De novo Aneurysms. How to manage?

Aneurismas de novo. Diagnóstico e tratamento

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RESUMO

Introdução: Pacientes submetidos a craniotomia e clipagem de aneurismas supostamente são dados como curados. Nós relatamos dois casos com cirurgia prévia para aneurisma roto que se apresentaram 10 e 14 anos após com aneurismas de novo.

Métodos: Foram revisados os prontuários de 39 pacientes submetidos a clipagem de 52 aneurismas intracranianos por um único cirurgião em uma única instituição entre julho de 1999 a junho de 2003. Foi realizada busca na literatura de língua inglesa publicada entre 1964 e 2003 sobre aneurismas de novo.

Resultados: Duas pacientes do sexo feminino, entre 39 do total (5%) foram identificadas como portadoras de aneurismas de novo. A idade média foi de 47 anos: sendo uma delas como novo episódio de hemorragia subaracnóide. Ambas apresentavam aneurismas múltiplos de menos de 6 mm. Na literatura revisada, encontramos 77 casos de aneurismas de novo, sendo 81% com manifestação de rotura. A idade de apresentação inicial foi de 42,2 anos com interval médio entre este diagnóstico e o diagnóstico de aneurisma de novo de 9,2 anos. A relação pacientes femininos e masculinos foi de 2:1. Aneurismas múltiplos foram encontrados em 17 (22%) e 16 (21%) dos pacientes na apresentação inicial e na apresentação de novo, respectivamente.

Conclusão: Pacientes submetidos a craniotomia e clipagem de aneurismas em idade jovem podem se beneficiar de exames de imagem por até 20 anos, especialmente através de angiotomografia helicoidal com reconstrução 3D, por suas características não-invasivas, face a possibilidade do surgimento de aneurismas de novo.

Palavras Chave: aneurisma, aneurisma de novo, hemorragia sub-aracnóide

ABSTRACT

Introduction: Patients who have undergone craniotomy and clipping of an aneurysm are believed to be cured. We report two cases with previous ruptured aneurysms who presented 10 and 14 years later with de novo aneurysms.

Methods: The charts of 39 patients who underwent craniotomy and clipping of 52 intracranial aneurysms by a single surgeon at a single institution from July 1999 to June 2003 were reviewed. Medline search for published English literature on de novo aneurysms was conducted from 1964 to 2003.

Results: Two female patients out of 39 (5%) were found to have de novo aneurysms in our series. Mean age was 47. One patient presented again with SAH. Both were found to have multiple aneurysms less than 6 mm in size. There are 77 cases of de novo aneurysms in the English literature. Sixty-two (81%) patients presented with ruptured de novo aneurysm. The mean age of initial aneurysm presentation was 42.2 years, with average time interval between this and diagnosis of de novo aneurysm formation was 9.2 years. The female to male ratio is 2:1. Multiple aneurysms were found in 17 (22%) and 16 (21%) patients in the initial presentation and the de novo presentation respectively.

Conclusions: Patients who undergo craniotomy and aneurysm clipping at an early age may benefit from follow up imaging studies for up to 20 years. Helicoidal CT angiogram with 3D reconstruction will allow for non-invasive follow up.

Keywords: aneurysm, de novo aneurysm, subarachnoid hemorrhage
INTRODUCTION

De novo aneurysms are defined as aneurysms not seen in a previous high definition imaging study of the Circle of Willis such as a four vessel cerebral angiogram or a CT angiogram with three-D reconstruction. It was first reported in 1964 by Graf and Hamby, and has been described associated with occlusion of major vessels supporting the hemodynamic theory (22) and without any changes in the blood flow of the parent vessel (1,3,5,6,8-11,15,16,17,18,20-27,29,30,31,32,33,35,36,38,39).

Though the exact mechanism is unknown, intracranial aneurysms are believed to be due to either or both congenital defects or acquired degenerative changes due to hemodynamic stress of the arterial wall. Forbus in 1930, described that aneurysms are acquired lesions that result from a combination of focal weakness in the vessel wall due to congenital muscularis defect, and degeneration of the elastic membrane due to continue overstretching. Crompton found medial defects, intimal cushions, and changes in the internal elastic in cerebral arterial forks at birth. Also, reported that these lesions increased in size and number with increasing age. Stehbens suggested that aneurysms are acquired lesions due to a combination of absence of media and hemodynamic stress upon the relatively unsupported arterial bifurcations of the cerebral arteries which are prone to degenerate due to their thin walls and lack of external elastic lamina (34).

Several risk factors have been reported to be related to aneurysm formation, which include smoking, hypertension, and the female sex (30,34).

Incidence

De novo aneurysms are rare. There have been twenty-eight reports, which include eighty-five cases of de novo aneurysms following a previous aneurysm clipping around the world in the English literature since 1964 (1,3,5,6,8-11,15,16,17,18,20-27,29,30,31,32,33,35,36,38,39). Patients with carotid ligation or hereditary disorders linked to aneurysm occurrence were excluded. David reported and incidence of 1.8 percent per year (5). In our personal series we have seen an incidence of 2 percent (7).

Few angiographic follow up studies on patients with intracranial aneurysms investigated the formation of De novo aneurysms (5, 12, 13, 37) (Table 1). The rate of formation ranges from 0.84 to 2.2 percent per year. Two studies were carried on patients who harbored unruptured aneurysms (12, 13), while the other two studies investigated patients with clipped cerebral aneurysms (5, 37). Juvela (14) explained the rate of aneurysm formation was lower in their second study (0.84 percent/year compared to 2.2 percent/year), as the follow-up was not restricted to a high risk population. Miller et al. (24) found the annual incidence to be 1% for known aneurysm patients. They suggested the true incidence may be higher, as some patients die before diagnosis.

Table 1: Review of the Literature of Angiographic Follow-Up Studies of Intracranial Aneurysms

<table>
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<tr>
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</thead>
<tbody>
<tr>
<td>Patient Group</td>
<td>Unruptured Aneurysms</td>
<td>Clipped Aneurysms</td>
<td>Unruptured Aneurysms</td>
<td>Clipped Aneurysms</td>
</tr>
<tr>
<td>No. of Patients in Study</td>
<td>31</td>
<td>102</td>
<td>89</td>
<td>112</td>
</tr>
<tr>
<td>Mean Follow-Up (years)</td>
<td>9.0</td>
<td>4.4</td>
<td>20.1</td>
<td>9.0</td>
</tr>
<tr>
<td>No. of Patients with De Novo Aneurysms</td>
<td>6</td>
<td>6</td>
<td>15</td>
<td>9</td>
</tr>
<tr>
<td>No. of De Novo Aneurysms</td>
<td>7</td>
<td>8</td>
<td>19</td>
<td>10</td>
</tr>
<tr>
<td>Rate of Formation (%/year)</td>
<td>2.2</td>
<td>1.8</td>
<td>0.84</td>
<td>0.89</td>
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</table>

Sex Distribution

The female to male ratio for De novo aneurysms is 2:1, which is comparable to literature reporting female preponderance for intracranial aneurysms (34). Women are believed to be at increased risk for aneurysm formation, and the mechanism is believed to be due to decreased collagen content of cerebral vessels secondary to estrogen deficiency of menopause (19).

Ethnicity

De novo aneurysms had been reported in multiple races. They are though reported more frequently in the Japanese population. They compromise 51 percent of the De novo aneurysms reported in the literature. Second in frequency is the Finnish population. This is similar to the incidence seen for sporadic subarachnoid hemorrhage (28). Additionally, the age at aneurysm rupture for their first episode of sub arachnoid
hemorrhage in the Japanese population were 15 to 21 years older compared to other population groups (Table 2).

**Table 2: Summary of De Novo Aneurysm Patients by Population Group**

<table>
<thead>
<tr>
<th>Population Group</th>
<th>Mean Age Years</th>
<th>Mean Time Interval Years</th>
<th>F:M Ratio</th>
<th>Multiple Aneurysms No. of Patients (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Finland N=10</td>
<td>34.2</td>
<td>17.2</td>
<td>4.0:1.0</td>
<td>First Presentation: 3 (30) De Novo Presentation: 0 (0)</td>
</tr>
<tr>
<td>Japan N=39</td>
<td>51.0</td>
<td>8.6</td>
<td>1.4:1.0</td>
<td>First Presentation: 9 (23) De Novo Presentation: 3 (8)</td>
</tr>
<tr>
<td>US and Canada N=13</td>
<td>36.1</td>
<td>6.4</td>
<td>5.5:1.0</td>
<td>First Presentation: 1 (8) De Novo Presentation: 7 (54)</td>
</tr>
<tr>
<td>*All other Cases N=15</td>
<td>30.0</td>
<td>8.2</td>
<td>1.5:1.0</td>
<td>First Presentation: 4 (27) De Novo Presentation: 6 (40)</td>
</tr>
</tbody>
</table>

*Cases from Australia, Austria, Brazil ’4, Germany, Holland ’2, Italy, Poland ’2, Scotland, UK ’2

**Size**

Although this is a very small group of patients, the size of the de novo aneurysms were reported in only 8 cases with an average of 6.2 mm.

We suggest that treatment of this group of patients may be necessary even at small size due to its high incidence of rupture.

**Location**

The most common location for the aneurysms in this group of patients was the middle cerebral artery and posterior communicating artery (Table 3). The frequency of the anterior communicating artery aneurysms was found to be 13 and 12 percent for the sporadic presentation and the De novo presentation respectively. This is significantly less frequent than the conventional anterior communicating artery aneurysm, which is reported around 30 percent (28). The location of the De novo aneurysm with respect to the original aneurysm was also evaluated. De novo aneurysms located in the contralateral circulation exclusively were found in 25 percent, and in the ipsilateral circulation exclusively in 26 percent. The remaining patients had their aneurysms bilaterally or in anterior or posterior circulations.

**Table 3: Location of Aneurysm**

<table>
<thead>
<tr>
<th>No. of Aneurysms (%)</th>
<th>*Location</th>
<th>First presentation N=96</th>
<th>De Novo Presentation N=101</th>
<th>**Rees et al. (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>MCA</td>
<td>30 (31)</td>
<td>31 (31)</td>
<td>20-25</td>
<td></td>
</tr>
<tr>
<td>ACoA/ACA</td>
<td>18 (19)</td>
<td>19 (19)</td>
<td>35-40</td>
<td></td>
</tr>
<tr>
<td>PCoA/ICA</td>
<td>41 (43)</td>
<td>36 (36)</td>
<td>30</td>
<td></td>
</tr>
<tr>
<td>Basilar</td>
<td>3 (3)</td>
<td>9 (9)</td>
<td>10</td>
<td></td>
</tr>
</tbody>
</table>

*MCA- middle cerebral artery; ACoA- anterior communicating artery; ACA- anterior cerebral artery; PCoA- posterior communicating artery; ICA- internal carotid artery. **Literature reported sites of cerebral aneurysms

**Multiple Aneurysms**

Multiple aneurysms are seen in 22 and 21 percent at the time of the sporadic subarachnoid hemorrhage and at the De novo presentation respectively. Multiple aneurysms in both presentations are seen in 29 percent. This is similar to the incidence described for multiple intracranial aneurysms of 20 to 30 percent (28). Therefore, we agree with Miller, et al (24) that multiple aneurysms are not a risk factor for the novo aneurysm formation.

**Mirror Aneurysms**

The incidence of mirror aneurysm at the sporadic subarachnoid hemorrhage is of 26 percent in this group of patients. It is most common in the middle cerebral artery, followed by the internal carotid artery, and the posterior communicating artery. In our personal experience (7), we found mirror aneurysms in both cases of De novo aneurysms. Alphen et al. (1) suggested the phenomenon of mirror aneurysms makes it likely that an inborn weakness of the vessel wall is one of the underlying causes. Recent studies by Casimiro et al. (4) investigated mirror aneurysms in patients with multiple aneurysms. They concluded that these patients have a strong congenital predisposition to vessel wall weakness, which promotes early rupture (<40 years) even in the absence of other risk factors. They found smoking followed by hypertension to be the most dangerous risk factors for promoting rupture later in life when combined with the proposed congenital predisposition. There was inadequate evidence to analyze smoking and hypertension in the de novo population.
Clinical Presentation

81 percent of patients with De novo aneurysm present with a new subarachnoid hemorrhage. Development of cranial nerve palsies are seen in 8 percent. De novo aneurysms were found by follow-up angiogram in 13 percent. The majority of De novo aneurysm patients (90 percent) had a history of previous subarachnoid hemorrhage. The fact that 89 percent of these group of patients have its De novo aneurysm either ruptured or showed signs of growth suggest that the risk of De novo aneurysm rupture is much higher than the newly diagnosed unrupture aneurysms, or than the group of patients with a known aneurysm with history of previous SAH reported in the International Study of Unruptured Intracranial Aneurysms Investigators (USIA) study (12, 13).

Age at Sporadic Aneurysm Rupture

Patients with documented De novo aneurysm had their first subarachnoid hemorrhage at an early age: 42.2 years (range 12-73 years). With 56 percent of them presenting between the ages 15-45 years (c2, P<0.005). These results are significantly lower than the reported peak age group of 55 to 60 years for sporadic aneurismal subarachnoid hemorrhage or the 20 percent incidence of aneurysm rupture in the younger adults aged 15 to 45 years (2). It is also a younger age of rupture than the familiar cases were by 50 years of age 70 percent have suffered hemorrhages. These findings support the idea this may be a different group of patients and that aneurismal subarachnoid hemorrhage at an early age may be a risk factor for De novo aneurysm formation. One explanation for this is that these patients live long enough for their cumulative risk for De novo aneurysm formation and rupture to be significant.

Time Interval for Diagnosis

The average time interval between the sporadic subarachnoid hemorrhage and diagnosis of De novo aneurysm formation was 9.2 years with 75 percent of patients presenting by 12.5 years. Although long follow up of patients with clipped aneurysm is not recommended, perhaps long follow up of this specific subset of patients may be necessary. Histogram plot of time interval data suggests the risk of de novo aneurysm presentation is low after 20 years (Figure 1).

Treatment

Due to the high incidence of aneurysm rupture, De novo aneurysms should be treated once diagnosed. The choice of treatment (coiling or clipping) will depend on many factors. Factors that may favor craniotomy and clipping include an aneurysm less than 2-3 mm, unfavorable neck/dome ratio, tortuosity of parent vessels, younger patients (< 50 years of age) and history of hypercoagulability. The experience of the neurosurgeon in either technique or the endovascular surgeon will also play a role.

The surgical approach to this aneurysm will depend on location of aneurysm and parent vessel. Typically the previous clip does not play a role since De novo aneurysm would be in a different location or a different side.

CASE EXAMPLE

Patient 1

A 46-year-old Caucasian smoker female presented to the emergency room with worse headache of her life. Computed tomography (CT) of the head was positive for diffuse subarachnoid hemorrhage (SAH). Four-vessel cerebral angiography showed a large irregular right middle cerebral artery trifurcation aneurysm, and a small left internal carotid artery bifurcation aneurysm. It was felt that the middle cerebral artery aneurysm was the ruptured aneurysm and subsequently underwent a right pterional craniotomy and clipping. Postoperative angiogram showed complete aneurysm obliteration.

The patient was again admitted 3 months later for an elective left pterional craniotomy and clipping of her left internal carotid artery aneurysm. Postoperative angiogram showed complete obliteration of her aneurysm.
Ten years later she returned to the emergency room because of severe headaches. She had being assaulted ten days ago and sustained a rib fracture. Head CT was negative. Due to the severity of the headache (10/10) and with the history of previous spontaneous SAH the patient underwent a lumbar puncture which was traumatic. A four-vessel cerebral angiogram revealed the presence of a 2 mm aneurysm on the anterior communicating artery and a 3 mm aneurysm on the left middle cerebral artery (Fig. 2). Both aneurysms were not seen in the original pre-operative cerebral angiogram or in the two post-operative angiograms 10 years ago. Patient subsequently underwent a left pterional craniotomy and clipping of both aneurysms. Her postoperative angiogram showed complete aneurysm obliteration (Fig. 3). Three years later the patient remains neurologically intact.

Patient 2

A 48-year-old Native American female presented at a different institution with a sudden onset worst headache of her life. She was found to have subarachnoid hemorrhage on a head CT and a ruptured right posterior communicating artery aneurysm on a four vessel cerebral angiogram. Patient underwent craniotomy and clipping. Postoperative angiogram showed no evidence of a residual aneurysm in this region, but a possible 3mm aneurysm of the right middle cerebral artery. Follow-up four vessel cerebral angiogram one year later did not showed any aneurysm.

Fourteen years later the patient presented with intraventricular hemorrhage, SAH, hydrocephalus, and a right sided craniotomy defect (Fig. 4). Patient had been complaining of a one-day history of severe headaches, which was followed by loss of consciousness.

Patient had a ventriculostomy placed in the emergency room and a subsequent four-vessel cerebral angiogram revealed a 2 mm aneurysm of the anterior communicating artery, 4 mm aneurysm on the left posterior communicating artery, and a 2 mm aneurysm of the left anterior choroidal artery (Fig. 5). A clip in the region of the right posterior communicating artery was also identified. It was felt that the anterior communicating artery aneurysm was the ruptured one and since there were two more aneurysms on the left side a left pterional craniotomy was performed with clipping of all three aneurysms. Postoperative angiography day showed complete obliteration of all three
aneurysms (Fig. 6). At six months follow-up the patient was found to be grade 2 of the modified Rankin outcome scale.

Figure 6: Postoperative anteroposterior cerebral angiogram showing complete aneurysm obliteration with new clips on ACoA, left PCoA, and left AchoA

**CONCLUSION**

Patients with De novo aneurysms present with subarachnoid hemorrhage at an early age (median: 42 years), although this is a small group of patients, these findings suggest that young patients with a history of spontaneous subarachnoid hemorrhage due to an aneurysm rupture may benefit from long-term follow up. New helicoidal CTA with 3D reconstructions allows non-invasively follow up of this group of patients.

Since the high incidence of De novo aneurysm rupture (81 percent) at an average of 9.2 years after first subarachnoid hemorrhage, it is recommended to treat those patients when diagnosed even at a small size. The choices of treatment, either clipping and/or endovascular coiling should be considered.

**REFERENCES**