Despite all of the recent advances in therapeutic approaches to IAs, some IAs cannot be sufficiently treated by endovascular strategies or clipping. When endovascular treatment is not possible and clipping cannot be adequately performed because of size, shape, or location of the aneurysm, reinforcement of the aneurysmal wall by wrapping or coating is an established alternative. Covering the aneurysm with muslin or cotton gauze and adhesives will induce local inflammation and subsequently generate a fibrotic scar that stabilizes the wall of the aneurysm. In some cases, however, the inflammatory reaction induced by wrapping materials, adhesives, or the combination of both may also cause damage to adjacent structures or the parent vessel, leading to parent artery narrowing or occlusion. This may occur early postoperatively or several months after the procedure, where extensive foreign-body inflammatory response is usually associated with the development of a granuloma formation, that is, a so-called muslinoma or gauze granuloma. Both of these conditions may lead to ischemic stroke. The absence of a study systematically investigating the frequency and type of such cerebrovascular complications following wrapping or coating of IAs with cotton gauze and human fibrin adhesives prompted us to review all patients who underwent such procedures at our hospital over a 5-year period, including a comprehensive analysis of their clinical records and neuroimaging data.

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Clinical article

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Object. Reinforcement of intracranial aneurysms (IAs) by wrapping or coating is a well-established therapeutic approach to those IAs not amenable to any other definitive treatment, but has been associated with complications such as parent artery narrowing, granuloma formation, and ischemic stroke. The goal of this study was to systematically investigate cerebrovascular complications following this procedure.

Methods. The authors’ hospital database was searched for all patients who underwent wrapping or coating of IAs with cotton gauze and human fibrin adhesives between October 2006 and October 2011. The follow-up records of these patients were extracted, including regular clinical visits and vascular imaging.

Results. Five hundred sixty-seven patients were treated for IAs over the 5-year period: 303 patients underwent endovascular strategies and 264 underwent craniotomies. Wrapping or coating of IAs was performed in 20 patients (3.5%). Parent artery narrowing occurred in 5 (25%) of the 20 patients and was associated with major ischemic strokes in 4 patients and severe headache in another. Ischemic strokes were associated with parent artery narrowing, which occurred early postoperatively in 2 patients or was a consequence of granuloma formation in 2 patients 1 and 2 months after the procedure, respectively.

Conclusions. These data should add to the awareness of significant cerebrovascular complications following wrapping or coating of IAs with cotton gauze and human fibrin adhesives and indicate that major ischemic strokes need to be included in the risk/benefit considerations during decision making for such treatment strategies. Patients who receive IA wrapping should be monitored and followed up closely for arterial narrowing and granuloma formation.

Key Words • intracranial aneurysm • gauze wrapping • arterial occlusion • ischemic stroke • vascular disorders

Abbreviations used in this paper: IA = intracranial aneurysm; MCA = middle cerebral artery; PICA = posterior inferior cerebellar artery; SAH = subarachnoid hemorrhage.

This article contains some figures that are displayed in color online but in black-and-white in the print edition.
Methods

We retrospectively reviewed all patients who underwent treatment for IAs at a primary and tertiary care university hospital (University Hospital of Graz) between October 2006 and October 2011. Among those patients, we identified all those in whom wrapping or coating of IAs with cotton gauze and human fibrin adhesives (Tisseel; Baxter AG) was performed and reviewed their medical records. Routine follow-up of all patients included clinical visits at 1, 6, 24, and 48 months postoperatively. Vascular imaging with multislice cerebral CT angiography and/or contrast-enhanced MR angiography at 3-T was routinely performed 6, 24, and 48 months after cranioectomy. Whenever patients reported new clinical signs or focal symptoms during a clinical visit, additional neuroimaging was initiated. For this study a trained interventional neuroradiologist (H.D.) blinded to the clinical data reevaluated the imaging data, looking especially for arterial narrowing/occlusions and evidence of ischemic strokes. All clinical data and imaging were generated during routine clinical workups. The study was approved by the local university ethics committee, which waived the need for explicit informed consent.

Results

Over the 5-year period, 567 patients were treated for IAs: 303 patients underwent endovascular strategies and 264 underwent craniotomies. Wrapping or coating of IAs was performed in 20 patients (3.5%). The 20 patients had a mean age of 54 years (range 27–71 years) and 13 (65%) were women. In the 20 patients, 24 IAs were treated. Demographic data, clinical characteristics, treatment strategies, complications, and follow-up data in each of the 20 patients are shown in Table 1. Overall significant parent artery narrowing occurred in 5 (25%) of the 20 patients and was associated with ischemic strokes (n = 4, 20%) or severe headache (n = 1, 5%).

In-Hospital Treatment Complications

In-hospital complications occurred in 8 patients, and only in those who had suffered from SAH (Table 1). Two patients (Cases 11 and 20) declined neurologically on Day 4 after treatment of right MCA aneurysms. Clinical examination at that point revealed a substantial left hemiparesis in both patients (Table 1). Unenhanced CT showed ischemic infarcts in the right MCA territory and transcranial Doppler ultrasonography revealed elevated flow velocities in the right MCA (198 cm/sec and 156 cm/sec in Cases 11 and 20, respectively) whereas flow velocities in all other cerebral vessels were normal. Computed tomography angiography (available in 1 patient [Case 11]; Table 1) also illustrated significant narrowing of only the right MCA while all other vessels appeared normal. Subsequent MRI confirmed ischemic infarctions in the MCA territory (Fig. 1). Flow velocities of those 2 patients (Cases 11 and 20) normalized on postoperative Days 18 and 21, respectively. Both patients were discharged to neurorehabilitation and significantly recovered from their focal neurological deficits. They were living independently at home with a residual weakness of the left arm at the 36-month (Case 11) and 12-month (Case 20) follow-up evaluations.

Follow-Up Complications

Follow-up data, including comprehensive neurological examinations and vascular imaging, were able to be obtained in 19 of the 20 patients after a mean (± SD) of 22 ± 15 months (range 6–50 months). One patient had died due to pneumonia 2 weeks after she had been discharged (Case 9).

During the follow-up period 3 of the 19 patients were readmitted, 2 with acute focal neurological deficits due to ischemic strokes (Cases 5 and 19, Table 1) and 1 with severe headache that was associated with significant parent artery narrowing (Case 4, Table 1). Focal deficits occurred 1 month (Case 5) and 2 months (Case 19) after wrapping of MCA aneurysms and consisted of sudden-onset hemiparesis and acute nonfluent aphasia. The first of the 3 patients who was readmitted during follow-up was a 41-year-old man (Case 5). He was admitted to the stroke unit of a local neurological department for evaluation of a sudden-onset, left-sided hemiparesis. One month previously he had undergone uneventful wrapping of an incidental right MCA aneurysm that had not been amenable to clipping because of its location at the MCA trifurcation. Acute imaging revealed significant narrowing of the right MCA, multiple acute infarctions in the right MCA territory, and a contrast-enhancing lesion at the site of the previously treated aneurysm (Fig. 2A–D). The patient’s clinical condition deteriorated and he was transferred to the university hospital. Brain CT at that point showed a space-occupying infarction in the right MCA territory (Fig. 2E). Transcranial Doppler ultrasonography revealed MCA occlusion. A decompressive hemicraniectomy was performed (Fig. 2F). During neurorehabilitation the patient slowly recovered from initial hemiplegia. He underwent uneventful cranioplasty 10 weeks after decompressive hemicraniectomy. Neuroimaging obtained at the 6-month follow-up revealed persistent MCA occlusion, and brain CT showed the old MCA infarct (Fig. 2G and H). At that point, the neurological examination revealed a severe spastic hemiparesis. The patient was able to walk with a cane but was dependent on help regarding his activities of daily living.

The second of the 3 readmitted patients, a 69-year-old woman (Case 19), had undergone uneventful coating of an unruptured left MCA aneurysm (Fig. 3A) that was not amenable to clipping due to significant calcifications. Postoperatively the patient did well and was discharged home on Day 5. On readmission 2 months later due to sudden onset of nonfluent aphasia, MRI showed a lobulated contrast-enhancing mass at the site of the previously treated aneurysm consistent with a muslinoma. Diffusion-weighted MRI illustrated multiple acute ischemic infarcts in the left MCA territory (Fig. 3B). Magnetic resonance angiography revealed occlusion of the left MCA. Dexamethasone at a dose of 40 mg/day and dual antiplatelet treatment with 75 mg/day of clopidogrel and 100 mg/day of acetylsalicylic acid was initiated. During follow-up, aphasia continuously improved and there were...
TABLE 1: Demographic data, clinical characteristics, treatment strategies, complications, and follow-up data in each of the 20 patients with IAs*

<table>
<thead>
<tr>
<th>Case No.</th>
<th>Age (yrs), Sex</th>
<th>Presentation</th>
<th>Location/Shape of IA (size)</th>
<th>Treatment</th>
<th>Intracranial Treatment Complications</th>
<th>Follow-Up (mos)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>46, F</td>
<td>3rd cranial nerve palsy</td>
<td>ICA/saccular (6 mm)</td>
<td>clip</td>
<td>none</td>
<td>3rd cranial nerve palsy improved (44)</td>
</tr>
<tr>
<td>2</td>
<td>51, F</td>
<td>SAH (1)</td>
<td>MCA/bifurcation, multilobulated (5 mm)</td>
<td>clip</td>
<td>cerebral edema</td>
<td>recovered (45)</td>
</tr>
<tr>
<td>3</td>
<td>39, M</td>
<td>incidental</td>
<td>MCA M2/M3/heavy calcification (1.5 cm)</td>
<td>wrap</td>
<td>none</td>
<td>unreventful (50)</td>
</tr>
<tr>
<td>4</td>
<td>51, M</td>
<td>SAH (2)</td>
<td>PICA/fusiform</td>
<td>wrap</td>
<td>none</td>
<td>reversible parent artery narrowing, headache (38)</td>
</tr>
<tr>
<td>5</td>
<td>41, M</td>
<td>incidental</td>
<td>MCA trifurcation/saccular (8 mm)</td>
<td>wrap</td>
<td>none</td>
<td>granuloma-formation, MCA narrowing/occlusion, stroke, hemiparesis (6)</td>
</tr>
<tr>
<td>6</td>
<td>71, M</td>
<td>SAH (1)</td>
<td>PA/fusiform</td>
<td>clip &amp; wrap</td>
<td>none</td>
<td>recovered (6)</td>
</tr>
<tr>
<td>7</td>
<td>27, F</td>
<td>SAH (3)</td>
<td>MCA bifurcation/saccular (9 mm)</td>
<td>clip &amp; wrap</td>
<td>diffuse vasospasm</td>
<td>recovered (36)</td>
</tr>
<tr>
<td>8</td>
<td>58, F</td>
<td>SAH (3)</td>
<td>ACA/ACoA/broad-based (3 mm)</td>
<td>clip &amp; wrap</td>
<td>diffuse vasospasm</td>
<td>recovered (6)</td>
</tr>
<tr>
<td>9</td>
<td>51, F</td>
<td>SAH (4)</td>
<td>VA/berry (3 mm)</td>
<td>clip &amp; wrap</td>
<td>hydrocephalus, EVD, ventriculitis, diffuse vasospasm</td>
<td>unreventful (12)</td>
</tr>
<tr>
<td>10</td>
<td>58, F</td>
<td>SAH (3)</td>
<td>ICA/multilobulated (8 mm)</td>
<td>clip &amp; wrap</td>
<td>hydrocephalus, EVD, ventriculitis, diffuse vasospasm</td>
<td>recovered (12)</td>
</tr>
<tr>
<td>11</td>
<td>68, F</td>
<td>SAH (2)</td>
<td>MCA/broad-based, multilobulated (9 mm)</td>
<td>clip &amp; wrap</td>
<td>MCA narrowing, stroke</td>
<td>hemiparesis improved (36)</td>
</tr>
<tr>
<td>12</td>
<td>50, F</td>
<td>SAH (2)</td>
<td>ACA/ACoA (2 mm)</td>
<td>wrap</td>
<td>hydrocephalus, EVD</td>
<td>recovered (24)</td>
</tr>
<tr>
<td>13</td>
<td>49, M</td>
<td>incidental</td>
<td>MCA bifurcation (4 mm)</td>
<td>clip &amp; wrap</td>
<td>none</td>
<td>unreventful (6)</td>
</tr>
<tr>
<td>14</td>
<td>59, M</td>
<td>incidental</td>
<td>PA/broad-based, berry (6 mm)</td>
<td>clip &amp; wrap</td>
<td>none</td>
<td>unreventful (24)</td>
</tr>
<tr>
<td>15</td>
<td>71, M</td>
<td>incidental</td>
<td>MCA bifurcation/multilobulated (8 mm)</td>
<td>clip &amp; wrap</td>
<td>none</td>
<td>unreventful (24)</td>
</tr>
<tr>
<td>16</td>
<td>58, F</td>
<td>hemiparesis, stroke not related to aneurysm</td>
<td>BA tip (9 mm)</td>
<td>wrap</td>
<td>none</td>
<td>unreventful, hemiparesis unchanged (15)</td>
</tr>
<tr>
<td>17</td>
<td>59, F</td>
<td>incidental</td>
<td>MCA bifurcation/multilobulated (5 mm)</td>
<td>wrap</td>
<td>none</td>
<td>unreventful (14)</td>
</tr>
<tr>
<td>18</td>
<td>54, F</td>
<td>incidental</td>
<td>MCA bifurcation/multilobulated (3 mm)</td>
<td>wrap</td>
<td>none</td>
<td>unreventful (14)</td>
</tr>
<tr>
<td>19</td>
<td>69, F</td>
<td>incidental</td>
<td>MCA bifurcation/broad-based, calcification (9 mm)</td>
<td>wrap</td>
<td>none</td>
<td>granuloma-formation, MCA narrowing/occlusion, stroke, aphasia improved (13)</td>
</tr>
<tr>
<td>20</td>
<td>59, F</td>
<td>SAH (1)</td>
<td>PA/saccular (11.5 mm)</td>
<td>coiled</td>
<td>isolated vasospasm, MCA, stroke</td>
<td>hemiparesis improved (12)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>MCA M2/broad-based (11 mm)</td>
<td>clip &amp; wrap</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>MCA bifurcation/multilobulated (2 mm)</td>
<td>wrap</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

* ACA = anterior cerebral artery; ACoA = anterior communicating artery; BA = basilar artery; EVD = external ventricular drainage; ICA = internal carotid artery; PA = pericallosal artery; VA = vertebral artery.
no further cerebrovascular events noted clinically or on MRI. Contrast-enhanced MRI showed a regression of the muslinoma (Fig. 3C and D) and persistent proximal left MCA occlusion was noted on MR angiography (Fig. 3E).

Discussion

In our series, the complication of ischemic stroke occurred in 20% of patients following wrapping or coating of IAs with cotton gauze and human fibrin adhesives. Ischemic strokes were associated with parent artery narrowing that occurred either early postoperatively or following granuloma formation 1 and 2 months after the procedure. Severe headache associated with parent artery narrowing was observed in 1 patient.

A variety of materials and adhesives have been used

in the distal left MCA branches (M₂, M₃), however, flow was visible, indicating that collateral leptomeningeal vascularization had occurred (Fig. 3F).

The third patient (Case 4), a 51-year-old man, was readmitted with severe headache that had started 3 weeks after wrapping of a left PICA aneurysm. Subsequent CT angiography revealed significant narrowing of the left PICA, which resolved without specific treatment. Aneurysmal regrowth was not observed and recurrent bleedings did not occur in any of the patients who had undergone wrapping procedures.

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A variety of materials and adhesives have been used
Cerebrovascular complications after gauze wrapping

for wrapping or coating IAs. Parent artery narrowing has been reported after wrapping procedures with cotton gauze and plastic or human-fibrin adhesives in single cases or small case series. Similar to our series, Yoon et al. used cotton gauze and human fibrin adhesives and described neuroimaging findings in 5 cases with muslinoma, and found parent artery narrowing in 2, which was associated with an ischemic stroke in 1 of their 5 patients. Our observation is consistent with their findings. However, we not only evaluated the cerebrovascular complications in patients with granuloma formation, but also systematically investigated arterial narrowing/occlusions and ischemic strokes by advanced vascular imaging methods. In the early postoperative phase we thus noted an isolated increase of flow velocities in the parent vessel of the aneurysm in 2 patients with SAH. This focal increase of flow velocities suggests an inflammatory response of the vessel wall to wrapping materials or adhesives, rather than vasospasm, in the context of coexisting SAH in which the cerebral vasculature tends to be more generally affected. Early parent artery narrowing following wrapping procedures has also been reported in the absence of SAH. In the case of coexisting SAH, however, early parent artery narrowing following gauze wrapping may not be distinguishable from vasospasms. Thus, the early cerebrovascular complications of the wrapping procedure itself may be underestimated, especially in patients with SAH.

Our study also includes the observation of various courses of disease in patients with late cerebrovascular complications following wrapping procedures. The development of ischemic strokes is likely dependent on 1) the rate of progression of a vascular stenosis of the parent artery, and 2) the rate of collateral (leptomeningeal) perfusion. The time course of the hemodynamic changes may play a crucial role. When parent artery narrowing rapidly progresses to occlusion, as evidenced by Case 5 in our series, severe strokes may develop. In such a scenario, urgent angioplasty or stent placement might have been beneficial to prevent further deterioration. When parent artery narrowing progresses more slowly as obviously encountered in Case 19, a more or less sufficient collateral vascularization (preventive of further infarction) may emerge. Close postoperative follow-up evaluation may aid early detection of parent artery narrowing and granuloma formation. In such an event, corticosteroid treatment may reduce inflammation in the vessel wall or adjacent structures and thereby not only inhibit parent artery narrowing, but also additional vessel compression due to a possible additional local space-occupying effect of the muslinoma. This treatment, together with antiplatelet treatment, may substantially decrease the risk of subsequent major strokes.

Our findings reflect the experience with wrapping IAs at a single center and are limited by sample size and retrospective design. Nevertheless, the observation of a high rate of cerebrovascular complications following wrapping procedures appears important and may dampen enthusiasm for gauze wrapping as a treatment modality and indicate caution in the application of cotton gauze and human fibrin adhesives in the treatment of IAs. Aneurysmal regrowth or recurrent bleedings were not observed in our series. Weighing such obviously positive aspects of the procedure against possible dangers may be challenging for vascular neurosurgeons in some situations and should include the notion of cerebrovascular complications.

Conclusions

Wrapping or coating of IAs with cotton gauze and human fibrin adhesives was associated with granuloma formation and a high rate of cerebrovascular complica-
tions in our series. Major ischemic strokes and granuloma formation need to be included in the risk/benefit considerations during decision making for such treatment strategies. Patients who receive wrapping or coating of IAs should at least be monitored closely for vessel narrowing and granuloma formation to initiate treatment and hopefully avoid subsequent ischemic infarctions.

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: Beitzke, Fazekas. Acquisition of data: Beitzke, Leber, Deutschmann, Gattringer, Poltrum. Analysis and interpretation of data: all authors. Drafting the article: Beitzke. 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: Beitzke. Study supervision: Fazekas.

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