Original Article
Surgical management of medulla oblongata hemangioblastomas in one institution: an analysis of 62 cases

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Abstract: Object: Hemangioblastomas of the central nervous system are highly vascularized benign tumors. When the tumors are located in the medulla oblongata, intraoperative bleeding can make the surgical procedure very difficult. Preoperative embolism has been performed in cases of hemangioblastoma in recent decades. However, the complications of the embolization can result in fatal consequences, especially when the lesions are located in the brainstem. In recent years, selectively blocking the suspicious feeding arteries of the tumors during operation in conjunction with intraoperative neurophysiological monitoring has been performed in the Department of Neurosurgery at the West China Hospital. The purpose of this study is to review all cases that underwent this surgical management and to evaluate their outcomes. Method: Between 2003 and 2014, 62 patients (36 female and 26 male, mean age 35.6 years) underwent microsurgery resection of 67 medulla oblongata hemangioblastomas. The suspicious feeding arteries were identified preoperatively by CTA or DSA. During the operation, the suspicious feeding arteries were blocked selectively by motor evoked potential (MEP) and somatosensory evoked potential monitoring (SEP). Based on the retrospectively review of the clinical records and outpatient long-term follow-up visits, their clinical courses were analyzed. Functional outcomes were evaluated according to the classification of McCormick and the Karnofsky Performance Scale. Result: The maximum tumor diameter ranged from 0.8 to 5.1 cm (mean, 2.9 cm). Total tumor resection was achieved in 60 patients. Sixty-one tumors were removed en bloc, and the other six were resected in a piecemeal fashion. The mean follow-up period was 47 months. During the follow-up period, 34 patients remained neurologically stable, 27 patients recovered to a better status and 16 patients developed new transient neurological dysfunction. One patient died. Karnofsky performance scale scores were 100 in 14 patients (22.9%), 90 in 18 patients (29.5%), 80 in 24 patients (39.3%) and 40 to 70 in 5 patients (8.2%). Seventeen cases were associated with von Hippel-Lindau (VHL) disease. In all the cases, tumor recurrence was observed during follow-up in only 2 patients. Conclusion: This study suggests that safe and effective surgical management of medulla oblongata hemangioblastomas can be achieved for most patients, even without preoperative embolization. With the assistance of intraoperative MEP and SEP, mistaken cutting of the vessels that feed the brainstem can be avoided. With improved microsurgical techniques, intraoperative neurophysiological monitoring and a better understanding of the vascular pattern of tumors, total and en bloc microsurgical removal can be performed with low mortality and favorable prognosis of neurological function.

Keywords: Hemangioblastoma, medulla oblongata

Introduction

Hemangioblastomas (HBs) are benign tumors of the central nervous system. HBs can develop spontaneously or as part of von Hippel-Lindau (VHL) syndrome, an autosomal dominant neoplastic syndrome with multiple affected organ systems [1]. HBs account for 1.5%-3.7% of all intracranial tumors [2-5] and 3%-4% of spinal tumors [2, 3]. The cerebellum is the most common location of the lesion, followed by the spinal cord and brainstem. Brainstem HBs are frequently located in the medulla oblongata and comprise 2% to 10% of all the intracranial HBs [6-12]. Although stereotactic radiosurgery has been suggested as an effective method to treat medulla oblongata HBs in recent decades [13-15], microsurgical resection remains the first
option [12, 16, 17]. However, because HBs are highly vascularized and largely solid lesions when they occur in medulla oblongata, resection is a challenge for neurosurgeons [12]. With the developments of neurosurgery in recent years, some new strategies have been adopted to address this disease, including pre-operative embolism. However, complications of embolism may develop, especially when the lesions are located in brainstem. These findings have been confirmed in the literature [18-20].

Between 2003 and 2014, a consecutive series of 62 patients with medulla oblongata HBs underwent microsurgery at the Department of Neurosurgery in West China Hospital. During the microsurgical procedure, blocking the suspicious feeding arteries of tumors selectively in conjunction with intraoperative neurophysiological monitoring was performed in all of the cases. Clinical records and long-term postoperative follow-up were reviewed retrospectively. The objective of this research is to share our experience with medulla oblongata HBs, to better understand the clinical presentation of these tumors, to analyze the outcomes of the microsurgical management for medulla oblongata HBs, and to evaluate the safety and efficacy of this microsurgical management.

Material and methods

Patient population

Sixty-two patients who underwent resection of medulla oblongata HBs at the Department of Neurosurgery in West China Hospital between 2003 and 2014 were identified. The 62 patients included 26 males and 36 females. The mean age was 35.6 years and ranged from 16 to 68 years. All of the patients underwent a total of 64 operations for the resection of 67 medulla oblongata HBs in our department during this period. The clinical information was obtained from hospital charts, clinical notes, and operative records.

Radiographic evaluation

Magnetic resonance imaging (MRI) was performed in each patient preoperatively and postoperatively. MRI provided information on tumor characteristics and the possibility of residual tumor. This radiographic evaluation, which was also performed in the follow-up period, was used to determine tumor recurrence. In the early period of this study, patients only underwent digital subtraction angiography (DSA). In recent years, because CTA can delineate the vascular structures around the lesions, patients underwent CTA first. If CTA was unable to provide information concerning the vascular anatomical information clearly, DSA was performed.

Neuophysiological monitoring

Somatosensory evoked potential (SEP) monitoring, motor evoked potential (MEP) monitoring and the Mapping technique were performed during the microsurgical procedures. SEP and MEP were mainly used to determine the impairment of sensory pathway and motor pathway, respectively. Changes from baseline recordings by SEP and MEP indicated possible damage of the medulla oblongata. SEP changes were defined as a decline of the wave amplitude of greater than 50% or more than one second prolongation of latency. MEP changes were defined as changes in the complexity of the waveform, either from polyphasic to biphasic, polyphasic to loss of waveform, or increases beyond a voltage threshold of 100 V or greater [21]. The Mapping technique was used to delineate the location of the nucleus in the medulla oblongata. During the operation, anesthesia induction with muscle relaxant was used as little as possible, and total intravenous anesthesia (TIVA) was applied to ensure the efficacy of neuropsychological monitoring.

Microsurgical techniques

The suboccipital midline approach and far-lateral approach were performed on lesions that were located in the dorsal part and ventrolateral part of the medulla oblongata, respectively. The microsurgical technique used for brainstem HBs resection by suboccipital midline approach has been previously described [11, 22]. In this study, all of the patients were placed in the three-quarters prone position. Cranietomy was performed with the addition of C-1 laminectomy. The purpose of these approaches was to create a bone window large enough for sufficient exposure of the tumors. Under an operative microscope, a Y-shaped dural incision was made. When the tumor was exposed, the suspicious feeding arteries and draining veins were detected according to the CTA or
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Table 1. McCormick clinical grading scale for neurological function*

<table>
<thead>
<tr>
<th>Grade</th>
<th>Definition</th>
</tr>
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<tbody>
<tr>
<td>I</td>
<td>Neurologically normal; mild focal deficit not significantly affecting function of involved limb; mild spasticity or reflex abnormality; normal gait</td>
</tr>
<tr>
<td>II</td>
<td>Presence of sensorimotor deficit affecting function of involved limb; mild to moderate gait difficulty; severe pain or dysesthetic syndrome impairing patient’s quality of life; still functions and ambulates independently</td>
</tr>
<tr>
<td>III</td>
<td>More severe neurological deficit; requires cane/brace for ambulation or significant bilateral upper-extremity impairment; may or may not function independently</td>
</tr>
<tr>
<td>IV</td>
<td>Severe deficit; requires wheelchair or cane/brace with bilateral upper-extremity impairment; usually not independent</td>
</tr>
</tbody>
</table>

*From McCormick et al., 1990 [23].

Table 2. Karnofsky Performance Scale scores and their definitions*

<table>
<thead>
<tr>
<th>Score</th>
<th>Performance Status</th>
</tr>
</thead>
<tbody>
<tr>
<td>100</td>
<td>Normal: no complaints, no evidence of disease</td>
</tr>
<tr>
<td>90</td>
<td>Able to carry on normal activity; minor symptoms</td>
</tr>
<tr>
<td>80</td>
<td>Normal activity w/effort; some symptoms</td>
</tr>
<tr>
<td>70</td>
<td>Cares for self; unable to carry on normal activities</td>
</tr>
<tr>
<td>60</td>
<td>Requires occasional assistance; cares for most needs</td>
</tr>
<tr>
<td>50</td>
<td>Requires considerable assistance &amp; frequent care</td>
</tr>
<tr>
<td>40</td>
<td>Disabled: requires special care &amp; assistance</td>
</tr>
<tr>
<td>30</td>
<td>Severely disabled: hospitalized but death not imminent</td>
</tr>
<tr>
<td>20</td>
<td>Very sick: active supportive care needed</td>
</tr>
<tr>
<td>10</td>
<td>Moribund: fatal processes are progressing rapidly</td>
</tr>
<tr>
<td>0</td>
<td>Dead</td>
</tr>
</tbody>
</table>

*Modified from the scale created by Karnofsky et al. [24].

Follow-up study

The detailed neurological function of each patient was assessed preoperatively, immediately postoperatively, and during the follow-up period (each six month interval). The neurological function was graded according to the classification scheme published by McCormick et al in JNS [23] (Table 1). KPS [24] scores (Table 2) were determined for each patient according to the clinical data obtained at the last interview of the follow-up period.

Results

Patient characteristics

Among the 62 patients, the most common preoperative symptoms and signs were related to hydrocephalus, intracranial hypertension, lower cranial nerve dysfunction, compression of the nucleus located in the medulla oblongata, and impaired sensory pathway or motor pathway. The details are presented in Table (Table 3). The average duration of symptoms and signs before presentation was 3.8 years (range, one week to 12 years).

The symptoms and signs were observed progressively in all the patients. The von Hippel-Lindau (VHL) germline analysis was performed in 56 of the 62 patients with the familial form of the disease by analyzing peripheral blood samples, as described in Chen et al [25]. Seventeen cases were confirmed to be associated with VHL disease.

Tumor characteristics

The characteristics of all of the 67 resected HBs were clearly identified by the preoperative contrast-enhanced MRI. Fifty-nine lesions were located in the dorsal part of the medulla oblongata, and the other 8 were located in the ventrolateral part. According to the texture of the lesions, the tumors included two types: solid (48 cases) and solid with peritumoral cyst (19 cases). The maximum diameter of the tumors ranged from 0.8 to 5.1 cm (mean, 2.9 cm). In this study, tumor size was determined by the
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maximum diameter, and tumors were divided into 3 groups based on size: Group I: diameter smaller than 1.5 cm; Group II: diameter between 1.5 cm and 3 cm; and Group III: diameter larger than 3 cm. Based on the relationship between the tumor and the medulla oblongata parenchyma, we divided the lesions into 3 types: Type I: completely intramedullary, Type II: intramedullary component larger than the extramedullary component, and Type III: intramedullary component smaller than the extramedullary component. The preoperative CTA or DSA delineated the anatomical localization of the suspicious feeding arteries for the tumors (sometimes the draining veins only by the DSA). However, in this series, the feeding arteries were identified in only 52 lesions. The blood supply largely arose from the PICA, AICA, PSA, ASA and BA. A few cases of tumors were fed by the SCA, VA, and branches of the meningeal arteries (SCA: superior cerebellar artery; AICA: anterior inferior cerebellar artery; PICA: posterior inferior cerebellar artery; VA: vertebral artery; PSA: posterior spinal artery; ASA: anterior spinal artery; and BA: basilar artery). The tumors were usually fed by multiple vessels. The details of the tumor characteristics are presented in table (Table 4).

Follow-up results

All of the patients underwent follow-up interviews. The duration of follow up ranged from 19 months to 128 months (mean 47 months). The neurological status before the operation and after different follow-up periods according to the McCormick grade is presented in table (Table 5).

Immediate outcomes (2 weeks post-operation): According to the MRI performed immediately after the operation, of all 67 tumors, total resection was achieved in 65 lesions in 60 patients. Sixty-one tumors were removed en bloc, and the remaining six were piecemeal resected. According to the McCormick grade, the immediate postoperative neurological function was stable in 55 (88.7%) patients. Among 31 Grade II cases, one patient (3.2%) improved to Grade I, one patient (3.2%) deteriorated to Grade IV and 3 patients (9.7%) deteriorated to Grade III. One (9.1%) of the Grade III patients deteriorated to Grade IV. Hydrocephalus improved in 25 patients, and the remaining 4 required V-P shunts. Gastrointestinal ulceration, which occurred in 12 (19.4%) patients after operation, was treated with a proton pump inhibitor. Eleven (17.7%) patients suffered pneumonia because of lower cranial nerves or respiratory center dysfunction. These patients were recovered with intravenous antibiotic administration and tube feeding, but one patient died secondary to respiratory and circulation failure. Four of the 11 patients required a tracheotomy. Cerebrospinal fluid leaks in 3 (4.8%) patients were successfully treated with lumbar drainage for 5-7 days.

Short-term outcomes (3-6 months after operation): The new neurological dysfunctions occurred during the early period post-operation and included hoarseness, swallowing difficulty, singultus hypesthesia, dysesthesia, and weakness; these dysfunctions were alleviated or disappeared in this period. Five Grade II patients and 1 Grade III patient improved to Grade I.
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Long-term outcomes (1.5-10 years after operation): Based on the neurological examination by McCormick grade at the most recent follow up, 18 patients (29.5%) remained improved, and 43 patients (70.5%) remained clinically stable. The Karnofsky performance scale scores were 100 in 14 patients (22.9%), 90 in 18 patients (29.5%), 80 in 24 patients (39.3%) and 40 to 70 in 5 patients (8.2%). In all of the cases, tumor recurrence was observed during follow-up in only 2 patients. Because the recurrent tumors did not cause any symptoms or signs, reoperation was not performed.

Discussion

Epidemiology and clinical presentation

HBs are benign neoplasms of uncertain histogenesis and are classified as grade I lesions according to the WHO, constituting 1.5-3.7% of all intracranial tumors and 7-12% of posterior fossa tumors in adults [2, 4, 30, 31]. The majority location is the cerebellar hemispheres; other locations, including supratentorially, brainstem, and cerebellopontine angle, are rare [20, 29, 32-35]. Brainstem tumors comprised 2 to 15% of hemangioblastomas [6-10, 12, 36]. Between 2003 and 2014, in our hospital, intracranial HBs accounted for approximately 2.8% of all intracranial tumors, and the incidence of medulla oblongata HBs were 7.6% of all the intracranial HBs. According to the literature, approximately 25%-35% of CNS HBs are associated with VHL disease [7, 9, 37, 38]. In this series, VHL disease was present in 17 (30.4%) patients.

The most common clinical symptoms and signs are related to intracranial hypertension, lower cranial nerve dysfunction, posterior column disturbances, and impaired motor pathway or sensory pathway [11, 22, 26, 28, 39, 40]. The clinical presentation of this study was similar to that reported in the literature (Tables 3, 6). In this series, because the lesions (88.1%) were usually located in the dorsal part of the medulla oblongata, they were apt to obstruct CSF outflow from the fourth ventricle, resulting in obstructive hydrocephalus and progressive symptoms of headache, papilledema, nausea, and vomiting. Hydrocephalus was induced by solid tumors more easily than by tumors with peritumoral cysts, even when the tumors with peritumoral cysts were bigger than the solid ones. However, if the solid tumor with a peritumoral cyst was a completely intramedullary lesion, obstructive hydrocephalus was very common. In the 29 patients with hydrocephalus, 23 cases were Type II or Type III, as shown in Table 4, and the remaining 6 cases were Type I. The incidence of obstructive hydrocephalus was 75% in Type I and was 38.9% in Type II and Type III. Twenty-seven lesions among the 29 patients exhibited a maximum tumor diameter larger than 1.5 cm. By analyzing the relationship between hydrocephalus and tumor classifications, we found that the incidence of hydrocephalus was obviously higher in patients

Table 4. The characteristics of the 67 resected medulla oblongata hemangioblastomas

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>N = 67 (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tumor texture</td>
<td></td>
</tr>
<tr>
<td>Solid</td>
<td>48 (71.7%)</td>
</tr>
<tr>
<td>Solid with peritumoral cyst</td>
<td>19 (28.3%)</td>
</tr>
<tr>
<td>Tumor size (maximum diameter)</td>
<td></td>
</tr>
<tr>
<td>Mean size</td>
<td>2.9 cm</td>
</tr>
<tr>
<td>Size range</td>
<td>0.8 cm-5.1 cm</td>
</tr>
<tr>
<td>Group I: ≤ 1.5 cm</td>
<td>11 (16.4%)</td>
</tr>
<tr>
<td>Group II: 1.5 cm-3 cm</td>
<td>36 (53.7%)</td>
</tr>
<tr>
<td>Group III: ≥ 3 cm</td>
<td>20 (29.9%)</td>
</tr>
<tr>
<td>Tumor location</td>
<td></td>
</tr>
<tr>
<td>Dorsal</td>
<td>59 (88.1%)</td>
</tr>
<tr>
<td>Ventrolateral</td>
<td>8 (11.9%)</td>
</tr>
<tr>
<td>Tumor relation to medulla oblongata</td>
<td></td>
</tr>
<tr>
<td>Type I: completely IM</td>
<td>8 (11.9%)</td>
</tr>
<tr>
<td>Type II: IM &gt; EM</td>
<td>16 (23.9%)</td>
</tr>
<tr>
<td>Type III: IM &lt; EM</td>
<td>43 (64.2%)</td>
</tr>
<tr>
<td>Feeding arteries of tumors</td>
<td></td>
</tr>
<tr>
<td>PICA</td>
<td>49 (73.1%)</td>
</tr>
<tr>
<td>AICA</td>
<td>34 (50.7%)</td>
</tr>
<tr>
<td>PSA</td>
<td>19 (28.4%)</td>
</tr>
<tr>
<td>ASA</td>
<td>16 (23.9%)</td>
</tr>
<tr>
<td>VA</td>
<td>14 (20.9%)</td>
</tr>
<tr>
<td>BA</td>
<td>13 (19.4%)</td>
</tr>
<tr>
<td>SCA</td>
<td>9 (13.4%)</td>
</tr>
<tr>
<td>Branches of the meningeal arteries</td>
<td>6 (8.9%)</td>
</tr>
<tr>
<td>Unknown</td>
<td>31 (36.3%)</td>
</tr>
</tbody>
</table>

who exhibited 4 characteristics: dorsal lesion, completely solid lesion, maximum diameter larger than 1.5 cm and completely intramedullary lesions. Similarly, according to the data of Table 6, the following three conditions contribute to cranial nerve dysfunction: ventrolateral lesions, intramedullary lesions, and lesions with a larger size. When lesions are located in the ventrolateral part of the medulla oblongata, the lower cranial nerves can be stretched or compressed by the body of the tumors. When the main component of the lesions is intramedullary, the nuclei of the lower cranial nerves are frequently impaired. Moreover, larger sized tumors more easily contribute to posterior column disturbances and impaired motor pathways or sensory pathways.

The average duration of symptoms and signs before presentation was 3.8 years. By analyzing the clinical data of all 62 patients, we observed that if the first symptoms or signs were associated with hydrocephalus, the average duration was 17.4 months, which was significantly shorter than otherwise. Therefore, if the patient exhibited the 4 characteristics that indicate obstructive hydrocephalus, the tumor should be resected early. Delayed microsurgery for these patients may lead to irreversible neurological deficits, such as visual disorders caused by intracranial hypertension.

**Radiographic implication**

MRI is the best diagnostic method for medulla oblongata HBs. Tumors exhibit isointensity or hypointensity on T1-weighted images and hyperintensity on T2-weighted images. On contrast-enhanced MRI, the tumors are markedly enhanced homogeneously or heterogeneously on T1-weighted images (Figures 1-3), with serpentine areas devoid of signal, often seen at the periphery or within the tumors. The serpen-
tine areas consist of the pathological vessels (Figure 1). MRI can indicate the location and the texture of the tumor and its relationship with the surrounding medulla oblongata tissues. However, MRI cannot delineate the feeding arteries or draining veins of the tumor clearly. In the early period of this study, we performed DSA to delineate the vascular architectures of the feeding and draining vessels (Figures 1, 2). However, in recent years, CTA has been demonstrated to be an effective method to replace DSA because it is noninvasive, takes less time, is easier to perform, requires lower x-ray doses and less contrast media, results in fewer complications, and offers high accuracy for delineating the feeding arteries [10]. Furthermore, CTA can provide detailed information about the relationship between the vessels, the tumor and the skull base (Figure 3). CTA is more useful than DSA in assisting neurosurgeons in preparing their surgical strategy before the operation. Sometimes, the CTA cannot delineate the vessels. In such cases, DSA should be performed. It is noteworthy that the DSA and CTA cannot detect the feeding arteries of some lesions. This type of tumor is always small in volume. In this study, the feeding arteries of 6 lesions were unable to be detected. The maximum diameter was smaller than 1.5 cm in 5 of the 6 lesions. According to the outcomes of CTA or DSA, PICA and AICA were the most common feeding arteries of medulla oblongata HBs. Tumors commonly drained into the straight, lateral, or petrosal sinuses (Figure 1).

**Microsurgical management**

Surgical resection of medulla oblongata HBs presents a challenge to neurosurgeons because the tumors exhibit significant vascularity, are typically solid lesions, and are associated with important neural tissue around or in the brainstem. In recent years, alternative methods such as stereotactic radiosurgery or chemotherapy have been used to treat these tumors, but the therapeutic effects are controversial. Thus, microsurgery remains the primary treatment option [27, 41-51]. According to the surgical morbidity and mortality rate associated with the resection of medulla oblongata HBs, which has been reported in the literature [27, 43-51], the prognosis of patients with this
Table 6. The relationships between tumor classification and clinical presentation

<table>
<thead>
<tr>
<th>Clinical presentation</th>
<th>Tumor texture</th>
<th>Tumor location</th>
<th>Tumor size</th>
<th>Tumor relation to medulla oblongata</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Solid N = 48 (%)</td>
<td>Solid with peritumoral cyst N = 19 (%)</td>
<td>Dorsal N = 59 (%)</td>
<td>Ventrolateral N = 8 (%)</td>
</tr>
<tr>
<td>Hydrocephalus (Headache, Nausea or vomiting, Papilledema) (N = 29)</td>
<td>23 (47.9%)</td>
<td>6 (31.6%)</td>
<td>28 (47.5%)</td>
<td>1 (12.5%)</td>
</tr>
<tr>
<td>Lower cranial nerves dysfunction (N = 24)</td>
<td>15 (31.3%)</td>
<td>9 (47.4%)</td>
<td>17 (28.8%)</td>
<td>7 (87.5%)</td>
</tr>
<tr>
<td>Posterior column disturbances (N = 18)</td>
<td>13 (27.1%)</td>
<td>5 (26.3%)</td>
<td>15 (25.4%)</td>
<td>3 (37.5%)</td>
</tr>
<tr>
<td>Impaired motor pathway or sensory pathway (N = 14)</td>
<td>8 (16.7%)</td>
<td>6 (31.6%)</td>
<td>12 (20.3%)</td>
<td>2 (25.0%)</td>
</tr>
</tbody>
</table>
Figure 1. A: Preoperative contrast-enhanced sagittal MR image revealing a large solid hemangioblastoma which was located on the dorsal part of medulla oblongata. B and D: Postoperative contrast-enhanced sagittal and axial MR images revealing total resection of the tumor. C: The arrows on the preoperative contrast-enhanced axial MR im-
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Some authors attribute the improvement to the application of operating microscopes, intraoperative neurophysiological monitoring, preoperative embolization, and Fluorescein angiography et al. In contrast, other authors oppose the application of preoperative embolization because this method has the potential to cause complications such as bleeding, tumor swelling and vessel occlusion with consecutive infarction [18-20, 22]. If the lesion is located in the medulla oblongata, these complications may be fatal. In consideration of these facts, none of the patients in our department underwent preoperative embolization.

Based on the analysis of the microsurgical management of this study, the following factors are considered important to achieve good microsurgical outcomes:

Surgical approach and exposure of tumor: The principle of choosing the microsurgical approach was the complete exposure of the tumor margins (Figure 3). Because the majority

Figure 2. (A and C) Preoperative contrast-enhanced sagittal and axial MR images revealing a large solid hemangioblastoma that was located on the ventrolateral part of the medulla oblongata. (B and D) Postoperative contrast-enhanced sagittal and axial MR images revealing total resection of the tumor. (E and F) On the preoperative DSA image (E) and the intraoperative photograph (F), the arrows pointed the feeding artery of the tumor, which derived from the AICA. (G) The tumor was resected en bloc.

type of tumor has improved progressively. Some authors attribute the improvement to the application of operating microscopes, intraoperative neurophysiological monitoring, preoperative embolization, and Fluorescein angiography et al. In contrast, other authors oppose the application of preoperative embolization because this method has the potential to cause complications such as bleeding, tumor swelling and vessel occlusion with consecutive infarction [18-20, 22]. If the lesion is located in the medulla oblongata, these complications may be fatal. In consideration of these facts, none of the patients in our department underwent preoperative embolization.

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of medulla oblongata HBs are located on the dorsal part of brainstem, the suboccipital midline approach provides an adequate operative field to expose the tumor margins. However, when the lesions are located on the ventrolateral part of brainstem or when the lesions expand from the dorsal part to the ventrolateral part, the far-lateral approach should be performed because the vessel structure on the ventrolateral boundary of the tumor could be exposed by this approach. Sometimes, expanding the craniotomy to the junction of the transverse sinus and sigmoid sinus should be performed in the far-lateral approach. In this series, all of the lesions were located near the foramen magnum and atlas, so craniotomy was performed with the addition of C-1 laminectomy, sometimes with C-2 laminectomy. A Y-shaped dural incision was made, and the dural edges were reflected laterally to expose the tumor margins. In this procedure, the underlying arachnoid and pia mater on the surface of the tumor should be kept intact. If the tumor is completely intramedullary, the solid component of the lesion should be detected by intraoperative ultrasonography. Intraoperative ultrasonography can provide the precise relationship between the solid tumor, the peritumoral cyst and the medulla oblongata tissues. Intraoperative sodium fluorescence for the resection of HBs was introduced in recent years [52]. However, we believed that intraoperative

Figure 3. A and B: Preoperative CTA images revealing a hemangioblastoma, which was fed by the VA and PICA. And the CTA images revealing the relationship between the tumor, the feeding arteries and the skull base structures. C and D: Preoperative and postoperative contrast-enhanced sagittal MR images revealing a total resection of a solid hemangioblastoma, which was located on the dorsal part of medulla oblongata. E: The arrow on the intraoperative photograph pointed a large draining vein of the tumor, and the tumor margins was exposed completely in this operative field. F: The arrow pointed the thin rim of the soft gliotic tissue between the surface of the tumor and the surrounding medulla oblongata. G: During the operation, the suspicious feeding artery that derived from PICA, which was pointed by the arrow, was temporary occluded by the tips of bipolar forceps for few minutes. H: Intraoperative photograph after total resection of the tumor.
ultrasonography is more convenience and precise. Because all intramedullary HBs are lesions with peritumoral cysts, the liquid in the cyst can help to locate the solid component. For the removal of intramedullary tumors, the medulla oblongata must be incised to expose the solid component of the tumor. The Mapping technique of neurophysiological monitoring was used to detect the location of the nucleus in the brainstem. Assisted by the information provided by intraoperative ultrasonography and neurophysiological monitoring, the incised position was determined. This position was safe because it was located at a distance from the important nuclei of the brainstem and near the solid component.

Resection of tumors: The principle of resection of medulla oblongata HBs should adhere to the principle of arteriovenous malformation: selective division of the feeding arteries followed by resection of the lesion with the preservation of the main draining veins; the division of the main draining veins should be performed at the last moment. In our experience, en bloc removal of the solid component of the lesions was also an important principle. Piecemeal resection is apt to result in uncontrollable bleeding during the operation and residual tumor. When the tumor is exposed, the arachnoid and pia mater should be incised sharply around the margins. Before the tumor resection procedure, the vessel construction and lower cranial nerves around the lesion should be investigated carefully. The major feeding arteries often arose from the ventral or ventrolateral sides of the lesions, and the main draining veins always crossed on the surface of the lesions (Figure 3). Because the tumors usually have several feeding arteries, the division of the arteries should be performed from the ventrolateral sides to the ventral sides progressively. Assisted by the MEP and SEP, the suspicious feeding arteries are temporary occluded by the tips of bipolar forceps for few minutes (Figure 3). If the MEP or SEP changed, the procedure should be stopped immediately, as the vessels may represent the normal brainstem feeding arteries that pass the lesions. If the lesion begins to shrink or if no changes are observed in the MEP and SEP, the vessels should be coagulated and divided as close to the margin of the lesions as possible by the properly low-set bipolar. If surgeons want to expose the feeding arteries on the ventral side, they must lift the lesions along the thin rim of the soft gliotic tissue between the surface of the lesions and the surrounding medulla oblongata tissues (Figure 3). The draining veins may potentially be impaired during this procedure. Gelfoam and cotton pieces should be placed on the surface of the lesions to protect the draining. When the lesions are rotated or retracted to identify the feeding arteries on the ventral side, it is very important to notice the changes of the MEP and SEP. The changes usually indicate compression or damage of the brainstem tissues. Because these tissues involve the respiratory and vasculomotor areas, the sensorimotor tracts on the extremities, and the nuclei of cranial nerves, damage can result in a poor prognosis in patients. However, fortunately, this damage is usually transient and recovers quickly after stopping manipulation. In this series, when the tumors were Type I or Type II (Table 4), especially lesions larger than 3 cm in diameter, these changes were observed frequently. If the diameter of the thinnest part of the medulla oblongata is smaller than 2 mm, the damages may be permanent or long-lasting. After division of almost all of the feeding arteries and the circumferential dissection of the lesion, the volume of the tumor should shrink. The main draining veins are then coagulated and cut, and the tumor is resected en bloc. Temporary occlusion of the suspicious feeding arteries assisted by MEP and SEP was not necessary for all of the cases in this series and was not performed when the feeding arteries of the tumors were clear or when the volume of the tumors was small. However, in some cases, when the diameter of the lesions was larger than 3 cm, the body of the tumors covered the feeding arteries completely. Meanwhile, the lower cranial nerves straddled the body of the tumors. Lifting the tumor would impair the nerves and could seriously compress or retract the brainstem. In such cases, it is too difficult to divide the feeding arteries before the resection of the tumors. Piecemeal resection was difficult to avoid. If the feeding arteries of this type of tumors were derived from the PICA, AICA, VA or PSA, the arteries were occasionally occluded temporarily by an aneurysm clip. This method may help decrease bleeding during piecemeal resection.

Neurophysiological monitoring implication: Intraoperative neurophysiological monitoring has been used in an attempt to prevent transient or permanent neurological impairment in
patients undergoing neurosurgery in recent decades. The SEP and MEP, which are used during the resection of intracerebral and intramedullary tumors [47, 53-57], have been introduced as reliable methods for the intraoperative monitoring of sensory and motor pathway function. In the resection of medulla oblongata HBs, the effectiveness of SEP and MEP are controversial [11]. In this series, based on the records of the intraoperative SEP and MEP, these methods were demonstrated to be very useful for determining the possibility of potential damage of brainstem. However, some issues are worth considering when SEP and MEP are performed during the operation. The sensory pathway in the dorsal part of the brainstem and the motor pathway in the ventral part are monitored by the SEP and MEP, respectively. If impairment or ischemia occurs in the brainstem during the operation, changes in the SEP and MEP can be observed. During the operation, these two methods must be performed in combination, and the changes in the methods must be analyzed comprehensively. SEP is used for continuous monitoring and can be performed during the entire operation. However, MEP is discontinuous. Because the muscles of the patient contract when MEP is performed, the operation may be disturbed. Therefore, when changes are observed on SEP, the operation should be stopped temporarily. Meanwhile MEP should be performed immediately to determine the potential impairment of the ventral part of the brainstem. Only after all changes on SEP and MEP recover should the operation be resumed. Because most medulla oblongata HBs are located on the dorsal part of the brainstem, changes in SEP usually appear first. However, when the tumors are ventrolateral lesions, changes in MEP can appear without changes in SEP. Therefore, when ventrolateral lesions are resected, MEP should be performed more frequently. In this study, suspicious feeding arteries of the tumors were occluded temporarily for 2-3 minutes; SEP and MEP were monitored for any changes compared with baseline recordings. The lack of changes indicated that the sacrifice of these arteries would not produce ischemic deficits in the brainstem.

Complications

In this series, the most common complications were gastrointestinal ulceration and pneumonia. These complications were related to the unique anatomy of the region in which these tumors were located. The major reason for the gastrointestinal ulceration was the injury of the dorsal motor nucleus of the vagus nerve, which may alter parasympathetic innervation of the gastrointestinal tract [58]. Using a proton pump inhibitor prophylactically in the perioperative period may reduce the incidence of this complication. The impairment of the lower cranial nerves and the respiratory center in the brainstem usually led to swallowing difficulties and respiratory depression. These dysfunctions may result in aspiration and expectoration difficulties, which are the main causes of pneumonia. To prevent this complication, patients should remain intubated and undergo tubal feeding until the full restoration of normal respiratory function. If expectoration difficulty does not recover in a few days, tracheostomy should be performed.

Tumor control and prognosis

Previous research has suggested that incomplete resection of HBs usually results in tumor recurrence [22]. In this series, the outcome of tumor control was similar to previous reports. Tumor recurrence occurred in only two patients who underwent subtotal resection of the tumors. Additionally, piecemeal resection of tumors, in our opinion, was also an important predictor of tumor recurrence because uncontrollable bleeding caused by the piecemeal resection made the boundary between the tumor surface and the brainstem tissues unclear. According to the neurological status measured by the classification of the McCormick grade scale before the operation and at the different follow-up periods, 34 patients remained neurologically stable, 27 patients recovered to a better status and 16 patients developed new transient neurological dysfunction. Combining these outcomes with the tumor characteristics of the 62 patients, we found that the tumor size, tumor location and the preoperative neurological status of the patient were not the best predictors of the neurological outcome. There is significant controversy with respect to factors affecting neurological outcomes [5, 11, 12, 22, 59]. In general, patients with large tumor sizes and severe neurological dysfunction before surgery are likely to exhibit a poor prognosis, although this is not always the case. Compared with these factors,
we believe that when the operation should be performed is a more important determinant of neurological outcomes. The microsurgery should be performed as soon as possible in symptomatic patients with medulla oblongata HBs. In asymptomatic patients, if the tumor growth is confirmed, the operation should be performed immediately.

Conclusion

Our study suggests that safe and effective surgical management of medulla oblongata HBs can be achieved for most patients, even without preoperative embolization. With the assistance of intraoperative MEP and SEP, mistaken cutting of the vessels that feed the brainstem can be avoided. With improved microsurgical techniques, intraoperative neurophysiological monitoring and a better understanding of the vascular pattern of tumors, total and en bloc microsurgical removal can be performed with low mortality and favorable prognosis of neurological function.

Disclosure of conflict of interest

None.

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References

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