The remaining 12 were "persisting" in that they cleared within several days, weeks, months or years, or that they never cleared. There seems to be a greater incidence of transient complications among those patients who had complications earlier than in those who had complications later. There does not appear to be any significant difference between the speed of the occlusion or its location or whether the clamp or ligature was opened again and the type of deficit (transient or persistent) (table 6). Except for one case in which there were two transient attacks of aphasia, there was not another case in which a complete loss of a function with entire or almost entire recovery within 24 hours was noted.

### TABLE 6

<table>
<thead>
<tr>
<th>Complication</th>
<th>Persistent</th>
<th>Transient</th>
</tr>
</thead>
<tbody>
<tr>
<td>Speed of occlusion</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Quick</td>
<td>3</td>
<td>7</td>
</tr>
<tr>
<td>Slow</td>
<td>6</td>
<td>5</td>
</tr>
<tr>
<td>Common carotid occlusion</td>
<td>5</td>
<td>6</td>
</tr>
<tr>
<td>Internal carotid occlusion</td>
<td>4</td>
<td>6</td>
</tr>
<tr>
<td>Clamp or ligature</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Opened</td>
<td>5</td>
<td>5</td>
</tr>
<tr>
<td>Not opened</td>
<td>4</td>
<td>7</td>
</tr>
</tbody>
</table>

### CASES FROM THE LITERATURE

Transient complications occurred less often in the cases reported in the literature (25 of 123 cases) than in our group (9 of 21) (table 7). There may be several reasons for this. (1) Transient episodes that cleared within 24 hours were not included, because the purpose of the study was to evaluate the surgical risk of this type of treatment of aneurysms. For example, this was true in the report by Schorstein (13) who gave details of eight patients with persistent deficits and mentioned only incidentally at least five other patients with transient neurological deficits. (2) Such patients have to be checked neurologically at relatively short intervals in order to detect minor and only short-lasting complications. This can be done best only in "intensive-care units," which are of rather recent origin.

In 23 of the 25 transient complications, the clamp or ligature was opened secondarily 12 times (nine for arterial aneurysms and three for arteriovenous aneurysms) and not opened 11 times (eight for arterial aneurysms and three for arteriovenous aneurysms). This lack of difference was also true in our series (table 6).

We have previously mentioned that transient complications are more likely to occur during the first hours after occlusion of the carotid artery. Since we did not have enough cases of transient complications in our own series, we combined our cases with those of the literature (table 8). The cases of arteriovenous aneurysms have been excluded. Of the 81 complications that occurred after carotid occlusion for arterial aneurysms, 26 (32%) were transient. Most of the transient complications
TABLE 7

<table>
<thead>
<tr>
<th>Complication</th>
<th>Transient</th>
<th>Persistent</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aneurysms</td>
<td>23 (6 AV-aneurysms)</td>
<td>59 (16 AV-aneurysms)</td>
<td>82</td>
</tr>
<tr>
<td>Tumors</td>
<td>2</td>
<td>22</td>
<td>24</td>
</tr>
<tr>
<td>Injuries</td>
<td>0</td>
<td>13</td>
<td>13</td>
</tr>
<tr>
<td>Infectious-processes</td>
<td>0</td>
<td>4</td>
<td>4</td>
</tr>
<tr>
<td>Total</td>
<td>25</td>
<td>98</td>
<td>123</td>
</tr>
</tbody>
</table>

TABLE 8

Frequency of Transient Complications in Certain Time Intervals After Total or Partial Occlusion of Carotid Artery. (Summary of Our Own Cases and of Cases From Literature—Evaluation of Arterial Aneurysms Only.)

<table>
<thead>
<tr>
<th>Time</th>
<th>Complications, no.</th>
<th>Transient complications</th>
</tr>
</thead>
<tbody>
<tr>
<td>Immediate to 10 min</td>
<td>8</td>
<td>2</td>
</tr>
<tr>
<td>10 min to 6 hr</td>
<td>18</td>
<td>13</td>
</tr>
<tr>
<td>7 to 12 hr</td>
<td>18</td>
<td>5</td>
</tr>
<tr>
<td>12 to 24 hr</td>
<td>17</td>
<td>4</td>
</tr>
<tr>
<td>After 24 hr</td>
<td>20</td>
<td>2</td>
</tr>
<tr>
<td>Total</td>
<td>81</td>
<td>26</td>
</tr>
</tbody>
</table>

occurred within the first six hours after occlusion of the vessel. A complication occurring within six hours therefore has a much greater probability of being transient as compared to one taking place, for example, during the second postoperative day, although both may be similar when they occur.

Discussion

SEX

In our series there was no difference in the relative frequency of complications between the sexes. However, more females than males underwent occlusion of the carotid artery. In their studies, McDonald and Korb (14), Dandy (15), and Taveras and Wood (16) noted more intracranial saccular aneurysms in the female than in the male, although Krayenbühl and Yasargil (17) found an equal incidence between the sexes.

AGE

The influence of the patient's age on the occurrence of complications cannot be precisely evaluated. While 75% of the patients who were 60 to 69 had complications, there were a significant number of complications in all ranges from 20-29 to 50-59 as depicted in table 3.

SITE OF LIGATURE

In the literature, one group of authors, among many, have recommended ligature of the common carotid artery as the less dangerous procedure, whereas another group favored ligation of the internal carotid, because of a smaller risk. The surgeons at the Mayo Clinic apparently have preferred to ligate the common carotid artery in patients 10 through 19 years old, 30 through 49 years old, and 70 through 79 years old. The more frequent occurrence of complications in patients with internal carotid occlusion is statistically not significant. In our series, there were 11 complications in 39 occlusions of the common carotid and 10 complications in 26 occlusions of the internal carotid.

SPEED OF OCCLUSION

Pool and Potts (18) believed that a slow occlusion of the attacked artery would allow the establishment of a collateral circulation and reduce the incidence of complications. This led to the construction of the "Silverstone clamp" and similar devices. Surprisingly, in our series there were 10 complications in 42 quick occlusions and 11 complications in 23 slow occlusions, the difference being statistically significant. However, it is important to remember that the surgeons have selected the cases for the different procedures and have, therefore, preferred to clamp the vessel slowly in patients who might have had some evidence
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of impaired cerebral circulation, although none of these signs was recorded in the medical records. We are not aware of any paper evaluating this question in a larger series.

INTERVAL BETWEEN TIME OF OCCLUSION AND APPEARANCE OF CEREBRAL SYMPTOMS

The first reports of Abernethy (6) in 1811 and Cooper (8) in 1809, concerned with patients who showed cerebral complications after carotid ligation, mentioned only incidentally that the symptoms appeared after a time interval. The same was true for the larger series of Norris (9) and Pilz (11). The first one to draw attention to this time interval directly, however, was Le Fort (10) in 1868 who used it as the most important support for his theory of the thrombotic origin of the complication. The existence of this interval has since then been repeatedly reported by many (12, 13, 15, 19-31). Mount (26) in 1959 reported an average interval of 13 hours 25 minutes for 27 patients; this agrees generally with our own finding of 17 hours (21 complications in 20 patients). The average interval in the cases of arterial aneurysms collected from the literature was 27 hours. Raskind (28) noted an interval of 7.7 days for eight surviving patients in his series.

INCIDENCE OF COMPLICATIONS

In recent years the frequency of cerebral complications has not changed greatly (15, 32-34). It is not possible to know how severe the symptoms of the complications had to be in order to be reported. From our own experiences with minor and transient complications, it is sometimes difficult to detect minor complications. The mortality rate has decreased gradually from 1847 (9) (36%) to the present date (5% (35), 6% (36), 5% (26), 0% (28), 3% in the present series).

Mechanisms of Cerebral Symptoms

Le Fort (10) in 1868 proposed for the first time that the occurrence of thrombosis in the distal part of the ligated vessel and its spread into the circle of Willis is responsible for the late onset of cerebral symptoms. This hypothesis was elaborated by Zimmermann (31) in 1891 who stated that not only can a thrombosis spread but also an embolus can originate from a small thrombus at the site of ligature and account for the symptoms. Since that time there has been an endless discussion in favor of the thromboembolic or the hemodynamic theory based on the existence of insufficient collaterals. This discussion has been at least partially ended by the doctrinary statement of Dandy (15) in 1944 who attributed the “immediate” complications (up to 8 to 12 hours) to an inadequate circulation and the “late” ones (after 12 hours) to thrombosis and embolism. Since this concept is oversimplified, we shall consider other aspects of the problem.

CIRCULATION TO BRAIN

Because the ligated vessel is the only supply to a certain area of the brain and because of the many anastomoses in the intracranial circulation, a congenital or acquired insufficiency of at least part of them can be assumed to cause cerebral symptoms. Since this is a structural, preexisting situation, its most marked effect occurs at the moment of ligation and regresses later because of dilatation of not fully patent channels. The clinical effects of such a situation, therefore, should be evident within a few minutes, perhaps even seconds. Thus, this mechanism might account for a maximum of 8 of the 81 cases of arterial aneurysm in our series and of those collected from the literature. It has, of course, to be considered that the Matas-Test (37), which was specifically designed to select patients with insufficient collaterals before surgery, reduced considerably the number of candidates for this kind of complication in the reported series. This mechanism can explain transient and persisting symptoms but cannot explain an occurrence of the complications after several minutes, hours, or days without any secondary and independent happening. The transitory character of the symptoms due to a sufficient dilatation of collaterals within reasonable time might be illustrated by a case reported by Rogers (38) although other theories can explain it too. In one patient in our series, with the use of local anesthesia, the left common carotid artery was tied and divided. Immediately upon tying and dividing, the patient became comatose and showed a right hemiplegia. Within seconds, she regained consciousness and the hemiplegia later disappeared.
FAILURE OF COLLATERAL CIRCULATION

A secondary, vascular occlusion, independent of the ligature, in one of the collateral vessels supplying blood to the area of the surgically occluded vessel can produce an infarct in this region of the brain. This seems to be extremely rare, and we are aware of only one such case in the literature (39).

SHUNTING

A blood shunt distal to the site of ligation may cause a decrease in the distal blood pressure that is more extensive than anticipated and may lead to cerebral ischemia. This shunting can theoretically be arteriovenous (most commonly through the intracavernous, arteriovenous aneurysm in which the symptoms should have been treated with the ligature) or arterial into another arterial system, such as the external carotid or vertebrobasilar region. Only the first (arteriovenous) type of shunt has been reported on in the literature as being a cause of complications; the second type never has been observed to cause troubles, although Sweet and Bennett (40) in 1948 have shown that in about one third of the cases an "external carotid steal" occurs. Since the shunting mechanism works immediately in the case of an arteriovenous connection, symptoms should appear within a very short period. Marsh and Raney (41) have shown that EEG changes and jacksonian seizures occur within 8 to 10 seconds. Complications after a longer interval probably need additional pathogenetic agents for their explanation.

REFLEX MECHANISMS

Two reflex mechanisms exist that might cause trouble after carotid ligation. The first one is the carotid sinus reflex which can bring on a cardiac arrest or severe bradycardia either immediately after the ligature is tied (42) or after a longer period by establishing a pressure hypersensitivity of its receptors (43). This mechanism should be detected relatively easily in an intensive-care unit; it never was seen in our series.

In regard to the second reflex, neuroradiologists know that a subarachnoid hemorrhage can cause spasms in the intracranial arteries. The surgeon, therefore, tries to delay the carotid ligation until this vasoconstricting phase has passed. A similar vasoconstriction is believed to be caused by a sympathetic irritation by the ligature. No one has ever been able to show why this reflex should start with a latency of several hours or days. Schorstein (13), in 1940, argued that the extremely strong stimulus of the accumulating CO₂ in a region that is not adequately perfused would be able to produce a dilatation powerful enough to overcome the constrictory impulses. Not even the periartrial sympathetomy of the internal carotid (44) or the postoperative irrigation of the superior cervical ganglion with anesthetics (45) has prevented complications.

TRANSIENT SYSTEMIC HYPOTENSION

Since the theory of the insufficiency of the collateral circulation fails to explain all complications occurring after a longer interval, an additional lowering of the systemic blood pressure has been assumed to fill this gap. Dorrance (21) in 1934 argued that emboli causing an infarction after carotid ligation have never been observed in animal experiments, whereas a lowering of blood pressure can easily produce an infarct. This is not common in humans with carotid ligations, because a decrease in blood pressure has been observed very rarely (26, 46) and was never seen in our own series. This mechanism may be important after injuries in which the ligation was done as an emergency procedure in shocked patients.

ANEMIA

Mount (26) stated in 1959 that three of his 27 patients who had complications suffered from anemia, the hemoglobin values being between 8.5 and 12.4 gm per 100 ml. The clamp was opened in all of them. One of these patients tolerated a second closure of the clamp; after that the hemoglobin value had risen from 10.8 to 13.6 gm. Siekert, Whisnant, and Millikan (47) in 1960 showed that an anemia combined with a spontaneous carotid occlusion can produce transient attacks of focal cerebral ischemia which could be stopped by correction of the anemia.

TRANSIENT SYSTEMIC HYPOGLYCEMIA

Transient hypoglycemia is well known as a factor capable of inducing cerebral infarction. However, we are not aware of a reported case in which this disturbance produced complications after carotid ligations.
PATHOGENESIS OF CEREBRAL INFARCTION

INCREASED PARENCHYMAL OXYGEN AND GLUCOSE CONSUMPTION

An increased consumption of oxygen and glucose can lead to cerebral infarction and dysfunction if the blood supply to a circumscribed part of the brain is already borderline. The increased consumption can be caused by fever, hyperthyroidism, and epileptic seizures. Pfeiffer (48) reported the case of a 20-year-old man who, immediately after the ligation of the left internal carotid artery, had a Jacksonian (motor) seizure on the right and afterward had motor aphasia, right hemiplegia, hemihypoaesthesia, right homonymous hemianopsia, and euphoria. These symptoms showed only minor improvement later. It is impossible to determine in this case whether the neurological deficit was caused by the seizure that was triggered by slight ischemia or whether the seizure was a part of the establishment of the neurological signs that would have appeared even without the convulsion.

THROMBUS FORMATION AT SITE OF LIGATURE AND PROPAGATION INTO CIRCLE OF WILLIS

The concept of a slowly forming thrombus in the internal carotid artery, starting at the site of ligation, spreading into the circle of Willis, and finally occluding vital branches of the system has been repeatedly proved in many reported autopsy cases (10, 15, 31). This mechanism explains the different latency of the cerebral symptoms; it is even able to explain the production of slowly progressing symptoms. The local thrombosis at the site of ligation is facilitated by the blood stasis, by the internal injuries caused by the ligation, and by the local inflammatory processes and arteriosclerotic changes in the ligated vessel.

THROMBOSIS AT THE SITE OF LIGATURE AND SECONDARY EMBOLIZATION

During surgical revision and removal of the ligature, it has been observed that the formerly occluded vessel afterward was patent and pulsating and showed no evidence of local thrombosis. The assumption, therefore, was that the complication had been caused by the insufficiency of the collaterals even if the symptoms occurred after a prolonged interval. This observation does not, of course, prove the cited statement. These late complications are explained more readily by the mechanism proposed by Zimmermann (31) who assumed that a thrombus is formed at the site of ligation where it can later become detached in its entirety from the wall and be transported into the circle of Willis or one of its branches, leaving the site of its formation empty. The same can happen if only a part of the thrombus breaks off. Both situations have been proved many times at autopsy. This mechanism even suggests that the ligation of the common carotid artery is more dangerous because it leaves a minor blood flow in the internal carotid which can help to displace the embolus. The reason for the breaking off of the embolus can only be elucidated in rare cases: The patient can trigger it himself by leaning out of his bed and reaching for an object (30), or it can be caused by the surgeon palpating the site of the ligation (33) or replacing a temporary clamp by a ligation (1). A local thrombus can be formed in a relatively short time and be displaced hours afterward, as, for example, is seen in the case of Perthes (27) who did, during neck surgery for a fibrosarcoma, a temporary clamping of the common carotid which was later reopened after control of the hemorrhage. A contralateral hemiplegia occurred in the evening of the first postoperative day. The local thrombosis even can be preexisting. Nunneley (49) reported on a patient who underwent the ligation of the left common carotid artery because of an intracranial arteriovenous aneurysm in the cavernous sinus. The patient showed an immediate right hemiplegia and aphasia and died 16 days later. Autopsy disclosed a coagulum in the intracranial part of the internal carotid artery, an ulceration in the common carotid at the site of ligation, but no local thrombus.

The thrombi also can start in the external carotid and grow into the carotid bifurcation if the ligature is not placed far enough from this point. Emboli can break off at their tips and cause cerebral complications. Lipps (50), Stierlin and Meyenburg (51), Herfarth (52), and Petermann (53) have documented this clearly at autopsy. The extremely long interval before complications appear represents the time needed by the thrombus to grow into the bloodstream of the common and internal carotid arteries.

A local thrombus can form if the carotid artery is only partially ligated (19). Complications can occur in this way at a stage in which
the remaining diameter of the vessel does not produce any decreased blood flow (54).

In 1900, Siegrist (29) proposed for the first time that an embolus, after plugging a cerebral artery for some time, can break apart, produce transient symptoms, but not be present at autopsy. This fragmentation of emboli is presently regarded as being responsible for the "transient focal cerebral ischemia" (55). A reestablishment of the preoperative blood pressure level by the opening of the clamp in the neck may help to fragment the embolus. However, opening the clamp may displace fragments of the local thrombus that are still left in place.

In one of our patients, a thrombus was formed in the common carotid during or after the clamp was turned down and probably obstructed the middle cerebral artery on the right side seven hours later. The embolus broke apart after the clamp was opened again and caused transient symptoms. The thrombus formed again when the clamp had been turned down only half way and led to the second complication, which also was transient. The second thrombosis perhaps was facilitated by intimal lesions that were produced by the first clamping.

Complications that occur within the first six hours are more likely to be transient and may be caused by fresh thrombi that are perhaps smaller and more brittle than older ones.

Coincidental Distal Thrombosis

The carotid ligation is done to decrease the blood pressure and its flow in the internal carotid artery up to its bifurcation, thus enabling a blood clot to be formed in the berry aneurysm (56). This blood clot can grow out of the neck of the aneurysm and invade the internal carotid artery and the circle of Willis (57). The same process of a local thrombosis can take place in any part of the vascular tree and change flow characteristics and alter some endothelial tissue. However, the occurring thrombosis may be purely coincidental, being unrelated to the ligation. This might perhaps explain the single case of a paradoxic hemiparesis that was observed in a 48-year-old woman by Hardy and associates (58).

The pressure of the thrombosed aneurysm on the middle cerebral artery has been reported to have caused the occlusion of this vessel from the outside (59). This is some-what hard to understand because there is no reason why a clot-filled aneurysm should exert a greater pressure on its underlying surface than should a blood-filled one. The occlusion was caused only by the lowering of the blood pressure in the affected vessel.

After all these different mechanisms of the complications occurring after carotid ligation are considered, it is evident that there exists a multitude of explanations that may fit any single case. Although the actual pathogenesis of complications often cannot be determined with certainty, it is clear that the thromboembolic theory can explain most of them.

Summary

The immediate postoperative cerebral complications of 65 carotid occlusions were evaluated. The occlusions were done in all but one case (extracranial, arterial aneurysm) for intracranial saccular aneurysms and were performed by either direct ligation (quick type) or slow turning down of a Silverstone clamp or similar device (slow occlusion). Cerebral complications occurred in 21 patients and varied from deficits that were minor and hardly detectable to hemiplegia, hemianesthesia of cortical type, hemianopsia, and aphasia. Two patients died as a result of the occurring infarction. The quick type of occlusion of the artery resulted in a complication rate of 24% whereas the slow type had a rate of 38%. Nine patients suffered only transient deficits; these cleared completely or almost completely within 24 hours, whereas the remaining 12 patients had persisting symptoms that cleared only after a prolonged interval or that never cleared. The symptoms occurred usually after an average interval of 17 hours, with extremes of two hours before occlusion and 80 hours after the occlusion. Symptoms were observed even in patients whose vessel was only half occluded. A total of 123 cases involving cerebral complications after carotid ligation were collected from the literature and evaluated. The combined total of 81 cases of transient complications that were collected from the literature and from our series showed that such deficits occur frequently from 10 minutes to six hours after the occlusion of the vessel.

The data were discussed in relation to the possible mechanisms of the complications.
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those discussed, the thromboembolic theory is the one that can explain most of the cerebral complications.

References

3. Lynn: The first ligation of the carotid artery ever performed in this country. Lancet 1: 63-64, 1832-33
5. Pilcher C, Thuss C: Cerebral blood flow: III and IV. III. Cerebral effects of occlusion of the common or internal carotid arteries. Arch Surg (Chicago) 29: 1024-1038 (Dec) 1934
6. Abernethy J: Surgical observations on injuries of the head: And on miscellaneous subjects. Philadelphia, Thomas Dobson, 1811, 299 pp
10. Le Fort L: De la valeur thérapeutique de la ligature de la carotide primitive. Gaz Hebd Med 5: 437-440; 465-467; 551-553 (July) 1868
17. Krayenbühl H, Yasargil MG: Das Hirnaneurysma, Docum Geigy, ser chir, 1958, no. 4, pp 1-143
22. Fetterman JL, Pritchard WH: Cerebral complications following ligation of the carotid artery. JAMA 112: 1317-1322 (April 8) 1939
34. Steelman HF, Hayes GJ, Rizzoli HV: Surgical treatment of saccular intracranial aneurysms:


Matas R: Discussion on papers of Drs. Elkin and Campbell, Dr. Matas and Dr. Gage. Amer J Surg 24: 692-698, 1934

Rogers L: Ligation of the common carotid artery: Report of 19 personal cases. Lancet 1: 949-950 (June 4) 1949

Sweet WH, Bennett HS: Changes in internal carotid pressure during carotid and jugular occlusion and their clinical significance. J Neurosurg 5: 178-195 (March) 1948


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