Preoperative Endovascular Embolization for Hemangioblastoma in the Posterior Fossa

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Abstract

Intracranial hemangioblastomas (HBs) are hypervascular neoplasms mainly located in the posterior fossa of the central nervous system. Preoperative embolization of the feeding arteries is one proposal for reduction of intraoperative hemorrhage, although indications for the procedures should be evaluated carefully due to the potential complications. This retrospective study investigated clinical outcomes and complications of 15 patients with HBs in the posterior fossa to evaluate the safety and effectiveness of endovascular procedures as well as angiographical procedures. Surgical excision without presurgical embolization was performed in 8 cases, and excision with presurgical embolization was performed in 7 cases, using Guglielmi detachable coils with or without polyvinyl alcohol (GDC ± PVA) in 4 cases and only n-butyl 2-cyanoacrylate (NBCA) in 3 cases. The embolization was applied for selected cases in which feeding arteries were located in a deep site and hard to coagulate surgically. Partial embolization was achieved in 5 cases, and all feeders were successfully embolized in 2 cases. Total removal was achieved in 12 cases, and subtotal/partial removal was achieved in 3 cases. Subarachnoid hemorrhage with intratumoral hemorrhage occurred in 1 case during the angiographic procedure and in 1 case during the embolization procedures. The mean volume of intraoperative blood loss was clearly less in the NBCA group than in the GDC ± PVA group. HBs are mainly located in the posterior cranial fossa, so the risk of severe clinical complication may be high if vascular problems occur. In our series, presurgical embolization using NBCA made tumor removal safe and reduced bleeding volume in posterior fossa HBs.

Key words: cerebellar lesion, complication, endovascular therapy, hemangioblastoma, n-butyl 2-cyanoacrylate

Introduction

Intracranial hemangioblastomas (HBs) are rare benign vascular neoplasms of the central nervous system which account for 1.5–2.5% of all central nervous system tumors and 7–12% of posterior cranial fossa tumors. HBs mainly occur in the posterior fossa, especially in the cerebellar hemisphere,10,11,17,18) but also in the spinal cord,17,18) and rarely in other regions including the nerve root.10) Resection of posterior fossa HBs requires great care due to the hypervascularity of the nodules and crucial normal structures near the tumors. Preoperative embolization of the nodules and/or the feeding arteries has been proposed.5,8,9,12,19–23,25,26) Theoretically, embolization should reduce hemorrhage and facilitate tumor removal. Previously, polyvinyl alcohol (PVA) has been used for the embolization of HBs.5,22,25) However, severe complications have occurred in some cases,4) so further evaluation of such endovascular procedures is necessary.

Here, we report the treatment of 15 patients with posterior fossa HBs and discuss the safety and effectiveness of the endovascular procedures as well as the angiographical procedures.

Patients and Methods

This retrospective study identified 15 consecutive
patients with pathologically verified HBs in the posterior fossa, treated with surgical resection with or without preoperative endovascular embolization between 1988 and 2011 in Tsukuba University Hospital. Only one of the 15 patients was re-treated because of tumor regrowth. Indications for preoperative embolization were decided for individual patients, especially if the feeding arteries were hard to coagulate surgically before handling the HB nodule, if the nodule was relatively large compared to the cyst component, and if the nodule located in a deep site. Endovascular embolization used Guglielmi detachable coils (GDCs) with or without PVA (GDC ± PVA) until 2006, and only n-butyl 2-cyanoacrylate (NBCA) from 2007. Endovascular procedures were performed under general anesthesia. Microcatheters were inserted into the tumor feeders. NBCA was diluted with lipiodol (NBCA concentration of 17%, 6-fold dilution) to delay polymerization of the NBCA and allow deeper penetration into the tumor. The glue was delivered under image acquisition at three images per second.

All embolization procedures were performed by neuroendovascular team members including two or more senior fellows of the Japanese Society for NeuroEndovascular Therapy. Tumor resection was performed by a skilled neurosurgeon, and other parts of procedures by one or two resident surgeons supervised by the skilled neurosurgeon. Therefore, operation time rather than bleeding volume may show a strong bias according to the training level of the resident surgeons. Age, sex, tumor location, tumor size, feeding arteries, complication of embolization, time to surgery after embolization, operation time, blood loss, and patient outcome were investigated.

**Results**

Table 1 presents the patient characteristics. The 8 males and 7 females were aged 12 to 60 years (mean 45 years). Only one patient (Case 13) with cerebellar HB, cervical HBs, and polycystic kidney was diagnosed with von Hippel-Lindau disease. The HBs were located in the intracerebellar region in 12 cases, the cerebellopontine angle in 1 case, the vermis in 1 case, and the medulla oblongata in 1 case. Nine tumors contained cystic lesions equal to or larger than 10 mm in maximal diameter. Ten patients presented with ataxia or vertigo, and 3 patients with headache on admission, probably caused by intracranial hypertension or hydrocephalus.

Table 2 shows the treatments, including embolization, and outcome for the cerebral HBs. Presurgical embolization was performed in 7 of the 15 cases, using GDC ± PVA in 4 patients and only NBCA in 3 patients. For procedures using GDC ± PVA, 2 or more coils in all 4 patients and PVA particles with 250-μm diameter in 2 patients were used for embolization. For example, 2 coils (GDC¹µm.10 UltraSoft⁴, 2 mm × 3 cm and 2 mm × 1 cm; Boston Scientific, Natick, Massachusetts, USA) were used for Case 12.

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**Table 1  Characteristics of patients with posterior fossa hemangioblastoma**

<table>
<thead>
<tr>
<th>Case No.</th>
<th>Age (yrs)/ Sex</th>
<th>Side</th>
<th>Tumor location</th>
<th>Nodule (maximal diameter, mm)</th>
<th>Cyst (maximal diameter, mm)</th>
<th>Hydrocephalus</th>
<th>Cerebellar or cerebral herniation</th>
<th>VHL disease</th>
<th>Feeders</th>
<th>Initial symptoms</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>28/M</td>
<td>rt</td>
<td>CH</td>
<td>20</td>
<td>50</td>
<td>+</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>PICA, tonsillar ataxia</td>
</tr>
<tr>
<td>2</td>
<td>36/M</td>
<td>rt</td>
<td>CH</td>
<td>45</td>
<td>&lt;10</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>AICA, PICA</td>
</tr>
<tr>
<td>3</td>
<td>51/M</td>
<td>rt</td>
<td>CH</td>
<td>40</td>
<td>30</td>
<td>+</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>AICA suspected ataxia, headache</td>
</tr>
<tr>
<td>4</td>
<td>49/F</td>
<td>lt</td>
<td>CH</td>
<td>10</td>
<td>40</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>PICA</td>
</tr>
<tr>
<td>5</td>
<td>36/M</td>
<td>lt</td>
<td>CH</td>
<td>&lt;10</td>
<td>40</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>AICA</td>
</tr>
<tr>
<td>6</td>
<td>60/F</td>
<td>lt</td>
<td>CH</td>
<td>17</td>
<td>15</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>AICA ataxia, nystagmus</td>
</tr>
<tr>
<td>7</td>
<td>53/F</td>
<td>lt</td>
<td>CH</td>
<td>38</td>
<td>&lt;10</td>
<td>–</td>
<td>+</td>
<td>–</td>
<td>–</td>
<td>PICA ataxia, nystagmus</td>
</tr>
<tr>
<td>8</td>
<td>60/F</td>
<td>lt</td>
<td>CH</td>
<td>&lt;10</td>
<td>31</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>PICA vertigo, ataxia</td>
</tr>
<tr>
<td>9</td>
<td>48/F</td>
<td>lt</td>
<td>CH</td>
<td>30</td>
<td>&lt;10</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>SCA</td>
</tr>
<tr>
<td>10</td>
<td>12/F median</td>
<td>CM</td>
<td>CH</td>
<td>40</td>
<td>&lt;10</td>
<td>+</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>bil PICAs, BA lower CN palsy</td>
</tr>
<tr>
<td>11*</td>
<td>56/M</td>
<td>rt</td>
<td>CH</td>
<td>36</td>
<td>&lt;10</td>
<td>+</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>PICA, AICA, OA ataxia</td>
</tr>
<tr>
<td>12</td>
<td>53/M</td>
<td>rt</td>
<td>CP</td>
<td>33</td>
<td>30</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>AICA ataxia, nystagmus</td>
</tr>
<tr>
<td>13</td>
<td>40/M</td>
<td>lt</td>
<td>CH</td>
<td>10</td>
<td>45</td>
<td>+</td>
<td>–</td>
<td>+</td>
<td>–</td>
<td>SCA vertigo, headache</td>
</tr>
<tr>
<td>14</td>
<td>41/M</td>
<td>rt</td>
<td>CH</td>
<td>47</td>
<td>50</td>
<td>+</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>SCA, PICA, SCA ataxia, nystagmus</td>
</tr>
<tr>
<td>15</td>
<td>59/F</td>
<td>lt</td>
<td>vermis</td>
<td>43</td>
<td>&lt;10</td>
<td>+</td>
<td>–</td>
<td>+</td>
<td>–</td>
<td>PICA, AICA, OA ataxia, SCA</td>
</tr>
</tbody>
</table>

Partial embolization was achieved in 5 cases, and all feeders were successfully embolized in 2 cases. The time to surgery after embolization was the same day in 3 patients, next day in 3 patients, and 6 days later in 1 patient. Total resection of the tumors was achieved in 5 patients without complications during and after all procedures, including the embolization. Intratumoral hemorrhage (ITH) and subarachnoid hemorrhage (SAH) occurred in 1 case (Case 9) during the embolization procedures. The patient died of hemorrhagic complication. In one patient (Case 10) pretreated with embolization using GDC and PVA, partial removal was performed because of unexpected intraoperative massive hemorrhage. In the 3 cases using NBCA, solid white arteries were seen directly in the microscopic fields during the operation. These vessels were used as markers for operative orientation. Superior outcomes were achieved in the patients without neurological complication.

Surgical excision without presurgical embolization was performed in 8 of the 15 cases. Total removal was achieved in 7 cases, and partial removal was achieved in 1 case. Hemorrhagic complications occurred in 1 patient (Case 7), who suffered SAH with mild ITH during the angiographic procedure. The other 7 patients had no complication.

Embolization (GDC ± PVA and NBCA) was performed less frequently for HBs located in the cerebellar hemisphere supplied by the posterior inferior cerebellar artery (PICA) or anterior inferior cerebellar artery, than in other regions (p = 0.0014, Fisher’s direct method). There was no difference in maximal diameter of the nodule or cyst between the non-embolization group, GDC ± PVA group, and NBCA group (24 mm, 35 mm, and 33 mm in the nodule, and 28 mm, 15 mm, and 35 mm in the cyst, respectively) (p > 0.05, one-way analysis of variance [ANOVA] test and Tukey’s honestly significant difference [HSD] test). Mean volumes of intraoperative blood loss were 467 ml in 8 cases of the non-embolization group, 1080 ml or more in 4 cases of the GDC ± PVA group, and 117 ml in 3 cases of the NBCA group. There was more massive blood loss in the GDC ± PVA group than in the others (p < 0.05, one-way ANOVA test and Tukey’s HSD test), and the least blood loss occurred in the NBCA group, although no statistical difference was found between the NBCA and non-embolization groups (Fig. 1 left). There was no association between intraoperative blood loss and other factors. Mean operation time was 6.8 hours in the non-embolization group, 12.4 hours in the GDC ± PVA group, and 9.0 hours in the NBCA group. The operation time in the GDC ± PVA group was significantly longer than in the Group 2.
Fig. 1 Comparison of mean volumes of intraoperative blood loss (left) and mean operation time (right) between the non-embolization group (Non), Guglielmi detachable coils with or without polyvinyl alcohol (GDC ± PVA) group, and n-butyl 2-cyanoacrylate (NBCA) group. *p < 0.05. One-way analysis of variance test and Tukey’s honestly significant difference test.

non-embolization group (p < 0.05, one-way ANOVA and Tukey’s HSD test) (Fig. 1 right).

Illustrative Cases

Case 7: A 53-year-old woman presented with cerebellar ataxia and nystagmus. She had a 9-month history of nausea and vertigo. Magnetic resonance (MR) imaging revealed the presence of a left cerebellar mass measuring 38 mm in diameter, compressing the dorsal portion of the medulla oblongata (Fig. 2A). Angiography disclosed a hypervascular tumor fed by the left PICA (Fig. 2B). During preparation for embolization of the feeding artery after routine diagnostic angiography, the patient complained of severe headache. She then lost consciousness and her breathing turned to snoring. Computed tomography revealed SAH with mild ITH (Fig. 2C, D). Right external ventricle drainage was performed, and the tumor was completely resected via the lateral suboccipital approach. She regained consciousness, and her abducens nerve palsy recovered one and a half months after the operation. Postoperative MR imaging detected no residual tumor (Fig. 2E). Histological examination revealed typical HB consisting of numerous vessels, capillary mesh, and stromal cells (Fig. 2F).

Case 14: A 41-year-old man complained of occipital headaches. MR imaging showed a single mass with cystic components in the right cerebellum (Fig. 3A). Angiography showed the tumor was supplied by the right superior cerebellar artery and the PICA (Fig. 3B). The patient underwent partial embolization of the nodule and the feeders using NBCA (Fig. 3C–E), and total removal of the tumor via lateral suboccipital craniotomy on the same day (Fig. 3F). The embolized feeding arteries were visible as solid white vessels directly in the microscopic fields during the operation, which was useful for operative orientation. The blood loss during the operation was limited (20 ml). His postoperative course was uneventful, and he was discharged without complaints.

Fig. 2 Case 7. A: T₁-weighted magnetic resonance (MR) image with gadolinium administration demonstrating a heterogeneously enhanced lesion in the left cerebellar hemisphere. B: Left vertebral angiogram showing a hypervascular tumor fed by several branches of the left posterior inferior cerebellar artery. C, D: Computed tomography scans revealing intratumoral hemorrhage (C) and subarachnoid hemorrhage (D). E: T₁-weighted MR image with gadolinium showing no residual tumor. F: Photomicrograph revealing typical hemangioblastoma consisting of numerous vessels, capillary mesh, and stromal cells. Hematoxylin and eosin stain, original magnification ×400.
Fig. 3 Case 14. A: T1-weighted magnetic resonance (MR) image with gadolinium showing an enhanced lesion with cystic component in the right cerebellum. B: Right vertebral angiogram showing a hypervascular mass supplied by the right superior cerebellar artery (SCA) and posterior inferior cerebellar artery (PICA). C–E: Right vertebral angiograms, before (C) and after (D) embolization using a guiding catheter (Envoy® MPD; Cordis Neurovascular, Miami Lakes, Florida, USA) in the vertebral artery showing a microcatheter (Mara-thon™; ev3 Inc.) inserted using a microguidewire (Mirage™ 0.08; ev3 Inc.), and 17% concentration of n-butyl 2-cyanoacrylate for feeder and nodule embolization, resulting in complete elimination of tumor staining through the PICA branches, and 20% decrease in tumor staining after embolization procedures though the PICA and SCA branches (E). F: T1-weighted MR image with gadolinium showing the lesion had disappeared.

Discussion

HB is a pathologically benign neoplasm, but should be removed totally and followed up carefully because recurrence is seen in up to 25% of cases.3) HB is a highly vascular tumor with fragile vessels.

Tumor diameter over 3 cm carries the risk of spontaneous hemorrhage, whereas diameter smaller than 1.5 cm is associated with no risk of spontaneous hemorrhage.6) Although spontaneous hemorrhage is a very uncommon event in the natural history of HB, uncontrollable intraoperative hemorrhage sometimes occurs. Endovascular embolization of the feeding artery and subsequent operative resection are the recommended procedures, because preoperative embolization can control the arterial supply and reduce tumor vascularity.5,12,20,22,25,26) On the other hand, preoperative embolization carries a high risk of cerebellar infarction and/or ITH.2,4,14) Embolization by PVA has the advantage of reducing intraoperative blood loss.5) However, one patient in this study worsened clinically within 12 hours of embolization, perhaps due to obstructive hydrocephalus resulting from tumor swelling.5) We recommend that endovascular embolization should be performed immediately or within a day before the tumor removal, to avoid worsening of the edema of the tumor or surrounding cerebellar tissue. Individual decisions about embolization are required for patients with HB, due to the substantial risk of peri-procedural morbidity.2,4,17)

The cause of tumor bleeding due to embolization is not clear. PVA reaching beyond the capillary bed and settling in the venous compartment may cause venous obstruction and subsequent congestion of the tumor vessels.2) Indeed, embolization material was found in the venous compartment at histological examination of a posterior fossa HB.14) In our series, intratumoral bleeding occurred in one case after complete feeder embolization by GDC and PVA. We speculate that embolization by PVA rather than GDC encouraged heterogeneous congestion in the fragile vessels resulting in the bleeding.

Pre-surgical embolization has been used in other brain lesions including meningioma or arteriovenous malformation, mainly located in the supratentorial regions.1,7,15,27) Embolization for these lesions can be performed with a high ratio of technical success without permanent neurological complications. On the other hand, HBs are mainly located in the posterior fossa. The risk of severe clinical complications may be higher in the posterior fossa lesions than in other supratentorial lesions, if the embolization causes vascular problems such as ITH and/or brain swelling. Surgeons may have to decide on presurgical embolization based only on whether the feeders will be hard to coagulate before handling the large nodule located in a deep site.

Recently, we have used NBCA for the preoperative embolization of HBs because we believe that NBCA causes more homogeneous embolization of...
fragile vessels of tumors as well as the feeding arteries, whereas PVA often encourages heterogeneous congestion of the tumor. This characteristic of NBCA may reduce the risk of ITH due to congestion. In our 3 cases using NBCA, solid white arteries were seen directly in the microscopic fields during the operation, which were useful for operative orientation. Moreover, better outcomes including total removal of HBs and no neurological complication were achieved in the NBCA group compared to the non-embolization group, whereas outcome in the GDC ± PVA group was worst of all groups. Hence, we speculate that the NBCA is more useful for embolization than PVA in posterior fossa HBs.

As limitations of this study, the present study did not assess various particle sizes of PVA, various concentrations of NBCA, and other types of embolic material, so does not prove the inferiority of all embolic materials compared to NBCA. The standard concentration of NBCA diluted with lipiodol is 10% to 50%, and the concentration alters the polymerization time of NBCA after mixing with blood. Therefore, surgeons determine empirically the concentration and administration volume according to the flow pattern of tumor. In this present study, all 3 cases were treated with low NBCA concentrations because the feeders were not high-flow type. In cases with high-flow feeders, it might be necessary to increase the NBCA concentration. Moreover, we cannot definitively conclude the usefulness of NBCA due to the limited number of patients, which will require large-scale studies. Recently, some authors report multiple cases of arteriovenous malformations and single case of HB using Onyx (ev3 Inc., Plymouth, Minnesota, USA) for presurgical embolization, which is a non-adhesive embolic material different from NBCA. NBCA must also be compared to Onyx.

The present study suggests that treatment strategy should be determined individually for patients with posterior fossa HB. If presurgical embolization is selected, NBCA may be the appropriate embolization material to ensure operation safety and minimum bleeding volume, because better outcomes were achieved in our limited experiences. Nevertheless, the hypervascularity and fragility of the nodule should always be considered, and invasive procedures including embolization should be performed just before tumor removal.

Conflict of Interest Notification

No conflict of interest exists.

References

15) n-BCA Trial Investigators: N-butyl cyanoacrylate embolization of cerebral arteriovenous malformations.


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