Angiographic frequency of saccular intracranial aneurysms in patients with spontaneous cervical artery dissection

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The pathogenesis of intracranial aneurysms and spontaneous cervical artery dissection is incompletely understood but a primary arteriopathy, possibly similar in both disorders, may be of importance. To investigate the frequency of intracranial aneurysms in patients with spontaneous cervical artery dissection, the angiograms of 164 patients who were diagnosed at the Mayo Clinic as having spontaneous extracranial carotid or vertebral artery dissection were reviewed. Thirteen intracranial aneurysms were detected in nine (5.5%) of the 164 patients: eight (8.8%) of the 91 female patients and one (1.4%) of the 73 male patients. The frequency of intracranial aneurysms in these patients was significantly higher ($p < 0.01$) than that observed in a recent angiographic study from the same institution, estimating the frequency of intracranial aneurysms in the general population (1.1%). The significance of these findings is discussed.

Key Words • angiography • aneurysm, dissecting • cerebral aneurysm • subarachnoid hemorrhage

Spontaneous dissections of the extracranial carotid or vertebral artery are increasingly diagnosed as a cause of transient ischemic attacks, ischemic stroke, unilateral headache accompanied by ipsilateral oculosympathetic palsy and/or pulsatile tinnitus, and lower cranial nerve palsies.12,25-27 The pathogenesis of cervical artery dissection has not been firmly established, but probably involves an underlying structural arterial defect and mechanical factors. Although a history of a more or less trivial traumatic precipitating event is regularly elicited, an underlying arteriopathy is generally suspected. Several factors support such a primary arteriopathy, including the occurrence of multiple arterial dissections in the same patient, subtle arterial wall defects of (segments of) arteries not affected by the dissection, and the familial occurrence of the disease.12,24-28 In addition, families with members suffering from either intracranial aneurysms or cervical artery dissections have been described.34

The presence of an intracranial aneurysm in a patient with cervical artery dissection is occasionally noted, but the frequency of this occurrence has not been established. The present study was undertaken to estimate the incidence of saccular intracranial aneurysms in patients with spontaneous dissection of the cervical arteries.

Clinical Material and Methods

All patients seen at the Mayo Clinic during the 20-year period between 1970 and 1989 with a diagnosis of spontaneous cervical artery dissection were identified, and their medical records were retrieved and reviewed. Their radiographic records were examined for the presence of an intracranial aneurysm and, when indicated and available, the angiograms were reviewed.

Of the 175 patients identified, 11 were excluded from the study: seven because only a single carotid artery was visualized during angiography and four others because only intravenous digital subtraction angiography had been performed. The study population therefore consisted of 164 patients. It was assumed that adequate visualization of the anterior cerebral circulation was assured in these patients, although their records did not always indicate this.

Results

Patient Population

The patient group included 91 (55.5%) females and 73 (44.5%) males with a mean age of 44.9 years. Age and sex distribution is shown in Fig. 1. Two vessels were visualized during angiography in 53 patients, three vessels in 67 patients, and four vessels in 44 patients. Dissection involved the internal carotid artery in 121 patients, the vertebral artery in 30 patients, and both the carotid and vertebral arteries in 13 patients. Multi-vessel arterial dissection was observed in 59 (36.0%) of the 164 patients: 45 (33.6%) of the 134 patients with internal carotid artery dissection and 27 (62.8%) of the 43 patients with vertebral artery dissection.
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Thirteen saccular intracranial aneurysms were found in nine (5.5%) patients (Table 1). This group consisted of eight women and one man; thus, saccular intracranial aneurysms were found in 8.8% of the female patients and in 1.4% of the male patients. The mean age of these nine patients was 44.4 years. Two (22.2%) had multivessel dissection.

Three women had a history of oral contraceptive use (Cases 5, 7, and 8) and one woman with uterine aplasia had received daily diethylstilbestrol for 16 years (Case 2). Four patients were current cigarette smokers (Cases 1, 5, 7, and 8), four had a history of migraine headaches (Cases 2, 5, 6, and 7), and three were hypertensive (Cases 1, 2, and 8). Mitral valve prolapse was diagnosed in two women (Cases 3 and 4). One woman suffered from multiple subclavian and renal artery aneurysms and pathologically confirmed fibromuscular dysplasia (Case 3).

**Evaluation and Treatment**

Three of four intracranial aneurysms were clipped in one patient (Case 6). Her basilar artery aneurysm and the intracranial aneurysms in all other patients (all < 7 mm in diameter) were left untreated. During an average follow-up period of 41 months (range 1 to 128 months), there has been no evidence of aneurysm rupture or other vascular events.

In addition to the intracranial aneurysms, the following incidental intracranial vascular anomalies were found in one patient each: arteriovenous malformation, cerebellar venous angioma, and dural arteriovenous malformation.

**Discussion**

**Frequency of Incidental Intracranial Aneurysms**

Numerous investigators have attempted to estimate the incidence of intracranial aneurysms in the general population by means of angiographic or autopsy studies. The results of these investigations have varied considerably. The more recent angiographic studies indicate an occurrence rate of 0.5% to 1%, 1,4,6 while autopsy studies disclose unruptured intracranial aneurysms of 0.5% to 5% of the population. 5,19,30,34 It is appropriate to compare the 5.5% incidence of saccular intracranial aneurysms in our study with that obtained from a recent study from our institution by Atkinson, et al., 1 that estimated the angiographic frequency of incidental intracranial aneurysms in a population with minimal bias toward the presence of an intracranial aneurysm. In that study, 287 anterior circulation angiograms were reviewed during a period of time in which the majority of the patients in this series were diagnosed. Intracranial aneurysms were detected in three patients for an incidence of 1.1%. The difference between the rates (5.5% vs. 1.1%) is statistically significant (Fisher's exact test; p < 0.0109). The true difference may be larger since the mean age of our patients as a group was lower (44.9 vs. 53 years) and adequate intracranial visualization was not always obtained in our series, primarily when the dissection had resulted in a significant stenosis or occlusion of the carotid artery. On the other hand, female patients were more common in our study (55.5% vs. 45.0%). The higher frequency of intracranial aneurysms in our patient population was due to the high incidence in the female patients, who harbored intracranial aneurysms in 8.8%; only 1.4% of the male patients were found to have an intracranial aneurysm, a figure similar to that reported by Atkinson, et al.

**Evidence for a Common Underlying Vasculopathy**

Various disorders affecting the extracellular matrix have been associated with both intracranial aneurysms and cervical artery dissections, including Ehlers-Danlos

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**TABLE 1**

*ICA = internal carotid artery; ACoA = anterior communicating artery; VA = vertebral artery; PCoA = posterior communicating artery; MCA = middle cerebral artery; BA = basilar artery.

<table>
<thead>
<tr>
<th>Case No.</th>
<th>Age (yrs)</th>
<th>Sex</th>
<th>Site of Dissection</th>
<th>Location &amp; Size of Aneurysm</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>43, M</td>
<td>Lt ICA</td>
<td>ACoA, &lt; 5 mm</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>40, F</td>
<td>rt ICA</td>
<td>Lt VA</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>44, F</td>
<td>rt ICA</td>
<td>Lt cavernous ICA, 5-6 mm</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>48, F</td>
<td>rt ICA</td>
<td>Lt supracerebral ICA, 2-3 mm</td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>47, F</td>
<td>Lt ICA</td>
<td>Lt cavernous ICA, &lt; 5 mm</td>
<td></td>
</tr>
<tr>
<td>6</td>
<td>50, F</td>
<td>Lt ICA</td>
<td>Lt supracerebral ICA, 22 mm</td>
<td></td>
</tr>
<tr>
<td>7</td>
<td>46, F</td>
<td>rt ICA</td>
<td>Lt supracerebral ICA, 3 mm</td>
<td></td>
</tr>
<tr>
<td>8</td>
<td>40, F</td>
<td>rt ICA</td>
<td>Lt PCoA, &lt; 5 mm</td>
<td></td>
</tr>
<tr>
<td>9</td>
<td>42, F</td>
<td>Lt VA</td>
<td>Lt supracerebral ICA, 3 mm</td>
<td></td>
</tr>
</tbody>
</table>

*An additional right-sided MCA aneurysm, measuring 2 mm in diameter, which had not been detected angiographically was found at surgery.
syndrome type IV, Marfan’s syndrome, \(^{2,7,37,39}\) and fibromuscular dysplasia. \(^{12,22,23,25-27}\) In our patients with both vascular disorders, there was no evidence of any of these or other generalized connective-tissue diseases that are characterized by dissection and aneurysm formation except in Case 3. This 44-year-old woman with mitral valve prolapse presented with symptomatic carotid artery dissection and was found to have multiple aneurysms. Pathological examination of a resected portion of subclavian artery revealed fibromuscular dysplasia.

Angiographic changes of fibromuscular dysplasia have been reported in approximately 15% of patients with spontaneous cervical artery dissection. \(^{12,22,23}\) George, et al., \(^{30}\) studied the cervical angiograms of 102 patients with ruptured intracranial aneurysms and observed arterial wall abnormalities compatible with fibromuscular dysplasia in 30% of the cases and with cervical artery dissection in 2%. However, the angiographic diagnosis of fibromuscular dysplasia may be quite challenging and other vasculopathies could mimic the angiographic appearance of fibromuscular dysplasia. \(^{24,35}\)

Abnormalities of collagen type III, one of the three major fibrillar collagens that constitutes approximately 40% of arterial walls, \(^{18}\) have been detected in a significant portion of patients with intracranial aneurysms. \(^{29,32}\) Similarly, collagen type III abnormalities have also been suggested to be involved in the pathogenesis of spontaneous cervical artery dissection. \(^{37}\) Studies are now underway to substantiate or refute this hypothesis.

Intracranial aneurysms were mainly observed in female patients with cervical artery dissections. The reason for this female preponderance is not apparent; however, inherited connective-tissue disorders and fibromuscular dysplasia are more frequently, but not exclusively, observed in women. Hormonal factors may have played a concomitant role in the pathogenesis of these vascular disorders.

Twenty-two percent of the nine patients with intracranial aneurysms had multivessel dissection compared to 36% of the total group of 164 patients. Although the number of cases is small, there does not appear to be a positive relationship between the number of vessels involved and the occurrence of intracranial aneurysms.

**Hemodynamic Considerations**

Although the increased frequency of intracranial aneurysms in the patients with dissection likely reflects the presence of an underlying vasculopathy, hemodynamic changes may have played an additional role in the development of the intracranial aneurysms. Patients who have undergone ligation of the cervical carotid artery, \(^{2,45}\) those with absence or hypoplasia of the carotid artery, \(^{15,44}\) and those with stenosis and occlusion of the carotid artery \(^{2}\) may have an increased chance of developing an intracranial aneurysm later in life, particularly an aneurysm of the anterior communicating or contralateral internal carotid artery. This is believed to be due to an increase in flow through the remaining patent arteries or to altered intracranial hemodynamics in general. An important role for a hemodynamic mechanism in the pathogenesis of the intracranial aneurysms in our patients seems unlikely since most of the angiograms showing the aneurysm were carried out within several months after the dissection, and hemodynamically significant stenoses or occlusions were observed in only a minority of patients. Furthermore, the aneurysms were located on the contralateral carotid artery in four of the eight patients with carotid artery dissection, on the ipsilateral carotid artery in three patients, and on the anterior communicating artery in one patient. Nevertheless, intracranial aneurysms may develop over a relatively short time \(^{12,45}\) and cervical artery dissections are dynamic lesions, the appearance of which may change considerably over a period of days or weeks. \(^{12,14,25}\) The one patient with posterior circulation dissections had bilateral vertebral artery involvement and bilateral internal carotid artery aneurysms.

**Aneurysm Characteristics**

The location of the intracranial aneurysms was unusual in that cavernous sinus aneurysms and those arising from the proximal supraclinoid/ophthalmic segment were overrepresented. These aneurysms were seen in seven of the nine patients and comprised 62% of the total number of aneurysms. In general, intracranial aneurysms at these locations are distinctly more common in women than men, but account for only 6% to 7% of all intracranial aneurysms. \(^{11,16}\) The reason for the preponderance of cavernous sinus and proximal supraclinoid aneurysms is a matter of speculation. It is of interest to note that intracranial aneurysms in patients with (suspected) connective-tissue disorders are frequently located in this particular region. \(^{6,7,9,13,21,33,36-39}\)

Of the 13 intracranial aneurysms in our study, six were less than 5 mm in diameter, four were between 5 and 10 mm, and three were between 10 and 25 mm. This is similar to the distribution in size of incidental intracranial aneurysms in general. \(^{42}\) The intracranial aneurysms were all saccular in nature and were not believed to be directly related to the dissection itself.

**Management**

The number of patients with intracranial aneurysms in addition to cervical artery dissection is small. However, since there is no evidence that intracranial aneurysms in these patients have a significantly different natural history from that of intracranial aneurysms in general, there is no apparent reason to manage these lesions differently. Much has been written about whether incidental intracranial aneurysms should be treated surgically \(^{36,42}\) and we shall not reiterate the arguments here. None of the intracranial aneurysms smaller than 7 mm was surgically treated in our series, while all of those larger than 10 mm (all in a single
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patient) were clipped. There has been no evidence of aneurysm rupture in any patient.

Theoretically, intracranial aneurysms distal to an occluded or pressure-significant stenotic cervical artery could increase in size following resolution of the dissected arterial segment secondary to a change in cervico-cerebral hemodynamics and increased intra-aneurysmal pressure. This should be taken into consideration as dissections frequently resolve spontaneously over a variable period of time, and follow-up monitoring with repeat arteriography or magnetic resonance angiography is indicated when the intracranial aneurysm is not initially considered for surgical treatment. This situation is comparable to that observed in patients with extracranial carotid artery disease and an ipsilateral incidental intracranial aneurysm who undergo carotid endarterectomy, except that in the case of dissection the time of resolution of the stenotic or occlusive lesion cannot be controlled. We have not had the opportunity to investigate the increased potential for aneurysm growth following resolution of a significantly stenotic or occluded dissection since none of the patients presented with this particular set of circumstances.

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References


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