Title:
Delayed rupture of a basilar artery aneurysm treated with coils: case report and review of the literature.

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Running head: Delayed Rupture of Saccular Coil-Packed Aneurysm

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Delayed rupture of a basilar artery aneurysm treated with coils: case report and review of the literature.

Summary
Delayed rupture of a previously unruptured cerebral aneurysm after uneventful saccular coil packing is rare singularly when the quality of aneurysm occlusion is appropriate (neck remnant or total occlusion). The present report describes a case of a 70-year-old woman with incidentally detected asymptomatic small basilar tip non-thrombosed aneurysm who experienced rupture of the aneurysm 2 years after coiling. Cerebral angiography taken on the day of rupture revealed only small recanalization of the aneurysmal neck without dome filling. This is the first report of delayed rupture due to the minor recurrence of a previously unruptured small asymptomatic cerebral aneurysm after saccular coil packing. A literature review of 26 reports of late bleeding after coil embolization of previously unruptured cerebral aneurysms is provided, showing that dome filling after coil embolization, symptomatic aneurysms and large/giant aneurysms all increase the risk of delayed rupture in saccular coil-packed, previously unruptured aneurysms.

Introduction
The efficacy of endovascular coil embolization in the management of unruptured cerebral aneurysm has been characterized in several large studies [1, 2]. Delayed rupture of a previously unruptured cerebral aneurysm after uneventful saccular coil packing is very rare [3, 4].

Case Report
A 70-year-old woman was incidentally diagnosed with asymptomatic basilar tip aneurysm on magnetic resonance imaging (Fig. 1) and magnetic resonance angiography (MRA). Her history was notable for hypertension, hyperlipidemia, and coronary artery disease (treated with aspirin 100 mg daily) but she had no history of subarachnoid hemorrhage. Transarterial coil embolization for this unruptured basilar tip aneurysm (diameter, 7.4 mm) (Fig. 2A, B, C, D), was performed, and 95% neck remnant occlusion of the aneurysm was achieved using a balloon neck remodeling technique (Fig. 2E). Computed tomography taken on the next day showed no subarachnoid hemorrhage (Fig. 3).
MRA taken 6 months after the first intervention revealed complete obliteration of the aneurysm (Fig. 4). MRA taken 18 months after the first intervention showed small recanalization at the neck of the aneurysm (Fig. 5).
Twenty-two months after the initial treatment, the patient presented with subarachnoid hemorrhage (Hunt and Hess grade 3, Fischer group 3) (Fig. 6A). Cerebral angiography demonstrated a small recurrence at the level of the neck of the basilar tip aneurysm without any other intracranial aneurysm (Fig. 6B, C, D). On the day of onset, transarterial coil embolization was performed using a balloon neck remodeling technique.
During the chronic phase of subarachnoid hemorrhage, endovascular treatment was performed using a stent-assisted coil embolization technique, deploying two Enterprise stents (Cordis Neurovascular, Miami, FL, USA) in a Y-configuration and depositing coils through the stents’ mesh (Fig. 6E). Triple antiplatelet therapy, using aspirin 100 mg daily, cilostazol 200 mg daily, and ozaqrel 160 mg daily, was maintained during the perioperative period of stent-assisted coiling. The patient experienced neurologic recovery to a modified Rankin Scale score of 1.

**Discussion**

**Delayed rupture after saccular coiling**

Within the published literature, there are 26 reports of late bleeding after coil embolization of previously unruptured aneurysms [5-21] (Table 1). Ten were symptomatic and only one was asymptomatic at the time of initial presentation. In the other 15 cases, the presence or absence of symptoms was not reported. However, two of these 15 cases developed new compressive symptoms in the postoperative follow-up period prior to rupture of the aneurysm. Symptomatic aneurysms, which suggest recent growth and wall instability [22], could be associated with an increased risk of delayed rupture.

Sixteen delayed ruptures occurred in large and giant aneurysms while only two were associated with small aneurysms. A high aspect ratio (dome high to neck ratio) correlates with aneurysm rupture [23]. Large and giant aneurysms tend to have a high aspect ratio and should therefore receive particular attention, even after coiling.

All reported cases of delayed rupture of previously unruptured aneurysms after saccular coil packing occurred in aneurysms with dome filling (residual aneurysm) [24, 25]. Seventeen of 26 aneurysms were incompletely occluded (residual aneurysm) at the time of initial embolization. Three aneurysms were occluded subtotally (residual neck) at the time of initial embolization; however, coil compaction and dome filling of the aneurysm were revealed on follow up cerebral angiography. There is no description regarding the degree of occlusion in the other six cases. No cases (except for the present case) ruptured without dome filling. Rupture occurs preferentially at the site of the aneurysm dome [23]; therefore, completely occluded or neck remnant occluded aneurysm for the prevention of aneurysm rupture is considered to be relatively safe.

**Delayed rupture after flow-diversion treatment**

Flow diverters are increasingly used for the treatment of wide-necked cerebral aneurysms. Delayed rupture of the treated unruptured aneurysm after flow diverter implantation has also been reported in some studies [26]. The mechanisms of delayed ruptures after flow-diversion treatment are probably different from those after saccular coiling. In our review of the literature, the delay between saccular coiling and rupture varied from 4 hours to 7 years. Most ruptures (18 of 20) occurred later than 3 months after the embolization (Table 1). By contrast, Kulcsar et al. [22] reported that delayed rupture after flow-diversion treatment had occurred more frequently within 3 months after the treatment [10 early (< 3 months) ruptures and three late (3-5 months) ruptures among the 13 delayed rupture cases reported in patients with previously unruptured cerebral aneurysm
treated using flow diverter]. Implantation of flow diverter caused significant flow changes around the aneurysm; however, inflow jets were still present immediately after treatment in most patients with delayed rupture [22]. Computational flow dynamics analysis of cerebral aneurysms that ruptured after employment of flow-diversion revealed that placement of a flow diverter could increase the intraaneurysmal pressure and thereby potentially cause the rupture of the aneurysm [27]. Potential mechanisms of delayed rupture may involve post-flow-diversion thrombosis of the aneurysm sac. Thrombosis of the sac can activate an inflammatory reaction at the aneurysmal wall, which may result in weakening cerebral aneurysms [28], even though thrombus formation is the first step leading to permanent aneurysm repair through cicatrization and reverse remodeling of the vessel wall. Dual antiplatelet therapy after flow-diversion treatment might also play a role in delayed rupture. Most patients treated with flow diverters were still receiving both aspirin and clopidogrel at the time of the rupture [22].

**Treatment of recanalized aneurysms**

This is the first report of delayed rupture due to minor recurrence of a previously unruptured small asymptomatic cerebral aneurysm after saccular coil packing. The present case indicates that while the risk of bleeding from minor recurrence of a saccular coil-packed previously unruptured cerebral aneurysm is far less than that for a previously ruptured cerebral aneurysm [12], bleeding can still occur. Therefore, re-operation should be considered when recurrence of the aneurysm is detected.

Several treatment strategies can be used for re-operation of recurred aneurysms, including balloon neck remodeling, stent-assisted coiling, and flow diverters; however, treatment may be difficult in cases with anatomically complex aneurysms, including small recurrence and/or wide neck. The balloon neck remodeling technique has equivalent safety and achieves better occlusion when compared with the standard coiling technique [29]; therefore, wide use of the remodeling technique can be proposed not only for recanalized unruptured aneurysms, but for ruptured/reruptured aneurysms as well. The stent-assisted coil embolization is also a helpful technique for re-embolization of minor recurrence in a wide-necked aneurysm [30] and was used to achieve total occlusion in the present case. However, aneurysm stent placement is associated with a higher mortality when compared with coiling with or without balloon neck remodeling [20]. Accordingly, wider use of stents is probably not recommended [29]. A flow diverter is another option for the initial treatment and re-treatment of anatomically complex aneurysms; however, treatment using flow diverters can be difficult in the context of dual antiplatelet therapy, particularly for ruptured/reruptured aneurysms.

**Conclusions**

The risk of bleeding from minor recurrence of a saccular coil-packed, previously unruptured cerebral aneurysm is very low. Dome filling after coil embolization, symptomatic aneurysms and large/giant aneurysms all increase the risk of delayed rupture in saccular coil-packed, previously unruptured aneurysms, usually occurring more than 3 months after the coil embolization.
Acknowledgments

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Conflict of Interest

No potential conflict of interest relevant to this article was reported.

References

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Fig. 1  Brain MRI T1- and T2-weighted images taken before the initial embolization. Basilar tip aneurysm is seen without thrombus or peri-aneurysmal edema.
Fig. 2  A, B, C, D. Pre-operative 3-dimensional digital subtraction angiography (A: antero-posterior view, B: rostro-caudal view) and right vertebral angiography (C: antero-posterior view, D: lateral view) shows a basilar tip aneurysm, 7.4 mm in diameter. E. Right vertebral angiography just after the initial saccular coiling shows 95% neck remnant occlusion of the aneurysm.
Fig. 3  Computed tomography taken on the day after initial embolization shows no intracranial hemorrhage.

Fig. 4  Follow-up magnetic resonance angiogram taken 6 months after the initial embolization shows complete occlusion of the aneurysm.
Fig. 5  Follow-up magnetic resonance angiogram taken 18 months after the initial embolization shows small recanalization at the neck of the aneurysm.
Fig. 6  A. Computed tomogram taken on the day of onset of loss of consciousness shows Fisher group 3 subarachnoid hemorrhage. B, C, D. Emergent 3-dimensional digital subtraction angiography (B: antero-posterior view, C: lateral view) and right vertebral angiography (D) taken on the day of onset shows small recurrence at the ventral part of the aneurysmal neck. E. Complete obliteration of the aneurysm was achieved using a stent-assisted coiling technique.
Table 1. Cases of delayed rupture of previously unruptured cerebral aneurysm after coil embolization in the published literature.

<table>
<thead>
<tr>
<th>Authors &amp; Year</th>
<th>Aneurysm Location</th>
<th>Size</th>
<th>Results of Embolization</th>
<th>Embolization Time at the Time of Rupture</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Guglielmi et al., 1992</td>
<td>basilar tip</td>
<td>giant</td>
<td>residual aneurysm</td>
<td>18 months</td>
<td>partially thrombosed aneurysm</td>
</tr>
<tr>
<td>ApSimon et al., 1995</td>
<td>basilar tip</td>
<td>large</td>
<td>residual aneurysm</td>
<td>7 months</td>
<td>partially thrombosed aneurysm</td>
</tr>
<tr>
<td>Malisch et al., 1997</td>
<td>-</td>
<td>giant</td>
<td>residual aneurysm</td>
<td>12–20 months</td>
<td>partially thrombosed aneurysm</td>
</tr>
<tr>
<td>Hodgson et al., 1998</td>
<td>middle cerebral artery</td>
<td>small</td>
<td>residual aneurysm</td>
<td>18 months</td>
<td>partially thrombosed aneurysm</td>
</tr>
<tr>
<td>Eskridge et al., 1998</td>
<td>-</td>
<td>giant</td>
<td>-</td>
<td>31–90 days</td>
<td>new compressive symptoms during follow up period</td>
</tr>
<tr>
<td>Murayama et al., 1999</td>
<td>posterior communicating artery</td>
<td>large</td>
<td>residual aneurysm</td>
<td>3 years</td>
<td>new compressive symptoms during follow up period</td>
</tr>
<tr>
<td>Gruber et al., 1999</td>
<td>superior artery</td>
<td>giant</td>
<td>residual aneurysm</td>
<td>4 hours</td>
<td>new compressive symptoms during follow up period</td>
</tr>
<tr>
<td>Johnston et al., 2000</td>
<td>-</td>
<td>-</td>
<td>residual aneurysm</td>
<td>-</td>
<td>new compressive symptoms during follow up period</td>
</tr>
<tr>
<td>Ng et al., 2002</td>
<td>-</td>
<td>-</td>
<td>residual aneurysm</td>
<td>7 months</td>
<td>partially thrombosed aneurysm</td>
</tr>
<tr>
<td>Horowitz et al., 2002</td>
<td>anterior communicating artery</td>
<td>small</td>
<td>residual neck</td>
<td>23 months</td>
<td>partially thrombosed aneurysm</td>
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<tr>
<td>Briolstra et al., 2004</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>2 months</td>
<td>partially thrombosed aneurysm</td>
</tr>
<tr>
<td>Gonzalez et al., 2004</td>
<td>-</td>
<td>giant</td>
<td>residual neck</td>
<td>8 months</td>
<td>partially thrombosed aneurysm</td>
</tr>
<tr>
<td>van Rooij et al., 2006</td>
<td>-</td>
<td>large</td>
<td>complete occlusion</td>
<td>13 months</td>
<td>partially thrombosed aneurysm</td>
</tr>
<tr>
<td>Standhardt et al., 2008</td>
<td>vertebro-basilar junction</td>
<td>giant</td>
<td>residual neck</td>
<td>4 years</td>
<td>partially thrombosed aneurysm</td>
</tr>
<tr>
<td>Piotin et al., 2010</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>stent-assited coiling</td>
</tr>
<tr>
<td>Pyysalo et al., 2010</td>
<td>-</td>
<td>large</td>
<td>residual aneurysm</td>
<td>7 years</td>
<td>partially thrombosed aneurysm</td>
</tr>
<tr>
<td>The present case</td>
<td>basilar tip</td>
<td>small</td>
<td>residual neck</td>
<td>22 months</td>
<td>partially thrombosed aneurysm</td>
</tr>
</tbody>
</table>

Data not described in the paper is indicated as “-”. Angiographic results at the initial embolization and at the time of rupture are classified according to the Montreal scale (complete occlusion; residual neck; residual aneurysm). The time between the initial embolization to rupture that was not precisely described in the paper is indicated as “12–20 months”.

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