Aneurysmal Forms of Cervical Artery Dissection

Associated Factors and Outcome

Emmanuel Touzé, MD; Bruno Randoux, MD; Eric Méary, MD; Caroline Arquizan, MD; Jean-François Meder, MD; Jean-Louis Mas, MD

Background and Purpose—The natural history of aneurysmal forms of cervical artery dissection (CAD) is ill defined. The aims of this study were to assess (1) clinical and anatomic outcome of aneurysmal forms of extracranial internal carotid artery (ICA) and vertebral artery (VA) dissections and (2) factors associated with aneurysmal forms of CAD.

Methods—Seventy-one consecutive patients with CAD were reviewed. Aneurysmal forms of CAD were identified from all available angiograms by 2 neuroradiologists. The frequency of arterial risk factors, of multiple vessel dissections, and of artery redundancies was compared in patients with and without aneurysm. Patients with aneurysm were invited by mail to undergo a final clinical and radiological evaluation.

Results—Of the 71 patients, 35 (49.3%) had a total of 42 aneurysms. Thirty aneurysms were located on a symptomatic artery (ICA, 23; VA, 7) and 12 on an asymptomatic artery (ICA, 10; VA, 2). Patients with aneurysm had multiple dissections of cervical vessels (18/35 versus 7/36; \( P = 0.005 \)) and arterial redundancies (20/35 versus 11/36; \( P = 0.02 \)) more frequently than patients without aneurysm. They were also more often migrainous (odds ratio = 2.7 [95% CI, 0.8 to 8.5]) and tobacco users (odds ratio = 2.2 [95% CI, 0.7 to 6.3]). Clinical and anatomic follow-up information was available for 35 (100%) and 33 patients (94%), respectively. During a mean follow-up of >3 years, no patient had signs of cerebral ischemia, local compression, or rupture. At follow-up, 46% of the aneurysms involving symptomatic ICA were unchanged, 36% had disappeared, and 18% had decreased in size. Resolution was more common for VA than for ICA aneurysms (83% versus 36%). None of the aneurysms located on an asymptomatic ICA had disappeared.

Conclusions—Although aneurysms due to CAD frequently persist, patients carry a very low risk of clinical complications. This favorable clinical outcome should be kept in mind before potential harmful treatment is contemplated. (Stroke. 2001;32:418-423.)

Key Words: aneurysm • carotid arteries • connective tissue disorders • dissection • magnetic resonance imaging • rehabilitation • vertebral artery

Cervical artery dissection (CAD) accounts for up to 20% of ischemic strokes in young adults.1,2 Although the exact pathogenesis of CAD remains unclear, an underlying arteriopathy leading to a so-called weakness of the vessel has been postulated.3,4 Three main angiographic patterns of dissection have been described, including stenotic, occlusive, and aneurysmal forms.5 Aneurysmal forms represent approximately one third of cases.6–14 While complete resolution of stenotic forms of dissection is the rule, the regression of aneurysms seems rare. The risk of late ischemic events associated with persistent aneurysms is not well known. Indeed, only one study has been specifically devoted to the clinical and anatomic outcome of aneurysmal forms of internal carotid artery (ICA) dissection.14 The proper strategy for secondary prevention in patients with persistent aneurysms is controversial. Therapeutic options include antiplatelet drugs or anticoagulants and invasive treatments, including surgery or endovascular procedures.15–19 All these therapeutic options have some risks, which must be weighed against natural history.

The aims of this study were to assess (1) the clinical and anatomic outcome of aneurysmal forms of cervical ICA and vertebral artery (VA) dissection and (2) the factors associated with aneurysmal forms of CAD.

Subjects and Methods From January 1990 through January 2000, 71 consecutive patients with recent CAD (extracranial) were admitted to our department. All patients had digital subtraction angiography (DSA) and/or magnetic resonance angiography (MRA) at the time of the diagnosis and, with the exception of 5 patients, at least 1 follow-up angiographic study. Axial neck MRI was performed in 64 patients. The diagnosis of dissection was based on classic angiographic signs, namely, irregular stenosis (“string sign”), double lumen, and intimal flaps.2,3 Occlusive
forms of CAD were confirmed by the presence of a mural hematoma on MRI.

Two experienced neuroradiologists reviewed all available angiograms and classified the patients into 2 groups: CAD with aneurysm and CAD without aneurysm. An aneurysm was defined as an extraluminal pouch (saccular aneurysm) or a segmental dilatation of the lumen diameter (fusiform aneurysm).14 The presence of multiple dissections and redundancies of the arteries was recorded. Redundancies were defined with classic criteria.20

The following risk factors were recorded prospectively in our stroke registry: history of hypertension, cigarette smoking, hypercholesterolemia, diabetes mellitus, history of migraine according to the International Headache Society criteria,21 oral contraceptives use, and recent (in the previous month) trauma or infection.

Between December 1999 and July 2000, all patients with aneurysmal forms of CAD were invited by mail to undergo a final clinical and standardized neuroradiological examination, including 2-dimensional (2D) time-of-flight (TOF) and gadolinium-enhanced MRA (see Imaging Protocol below) and cranial MRI to detect redundancies and to classify aneurysms. The sites of dissections and aneurysms are shown in Figure 1. Twenty-five patients had 1 (n=24) or 2 (n=1) aneurysms involving the artery responsible for acute symptoms (symptomatic artery). Five patients had 1 aneurysm involving the symptomatic artery, associated with an aneurysm on an asymptomatic artery. Five patients had 1 (n=4) or 2 (n=1) aneurysms involving an asymptomatic artery. Therefore, 30 aneurysms involved arteries responsible for acute symptoms (ICA, 23; VA, 7), and 12 aneurysms involved asymptomatic arteries (ICA, 10; VA, 2). Of the 42 aneurysms, 36 were identified in the acute stage of the dissection and 6 on a follow-up angiography performed 1.3 to 4.2 months later. Of these 6 patients, 1 had DSA and 5 MRA as initial angiography. ICA aneurysms were located in the following segments of the artery: subpetrous (n=26), medio-cervical (n=3), and postbulbar (n=4). All VA aneurysms involved the third segment of the artery. Of the 42 aneurysms, 27 were fusiform (ICA, 20; VA, 7) and 15 saccular (ICA, 13; VA, 2). Fourteen ICA aneurysms were near or within a redundancy.

Comparison of CAD With and Without Aneurysm

Table 1 shows the characteristics of patients with and without aneurysm. Clinical presentation did not differ significantly between the 2 groups, but painful Horner’s syndrome and/or dysfunction of cranial nerves IX to XII were slightly more frequent in patients with aneurysm. Migraine and smoking were more frequent in patients with aneurysm, but the difference did not reach statistical significance. In a multivariate logistic regression analysis including age, sex, tobacco use, and migraine as explicative variables, ORs were 2.7 (95% CI, 0.8 to 8.5; P=0.10) for migraine and 2.2 (95% CI, 0.7 to 6.3; P=0.16) for cigarette smoking. Dissections of multiple vessels were significantly more frequent in patients with aneurysm than in those without aneurysm (18/35 versus 7/36; P=0.005), as were redundancies (20/35 versus 11/36, P=0.02). Bilateral redundancies were more frequent in patients with aneurysm (11/35 versus 5/36; P=0.08), but the association was not statistically significant.

Follow-Up

Of the 35 patients with an aneurysmal form of CAD who were invited by mail, 28 (80%) accepted the request to

![Figure 1. DSA. A, Saccular aneurysm; B, fusiform aneurysm.](image-url)
undergo a final clinical and MRA examination, 3 refused MRA examination but related no clinical event since their first admission, and 4 could not be contacted, but clinical follow-up information was available in their medical chart (mean clinical follow-up of 49.7 months). Among the 7 patients who did not have the final MRA examination, 5 had had at least 1 follow-up angiography (mean anatomic follow-up, 13.5 months; range, 3.8 to 36.9 months). Therefore, 35 patients (100%) had at least 1 clinical follow-up visit, and 33 (94.3%) had at least 1 follow-up angiography.

**Clinical Outcome**
For a mean follow-up period of 41.6 months (range, 3.5 to 109.3 months), none of the 35 patients had transient ischemic attack, stroke, or clinical symptoms suggestive of aneurysmal rupture or compression. At the time of the last follow-up visit, 29 patients received antiplatelet therapy, 2 oral anticoagulants, and 4 no antithrombotic therapy. No patient had new lesions on cranial MRI.

**Anatomic Outcome**
After a mean anatomic follow-up of 36.6 months on average (range, 3.5 to 106.6 months), 22 of 33 patients (67%) had at least 1 persistent aneurysm. In 3 of them, the

### TABLE 1. Comparison of CAD With and Without Aneurysm

<table>
<thead>
<tr>
<th></th>
<th>CAD With Aneurysm (n=35)</th>
<th>CAD Without Aneurysm (n=36)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Baseline characteristics</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age, mean ± SD, y</td>
<td>44.3 ± 9.2</td>
<td>41.9 ± 10.2</td>
<td>0.31</td>
</tr>
<tr>
<td>Sex, M/F</td>
<td>20/15</td>
<td>18/18</td>
<td>0.55</td>
</tr>
<tr>
<td>High blood pressure</td>
<td>6</td>
<td>4</td>
<td>0.47</td>
</tr>
<tr>
<td>Tobacco use</td>
<td>18</td>
<td>12</td>
<td>0.10</td>
</tr>
<tr>
<td>Diabetes</td>
<td>1</td>
<td>0</td>
<td>...</td>
</tr>
<tr>
<td>Hypercholesterolemia</td>
<td>6</td>
<td>2</td>
<td>0.13</td>
</tr>
<tr>
<td>Contraceptive use</td>
<td>4</td>
<td>6</td>
<td>0.52</td>
</tr>
<tr>
<td>Migraine</td>
<td>15</td>
<td>9</td>
<td>0.07</td>
</tr>
<tr>
<td>Recent trauma</td>
<td>13</td>
<td>15</td>
<td>0.70</td>
</tr>
<tr>
<td>Recent infection</td>
<td>2</td>
<td>4</td>
<td>0.44</td>
</tr>
<tr>
<td>Delay between first symptom and admission, d</td>
<td>11.6</td>
<td>15.2</td>
<td>0.57</td>
</tr>
<tr>
<td><strong>Clinical presentation</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Stroke</td>
<td>22</td>
<td>27</td>
<td>0.62</td>
</tr>
<tr>
<td>Transient ischemic attack</td>
<td>2</td>
<td>3</td>
<td>...</td>
</tr>
<tr>
<td>Painful Horner’s syndrome and/or cranial nerve IX to XII dysfunction</td>
<td>6</td>
<td>2</td>
<td>...</td>
</tr>
<tr>
<td>Subarachnoid hemorrhage*</td>
<td>2</td>
<td>1</td>
<td>...</td>
</tr>
<tr>
<td>Isolated neck pain or headache</td>
<td>3</td>
<td>3</td>
<td>...</td>
</tr>
<tr>
<td><strong>Angiographic features</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Initial evaluation by DSA</td>
<td>25</td>
<td>23</td>
<td>0.61</td>
</tr>
<tr>
<td>Multiple vessel dissection</td>
<td>18</td>
<td>7</td>
<td>0.005</td>
</tr>
<tr>
<td>Redundancies</td>
<td>20</td>
<td>11</td>
<td>0.02</td>
</tr>
<tr>
<td><strong>Site of dissection</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ICA (unilateral)</td>
<td>14</td>
<td>19</td>
<td>...</td>
</tr>
<tr>
<td>ICA (bilateral)</td>
<td>11</td>
<td>3</td>
<td>...</td>
</tr>
<tr>
<td>VA (unilateral)</td>
<td>3</td>
<td>10</td>
<td>...</td>
</tr>
<tr>
<td>VA (bilateral)</td>
<td>4</td>
<td>2</td>
<td>...</td>
</tr>
<tr>
<td>ICA + VA</td>
<td>3</td>
<td>2</td>
<td>...</td>
</tr>
<tr>
<td><strong>Site of aneurysm</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ICA (unilateral)</td>
<td>23</td>
<td>...</td>
<td>...</td>
</tr>
<tr>
<td>ICA (bilateral)</td>
<td>4</td>
<td>...</td>
<td>...</td>
</tr>
<tr>
<td>VA (unilateral)</td>
<td>6†</td>
<td>...</td>
<td>...</td>
</tr>
<tr>
<td>ICA + VA</td>
<td>2</td>
<td>...</td>
<td>...</td>
</tr>
</tbody>
</table>

Values are number of subjects unless indicated otherwise.
*These patients also had intracranial dissection.
†One patient with 2 aneurysms on the same artery.
aneurysm was visible on gadolinium-enhanced MRA but not on 2D TOF MRA. Table 2 shows the anatomic outcome of the 40 carotid or vertebral aneurysms of these 33 patients, according to whether they were located on a symptomatic or an asymptomatic artery. Of the 22 symptomatic carotid aneurysms, 10 (46%) were unchanged, 4 (18%) decreased in size (Figure 2), and 8 (36%) disappeared. Complete resolution was significantly more frequent for vertebral than for carotid symptomatic aneurysms (83% versus 36%; \( P=0.05 \)) (Figure 3), but aneurysm type (fusiform/saccular) did not influence anatomic outcome. The large majority of aneurysms located on an asymptomatic carotid artery were unchanged. When only the 28 patients who had the final standardized neuroradiological examination (2D TOF and gadolinium-enhanced MRA) were analyzed, the anatomic outcome of symptomatic and asymptomatic aneurysms was similar.

### Discussion

The frequency of aneurysmal forms of CAD found in our study (49.3%) is consistent with values reported in previous studies ranging from 13% to 48% for ICA\(^6,7,10–14\) and from 10% to 46% for VA.\(^8,9,22\) The differences in the proportion of aneurysmal forms of CAD between studies may reflect different definitions of dissecting aneurysms or referral biases. In addition, some aneurysms may be missed if only an acute-stage angiography is performed, because blood flow distal to the stenosis may be insufficient to fulfill the aneurysm. Indeed, in our series, 6 aneurysms were identified only on a follow-up angiography.

### Factors Associated With Aneurysmal Forms of CAD

Dissections of multiple vessels and redundancies are frequent in patients with connective tissue disorders,\(^23\) which argues in favor of an underlying arteriopathy in patients with CAD. Our findings, that dissections of multiple vessels and redundancies were significantly more common in patients with aneurysm than in those without aneurysm (Table 1), suggest a more severe underlying arteriopathy in patients with aneurysmal form of CAD.

We also found that patients with aneurysmal form of CAD were more often migraineurs and tobacco users. Migraine has been associated with CAD in a case-control study.\(^24\) The underlying mechanisms are unknown, but a recent study found that patients with migraine had a higher serum elastase activity level, suggesting an increase in extracellular matrix degradation.\(^25\) Tobacco has been shown to decrease activity of \(\alpha_1\)-antitrypsin, an enzyme that has a crucial role in maintaining the integrity of connective tissue.\(^26,27\) However, no association between smoking and CAD has been established. Finally, we did not find any relation between aneurysmal form of CAD and previous cervical or cranial trauma.\(^11\)

### Clinical Outcome

In the present study none of the patients with aneurysmal form of CAD had recurrent ischemic events, rupture, or local compressive signs under antithrombotic treatment (mainly aspirin) after a mean follow-up of >3 years. This result is consistent with the study of Guillon et al.\(^14\) who

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**TABLE 2. Anatomic Outcome of 40 Aneurysms (33 Patients)**

<table>
<thead>
<tr>
<th>Evolution</th>
<th>Symptomatic Artery</th>
<th>Asymptomatic Artery</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>ICA (n=22)</td>
<td>VA (n=6)</td>
</tr>
<tr>
<td>Resolved</td>
<td>8</td>
<td>5</td>
</tr>
<tr>
<td>Decreased</td>
<td>4</td>
<td>...</td>
</tr>
<tr>
<td>Unchanged</td>
<td>10</td>
<td>1</td>
</tr>
</tbody>
</table>

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**Figure 2.** A, Initial DSA shows severe stenosis of the right ICA but no obvious aneurysm. B, Follow-up DSA performed 3 months later shows resolution of the stenosis and appearance of a saccular aneurysm. C, Follow-up gadolinium-enhanced MRA performed 50 months later shows that the aneurysm decreased in size.

**Figure 3.** A, Initial 2D TOF MRA shows stenosis and 2 fusiform aneurysms on left VA. B, Follow-up gadolinium-enhanced MRA shows resolution of the stenosis and the aneurysms.
did not observe any recurrent event in 16 patients with aneurysmal form of ICA dissections followed up for an average of 3 years. In addition, our findings suggest that patients with aneurysmal form of VA dissection have an excellent clinical outcome. These results are also consistent with studies that assessed the overall risk of late recurrent stroke in patients with CAD and found that none of the late ischemic attacks were related to persistent aneurysm.28,29

Very few cases of stroke due to cervical ICA aneurysm have been reported. In some patients a thrombus was found in the aneurysm at surgery.30,31 However, the aneurysm was thought to represent an old dissection only in a few patients.30 To our knowledge, no case of arterial rupture or mass effect due to persistent aneurysm after CAD has been reported.

Anatomic Outcome
In our study, as in that of Guillou et al.14 no increase in size of the aneurysm was observed at follow-up angiographies. In both studies, most patients had a persistent ICA aneurysm: 95%14 versus 67% in our study. The proportion of complete resolution of ICA aneurysms in our series (36%) was similar to that compiled from series of cervical ICA dissections.6,7,10–13 Aneurysmal forms of cervical VA dissection seem to have a better anatomic outcome than aneurysmal forms of ICA dissections, since approximately 80% of the former resolved in our series, which is consistent with the rate of disappearance (65%) compiled from the different series of cervical VA dissections.6,9,22

An important difficulty is to know whether an aneurysm involving an asymptomatic artery represents a previous dissection and is present for many years or represents a purely aneurysmal form of acute dissection. In our series, 12 of 22 aneurysms (55%) involving a symptomatic carotid artery resolved or decreased in size during follow-up, compared with only 1 of the 10 aneurysms (10%) involving an asymptomatic carotid artery. This suggests that some aneurysms involving an asymptomatic artery are probably due to a previous silent dissection.

MRA has been considered a valuable technique for the diagnosis and follow-up of CAD.32,33 Recent advances have been made by the use of gadolinium infusion, which reduces artifacts and allows high-quality images of supra-aortic vessels.34 However, no study has compared different modalities of MRA in the diagnosis and follow-up of CAD with or without aneurysm. Our study is the first to use TOF MRA and gadolinium-enhanced MRA in the follow-up of aneurysmal forms of CAD. We found that TOF MRA missed aneurysm in 3 cases, which suggests that gadolinium-enhanced MRA allows a more accurate visualization of aneurysms than TOF MRA.

In conclusion, this study shows that aneurysms associated with cervical ICA dissection frequently persist, while those associated with cervical VA dissection seem to have a better anatomic outcome. The persistence of cervical ICA or VA aneurysm carries very little risk of ischemic event or other complication under antiplatelet therapy. This favorable clinical outcome should be kept in mind before potentially harmful treatment of patients with aneurysmal form of CAD is contemplated. Otherwise, there is a risk of exposing patients to unnecessary complications of treatment. Conservative management with antiplatelet therapy seems a prudent strategy pending further information.

References


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