High incidence of ICA anterior wall aneurysms in patients with an anomalous origin of the ophthalmic artery: possible relevance to the pathogenesis of aneurysm formation

Clinical article

MASAHIRO INDO, M.D.,1 SOICHI OYA, M.D., PH.D.,1 MICHIHIRO TANAKA, M.D., PH.D.,2 AND TORU MATSUI, M.D., D.M.Sc.1

1Department of Neurosurgery, Saitama Medical Center, Saitama Medical University, Saitama; and 2Department of Neurosurgery, Kameda Medical Center, Chiba, Japan

Object. Surgery for aneurysms at the anterior wall of the internal carotid artery (ICA), which are also referred to as ICA anterior wall aneurysms, is often challenging. A treatment strategy needs to be determined according to the pathology of the aneurysm—namely, whether the aneurysm is a saccular aneurysm with firm neck walls that would tolerate clipping or coiling, a dissecting aneurysm, or a blood blister–like aneurysm. However, it is not always possible to properly evaluate the condition of the aneurysm before surgery solely based on angiographic findings.

Methods. The authors focused on the location of the ophthalmic artery (OA) in determining the pathology of ICA anterior wall aneurysms. Between January 2006 and December 2012, diagnostic cerebral angiography, for any reason, was performed on 1643 ICAs in 855 patients at Saitama Medical Center. The authors also investigated the relationship between the origin of the OA and the incidence of ICA anterior wall aneurysms. The pathogenesis was also evaluated for each aneurysm based on findings from both angiography and open surgery to identify any correlation between the location where the OA originated and the conditions of the aneurysm walls.

Results. Among 1643 ICAs, 31 arteries (1.89%) were accompanied by an anomalous origin of the OA, including 26 OAs originating from the C3 portion, 3 originating from the C4 portion, and 2 originating from the anterior cerebral artery. The incidence of an anomalous origin of the OA had no relationship to age, sex, or side. Internal carotid artery anterior wall aneurysms were observed in 16 (0.97%) of 1643 ICAs. Female patients had a significantly higher risk of having ICA anterior wall aneurysms (p = 0.026). The risk of ICA anterior wall aneurysms formation was approximately 50 times higher in patients with an anomalous origin of the OA (25.8% [8 of 31]) than in those with a normal OA (0.5% [8 of 1612], p < 0.0001). Based on angiographic classifications, saccular aneurysms were significantly more common in patients with an anomalous origin of the OA than in those with a normal OA (p = 0.041). Ten of 16 patients with ICA anterior wall aneurysms underwent craniotomies. Based on the intraoperative findings, all 6 aneurysms with normal OAs were dissecting or blood blister–like aneurysms, not saccular aneurysms.

Conclusions. There was a close relationship between the location of the OA origin and the predisposition to ICA anterior wall aneurysms. Developmental failure of the OA and subsequent weakness of the vessel wall might account for this phenomenon, as previously reported regarding other aneurysms related to the anomalous development of parent arteries. The data also appear to indicate that ICA anterior wall aneurysms in patients with an anomalous origin of the OA tend to be saccular aneurysms with normal neck walls. These findings provide critical information in determining therapeutic strategies for ICA anterior wall aneurysms.

(http://thejns.org/doi/abs/10.3171/2013.9.JNS131030)

Key Words • internal carotid artery • cerebral aneurysm • ICA anterior wall aneurysm • ophthalmic artery • vascular disorders

Cerebral aneurysms at nonbranching sites of the internal carotid artery (ICA) are relatively rare, accounting for 0.9%–6.6% of all ICA aneurysms.39,46 Among these ICA aneurysms, those arising from the anterior wall of the ICA are the most common23 and have variously been referred to as dorsal wall,17,26,38,41 distal medial wall,46 superior wall,14 and ventral paraclinoid30 aneurysms. In the recent literature, the term “ICA anterior wall aneurysm” has been used frequently.8,18,20,25,28,43,47 Although the term “ICA anterior wall” specifically refers to the site of the aneurysm, it in fact involves various pathologies of an aneurysm, such as saccular aneurysms with normal neck walls, dissecting aneurysms, and blood blister–like aneurysms (BBAs). Treatment for ICA anterior wall aneurysms carries significant risk related to the difficulty of diagnosis,5 intraoperative rupture,5,15,31,42 and
postoperative ischemic complications caused by ICA stenosis or occlusion.23,25

While direct clipping is feasible in most cases of true berry aneurysms, which have firm vessel walls that tolerate clipping or coiling, BBAs and dissecting aneurysms frequently require more complicated surgical procedures, including clipping on wrapping materials,15,19,24 ICA trapping with or without a bypass,16,23,25,32 and endovascular treatment with a variety of advanced assisting techniques.9,22,34,47 Therefore, the pathogenesis of the aneurysm is obviously critical in determining the treatment strategy for ICA anterior wall aneurysms. Unfortunately, the preoperative information available regarding the wall conditions is very limited and unreliable. Although conventional angiography, CT angiography,10 and MRI13 are used to evaluate the pathology of ICA anterior wall aneurysms, it is not always possible to definitively determine the pathology of an aneurysm before surgery, as the angiographic finding of a saccular shape does not always correlate with the conditions of the aneurysm wall.31,32 In this study, we focused on the location of the ophthalmic artery (OA) in determining the pathology of ICA anterior wall aneurysms. We also investigated the relationship between the origin of the OA and the incidence of ICA anterior wall aneurysms.

Methods

This study was approved by the institutional review board at Saitama Medical Center. We conducted a retrospective review of the clinical records collected between January 2006 and December 2012 at Saitama Medical Center. We examined the results of all cerebral angiography studies performed during this period and collected data on each patient’s age, sex, side, reasons for angiography, clinical presentations, and pathologies of each aneurysm. Patients with moyamoya disease, severe stenosis, or occlusive lesions of the ICA were excluded from this study. Diagnosis of an ICA anterior wall aneurysm was defined as an aneurysm of any shape at the nonbranching anterior wall between the anterior clinoid and terminus of the ICA. Arteriosclerotic changes causing irregularity of the ICA lumen were cautiously excluded. We also carefully evaluated the origin of the OA. The OA normally originates from the supraclinoid portion of the ICA (Fig. 1A).21 However, we found other variations, such as OAs originating from the C3 segment of the ICA (Fig. 1B), OAs originating from the C4 segment (Fig. 1C), and OAs originating from the anterior cerebral artery (Fig. 1D). The quality of the angiogram was satisfactory for the diagnosis of ICA aneurysms in all cases, regardless of whether common carotid artery angiography or selective ICA angiography was performed.

Pearson’s chi-square test and Fisher exact test were used to compare the categorical variables. An unpaired Student t-test was used to analyze significant differences between the means of the continuous variables. A p value < 0.05 was considered significant.

Results

A summary of data is shown in Table 1. This study included 1643 ICAs in 855 patients (male/female ratio 337:518). The mean age of patients was 57.2 years (range 2–89 years). The numbers of right ICA and left ICA examined were 820 and 823, respectively. Angiography was performed in the evaluation of cerebrovascular disease (83.0% [710 of 855 patients]), brain tumor (16.4%), trauma (0.2%), and others (0.4%).

Among 1643 ICAs, an anomalous origin of the OA was found in 31 arteries (1.89%), including 26 OAs originating from the C3 portion, 3 OAs from the C4 portion, and 2 OAs from the anterior cerebral artery. There were no statistically significant differences in the mean age, sex, and side among patients with and without an anomalous origin (p = 0.82, 0.91, and 0.85, respectively). Internal carotid artery anterior wall aneurysms were found in 16 patients (0.97%, male/female ratio 2:14). The incidence of ICA anterior wall aneurysms was associated with sex (p = 0.026), with a higher incidence in females, but was not associated with age (p = 0.38) or side (p = 0.32). An ICA anterior wall aneurysm was found only in 0.5% of the I16 ICAs in patients with a normal OA (8 of 1626 vessels). On the other hand, an ICA anterior wall aneurysm was found in 8 (25.8%) of 31 ICAs in patients with an anomalous origin of the OA (p < 0.0001). The relative risk of aneurysm formation at this portion of the ICA was approximately 50 times higher for patients with an anomalous origin of the OA than those with a normal OA. The risk of ICA anterior wall aneurysm formation was the highest for women with an anomalous origin of the OA (31.6% [6 of 19 vessels]), while no men with normal OAs had an aneurysm at this site (0 of 639 vessels).

Next we focused on the pathology of these aneurysms. As shown in Table 2, when the OA originated from an anomalous location, aneurysms tended to take a saccular form, as indicated by angiography. In contrast, ICA anterior wall aneurysms without an anomalous origin of the OA were prone to having nonsaccular shapes, as indicated by angiography. This association was statistically significant (p = 0.04, Fisher exact test). We were able to directly confirm the pathogenesis of the aneurysm in 10 of 16 patients because they had undergone craniotomy (Table 3).
Ophthalmic artery and ICA anterior wall aneurysm

Intraoperative findings indicated that all 6 patients with a normal OA had nonsaccular aneurysms, although this did not reach statistical significance (p = 0.13).

Illustrative Cases

Case 1
This 51-year-old woman had a sudden onset of headache and was taken to our hospital. An emergency CT scan showed a thick subarachnoid hemorrhage (SAH) in the basal cistern (Fig. 2A). Cerebral angiograms showed an ICA anterior wall aneurysm and the OA originating from the cavernous C3 portion of the ICA (Fig. 2B). She underwent craniotomy and was found to have a ruptured saccular aneurysm with firm walls (Fig. 2C). Clipping was performed safely, preserving a good patency within the ICA.

Case 2
This 70-year-old woman with SAH (Fig. 3A) had been diagnosed with a ruptured ICA anterior wall aneurysm (Fig. 3B) and had a normal OA (Fig. 3C). Therefore, we suspected that the conditions of the walls of this aneurysm would not be suitable for ordinary clipping. We decided to perform a high-flow bypass using a radial artery graft in case of prolonged intraoperative ICA trapping or ICA sacrifice. Her aneurysm was intraoperatively confirmed to be a BBA with fragile walls (Fig. 3D). We were able to clip this aneurysm, with ICA stenosis safely managed by bypass flow via the radial artery graft.

Discussion

Relationship Between ICA Anterior Wall Aneurysm and a Developmental Anomaly of the OA

Our data showed that an anomalous origin of the OA was associated with an increased risk of the formation of ICA anterior wall aneurysms. The embryology of the OA has been described in detail by Padget through observations of sectioned embryos.33 Lasjaunias et al. revised the theory proposed by Padget to incorporate clinical observations in anomalous variations of the OA (Fig. 4). The OA begins to form when the crown-rump length is 4–8 mm.21 The primitive ophthalmic artery (POA) is formed by the fusion of the primitive ventral ophthalmic artery (PVOA) and the primitive dorsal ophthalmic artery (PDOA) in the orbit. Whereas the PVOA begins at the future anterior cerebral artery and passes through the optic canal, the PDOA originates from the cavernous portion and passes through the superior orbital fissure (SOF). The PVOA develops toward the retinal artery and nasal ciliary artery, whereas the PDOA grows toward the temporal ciliary artery.23 These arteries normally anastomose near the optic nerve in the orbit. Then, the PVOA fuses at its proximal portion with the supraclinoid portion of the intradural

---

**TABLE 1**: Summary of data in 855 patients with 1643 ICAs

<table>
<thead>
<tr>
<th>Characteristics (no. of ICAs)</th>
<th>ICA w/ Normal OA (n = 1612)</th>
<th>ICA w/ Anomalous Origin of OA (n = 31)</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>mean patient age in yrs</td>
<td>57.0</td>
<td>56.4</td>
<td>0.82</td>
</tr>
<tr>
<td>sex</td>
<td></td>
<td></td>
<td>0.91</td>
</tr>
<tr>
<td>male (n = 651)</td>
<td>639 (98.16%)</td>
<td>12 (1.84%)</td>
<td></td>
</tr>
<tr>
<td>female (n = 992)</td>
<td>973 (98.08%)</td>
<td>19 (1.92%)</td>
<td></td>
</tr>
<tr>
<td>side</td>
<td></td>
<td></td>
<td>0.85</td>
</tr>
<tr>
<td>right (n = 820)</td>
<td>804 (98.05%)</td>
<td>16 (1.95%)</td>
<td></td>
</tr>
<tr>
<td>left (n = 823)</td>
<td>808 (98.18%)</td>
<td>15 (1.82%)</td>
<td></td>
</tr>
<tr>
<td>diseases</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CVD (n = 1359)</td>
<td>1331</td>
<td>28</td>
<td></td>
</tr>
<tr>
<td>tumor (n = 275)</td>
<td>272</td>
<td>3</td>
<td></td>
</tr>
<tr>
<td>trauma (n = 3)</td>
<td>3</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>others (n = 6)</td>
<td>6</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>ICA anterior wall aneurysm</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>yes (n = 16)</td>
<td>8 (0.5%)</td>
<td>8 (25.8%)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>no (n = 1627)</td>
<td>1604 (99.5%)</td>
<td>23 (74.2%)</td>
<td></td>
</tr>
</tbody>
</table>

* CVD = cerebrovascular disease.

**TABLE 2**: Association between the shape of an aneurysm and an anomalous origin of the OA in 16 cases

<table>
<thead>
<tr>
<th>Origin of OA</th>
<th>Saccular Shape</th>
<th>Nonsaccular Shape</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>normal</td>
<td>1</td>
<td>7</td>
<td>0.041</td>
</tr>
<tr>
<td>anomalous</td>
<td>6</td>
<td>2</td>
<td></td>
</tr>
</tbody>
</table>

**TABLE 3**: Association between the intraoperative findings and an anomalous origin of the OA in 10 cases

<table>
<thead>
<tr>
<th>Origin of OA</th>
<th>Saccular Aneurysm w/ Firm Walls</th>
<th>BBA or Dissecting Aneurysm</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>normal</td>
<td>0</td>
<td>6</td>
<td>0.13</td>
</tr>
<tr>
<td>anomalous</td>
<td>2</td>
<td>2</td>
<td></td>
</tr>
</tbody>
</table>
ICA near the optic canal, and the continuation from the anterior cerebral artery regresses to give rise to the OA. Meanwhile, the PDOA regresses near the SOF, resulting in the formation of the trigeminal nerve at the SOF, the foramen rotundum, and the roof of the cavernous sinus.

Anomalous origins can result from anomalies in development, annexation, or disappearance of embryonic OAs and the orbital branch of the stapedial artery. Examples of these variants include the OA originating from the anterior cerebral artery, the cavernous portion, the middle meningeal artery, or the basilar artery. The incidence of an anomalous origin of the OA was 1.89% in this study. The previous literature indicates that 83% of OAs arose from within the subarachnoid space after the ICA had emerged from the cavernous sinus.

We found ICA anterior wall aneurysms in approximately 25% of ICAs from patients with an anomalous origin of the OA, whereas they were found in only 0.5% of ICAs from patients with a normal OA. This higher frequency of ICA anterior wall aneurysms in ICAs from patients with an anomalous origin of the OA may be due to a failed fusion of the primitive OA in the early embryogenesis, which might cause a congenital weakness of the anterior wall of the ICA. Such a congenital weakness has been well documented in aneurysms associated with arterial fenestrations in the middle cerebral artery or vertebrobasilar artery.

Recent extensive investigations about the natural history of unruptured intracranial aneurysms revealed that the location of the aneurysm affects the risk of rupture. Since none of the 31 patients with an anomalous origin of the OA underwent repeated angiography at an interval longer than 1 year in our study, we could not draw conclusions regarding the potential benefits of setting up a specific follow-up for patients with an anomalous origin of the OA. Based on our results, however, it might be valuable to plan more cautious follow-ups for patients with anomalous origins of the OA.

**Possible Usefulness in Determining the Surgical Strategy**

Regarding surgical strategies, ICA anterior wall aneurysms are often difficult to treat by either direct clipping or endovascular treatment. Although information on the pathogenesis of aneurysms is critical to determine the treatment strategy, evaluating the conditions of the aneurysm walls may be difficult because preoperative angiograms can show aneurysms to have various morphologies. True saccular aneurysms with firm wall structures are usually amenable to both conventional clipping and coil embolization during the acute phase of SAH. However, some saccular-shaped aneurysms may actually be BBAs with fragile walls, as shown in Case 2. In addi-
Ophthalmic artery and ICA anterior wall aneurysm

Fig. 4. Schematic drawings showing the development of the OA and our hypothesis. A: The PVOA and PDOA supply the orbit. B: Initially, the PVOA and PDOA anastomose in the orbit. C: Then the PVOA fuses at its proximal portion with the supraciliary portion of the intradural ICA near the optic canal. The continuation from the anterior cerebral artery regresses, resulting in the formation of a POA. D: We hypothesize that this failure of fusion might cause the fragility of the vessel wall at the portion where it is supposed to accommodate the PVOA, leading to a predisposition toward ICA anterior wall aneurysms. ILT = inferolateral trunk; OC = optic canal. Copyright Masahiro Indo. Published with permission.

tion, the conditions of the aneurysm wall should be carefully evaluated for endovascular treatment to minimize the risk of intraoperative complications and to prevent re-growth and rebleeding in the long term.13 However, there is no definitive method to correctly judge the conditions of the aneurysm wall without performing a craniotomy, and thus determining the appropriate surgical strategy for ICA anterior wall aneurysms may be difficult. Although MRI is valuable in assessing the conditions of the aneurysm wall,13 it might be difficult to obtain MR images during the acute phases of hemorrhage. Our findings regarding the correlation between the location of the OA and the pathogenesis of the aneurysm might provide useful information for determining the conditions of the aneurysm wall, if this information is effectively combined with other radiological examinations.

Conclusions

Based on our data, ICA anterior wall aneurysms are found approximately 50 times more frequently in patients with an anomalous origin of the OA than in those with normal OAs. Our study also suggests that a correlation may exist between the location of the OA and the pathogenesis of ICA anterior wall aneurysms. Although the accumulation of more data based on intraoperative findings and pathological investigations is necessary to establish a definitive relationship between the origin of the OA and the condition of aneurysm walls, the results of this study might contribute to the decision-making process in the treatment of ICA anterior wall aneurysms and the follow-up strategy for patients with abnormal origins of the OA.

Disclosure

The authors report no conflict of interest concerning the materials or methods used in this study or the findings specified in this paper.

Author contributions to the study and manuscript preparation include the following. Conception and design: Indo. Acquisition of data: Indo. Analysis and interpretation of data: Oya, Indo. Drafting of the article: Indo. Critically revising the article: all authors. Reviewed submitted version of manuscript: all authors. Approved the final version of the manuscript on behalf of all authors: Oya. Statistical analysis: Oya. Administrative/technical/material support: Oya, Matsui. Study supervision: Tanaka, Matsui.

References


Manuscript submitted May 18, 2013. Accepted September 23, 2013.

Please include this information when citing this paper: published online November 1, 2013; DOI: 10.3171/2013.9.JNS131030.

Address correspondence to: Soichi Oya, M.D., Ph.D., Department of Neurosurgery, Saitama Medical Center, 1981 Kamoda, Kawagoe, Saitama 350-8550, Japan. email: sooya-tky@umin.ac.jp.