Patients with Spinal Ependymomas Attached to the Anterior Median Septum are at Risks for Postoperative Functional Impairment: A Correlating Analysis

Satoru Shimizu, M.D.*1, Kimihiko Mii, M.D.*2, Daitoku Mishima, M.D.*2, and Kiyotaka Fujii, M.D.*3

Abstract

When operating on spinal ependymomas, careful dissection of tumors in the ventral attachment is important because the tumor-feeding arteries and the central vessels of the cord, both of which branch from the anterior spinal artery, are located close to the anterior median septum (AMS), which is an extension of the pia in the cord. In this study, we examined the clinical features of tumor attachment to the AMS.

We divided 10 patients who underwent total removal of spinal ependymomas into 2 groups based on the ventral attachment of their tumors. In Group A (n=5), the tumor was attached to the AMS, and in Group B (n=5), it was not attached to the AMS. We recorded the patients' modified McCormick grades at the time of admission, immediately, and 4 weeks after surgery. Pre- and postoperative changes in their functional status were evaluated by a deterioration/amelioration scoring system where 0=no change of grade, −1, −2=deterioration by 1 or 2 grades, and +1=improvement by 1 grade. We compared the scores recorded for Group A and B patients just after and 4 weeks after surgery. In addition, we compared the motor evoked potentials (MEPs), preoperative magnetic resonance imaging (MRI) results (proportion of the tumor to the cord, intratumoral cyst, and syrinx), and pathological findings (anaplastic changes and MIB-1 index) in the 2 groups.

In Group A, tight adhesion of the tumor to the AMS rendered selective division of the feeding arteries difficult. The mean deterioration/amelioration scores immediately and 4 weeks after surgery were −1.2 (range 0 to −2) and −0.6 (range +1 to −2), respectively in Group A. They were −0.8 (range 0 to −2) and +0.2 (range +1 to −1) respectively in Group B. Four weeks after surgery, one patient of Group A was scored −2, whereas no patient of Group B had a score of −2. Both groups, manifested decreases in MEP amplitudes. There were no specific MRI and pathological findings pertinent to the pattern of a attachment to the septum.

Tumors with adhesion to the AMS raise the risks of damage to the central vessels, tend to produce deterioration, and result in delayed postoperative recovery. Careful dissection that is based on an understanding of the anatomical relationship between the AMS and the central vessels and feeding arteries facilitates the safe detachment of these tumors from the AMS.

(Received: October 15, 2012; accepted: April 8, 2013)

Key words
anatomy, anterior median septum, central vessel, spinal ependymoma, surgery
Table 1  Characteristics of patients with spinal ependymomas (at presentation)

<table>
<thead>
<tr>
<th>Case no.</th>
<th>Age/Sex</th>
<th>Tumor location</th>
<th>Chief complaint</th>
<th>Symptom duration</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>64/F</td>
<td>T10/11</td>
<td>paraparesis</td>
<td>4 mos</td>
</tr>
<tr>
<td>2</td>
<td>49/M</td>
<td>C7</td>
<td>arm paresthesia</td>
<td>3 mos</td>
</tr>
<tr>
<td>3</td>
<td>27/F</td>
<td>T10–12</td>
<td>paraparesis</td>
<td>6 mos</td>
</tr>
<tr>
<td>4</td>
<td>33/M</td>
<td>C6–T1</td>
<td>paraparesis</td>
<td>4 mos</td>
</tr>
<tr>
<td>5</td>
<td>68/M</td>
<td>T3–4</td>
<td>paraparesis</td>
<td>6 mos</td>
</tr>
<tr>
<td>6</td>
<td>42/M</td>
<td>C1–2</td>
<td>quadriparesis</td>
<td>5 mos</td>
</tr>
<tr>
<td>7</td>
<td>45/F</td>
<td>C3/4–5</td>
<td>quadriparesis</td>
<td>3 yrs</td>
</tr>
<tr>
<td>8</td>
<td>45/M</td>
<td>C6–T2</td>
<td>quadriparesis</td>
<td>3 yrs</td>
</tr>
<tr>
<td>9</td>
<td>27/M</td>
<td>T4–12</td>
<td>paraparesis</td>
<td>1 yr</td>
</tr>
<tr>
<td>10</td>
<td>45/F</td>
<td>T5</td>
<td>breast paresthesia</td>
<td>4 yrs</td>
</tr>
</tbody>
</table>

Introduction

During surgeries for spinal intramedullary ependymomas, dissection of the ventral plane of the tumor is an important issue. Tumors that arise from ependymal cells lining the central canal are often fed by branches of the anterior spinal artery and the central artery (sulcal artery). These feeders should be cautiously dissected without damaging normal cord vessels. However, this process is complicated if the tumor is attached to the anterior median septum (AMS), which is an extension of the pia that is embedded in the ventral median part of the cord and contains the central vessels and feeding arteries.

We present the intraoperative and clinical findings of 10 patients, who were treated for spinal intramedullary ependymomas, and discuss the importance of understanding of the AMS for the safe surgical treatment of these tumors.

Materials and Methods

Patient Population

Between 1997 and 2011, 13 adults with spinal intramedullary ependymomas were surgically treated at Sagamihara Hospital. Patients with myxopapillary ependymomas in the filum terminale were excluded from this retrospective study. After reviewing patients’ medical records, operative notes, and video tapes of the operations, we included 10 patients who had undergone complete removal of tumor. We excluded 3 patients who were treated by partial removal; 2 of these presented with tight adhesions of the tumor to the lateral fasciculus, and 1 with excessive swelling of the cord.

Our study population consisted of 6 men and 4 women of age ranging from 27 to 68 years (mean, 44.5 years) (Table 1). The tumor, identified on contrast-enhanced magnetic resonance imaging (MRI) by using a 1.0–1.5 Tesla scanner, was located in the cervical region in 3 patients, cervicothoracic region in 2, and thoracic region in 5.

Surgery and Classification of Tumor Attachment

All operations were performed by or directed by the senior author (KM). After the induction of general anesthesia, the patient was placed in the prone position for an osteoplastic laminotomy or laminectomy. The extent of the tumors was confirmed by ultrasonography. While viewing through a microscope, the tumors were exposed by sharp dissection of the epipial layer on the posterior median sulcus and traction-assisted opening of the sulcus. After exposing the entire length of the tumor, its volume was reduced with a Cavitron ultrasonic surgical aspirator, and the tumor was dissected laterally to identify the cleavage plane. The tumor was lifted cephalad to caudal, caudal to cephalad (usually, the pole of the tumor adjacent to the associated syrinx was chosen as an entry), or dorsolateral to ventromedial.

The tumors were divided into 2 groups on the basis of their attachment at the ventral aspect. Group A tumors (n=5) were attached to the AMS. They presented as a whitish, tough, and fibrous line in the midline and could not be lifted because of their tight attachment. Group B tumors (n=5) were without attachment to the AMS. Because they were connected to the ventral parenchyma of the cord by only the feeding vessels, they could be lifted easily. In both groups, hemosiderin deposits on the parenchyma were observed, and this suggested an earlier hemorrhage.
we recorded the score as 0. We compared the scores that were recorded immediately after and 4 weeks after the surgery in Group A and B patients. Because 6 patients were transferred to regional facilities, we were unable to compare their scores during the latest examinations.

4 Radiological and Pathological Evaluation

We reviewed the MRI findings at presentation and the pathological results to assess whether there were specific findings reflective of tumor attachment to the AMS. The thickness of the cord parenchyma ventral to the tumor region with the largest diameter and the proportion of tumor–to–cord on the midsagittal plane were measured on MR images by using the SYNAPSE Enterprise–PACS software (FUJIFILM Holdings Corporation, Tokyo, Japan). The proportion was defined as 100% when the parenchyma surrounding the tumor could not be visualized. Any associated intratumoral cysts and syringes were also recorded. The pathological evaluation comprised of a tumor diagnosis that included its subtype, anaplastic changes, and the MIB-1 index for evaluating its proliferation potency.
The intraoperative findings and functional outcomes are detailed in Table 3. In the 5 patients who showed tight attachment of the tumor to the AMS (Group A), the tumor margin on the AMS was unclear, and after detaching the main mass, small tumor fragments were left at its tip to preserve the central vessels that were embedded at that site (Fig. 1a, c). The tumor–feeding arteries were meticulously coagulated by bipolar cautery and separated from the surrounding tissues comprising the tumor or the AMS. After removal of the main mass, the residual tumor fragments were removed piecemeal from the tip of the AMS. In patient 3, the ventral pia was exposed through a thin gliotic parenchyma (Fig. 1b, c).

In the 5 Group B patients, the tumors were connected to the ventral parenchyma by only the feeding vessels that passed through the anterior raphe, and the feeders could be identified easily by lifting the tumor. We then performed coagulation and separation along the tumor (Fig. 1d, e).

Results

The intraoperative findings and functional outcomes are detailed in Table 3. In the 5 patients who showed tight attachment of the tumor to the AMS (Group A), the tumor margin on the AMS was unclear, and after detaching the main mass, small tumor fragments were left at its tip to preserve the central vessels that were embedded at that site (Fig. 1a, c). The tumor–feeding arteries were meticulously coagulated by bipolar cautery and separated from the surrounding tissues comprising the tumor or the AMS. After removal of the main mass, the residual tumor fragments were removed piecemeal from the tip of the AMS. In patient 3, the ventral pia was exposed through a thin gliotic parenchyma (Fig. 1b, c).

In the 5 Group B patients, the tumors were connected to the ventral parenchyma by only the feeding vessels that passed through the anterior raphe, and the feeders could be identified easily by lifting the tumor. We then performed coagulation and separation along the tumor (Fig. 1d, e).

Hemosiderin deposits were observed in 2 Group A patients and 1 Group B patient. In both groups, we observed a 50% decrease in the MEP amplitude in 4 patients in Group A and 2 in Group B. Dissection of the tumor in the ventral part tended to cause MEP deterioration, especially in Group A. We could not compare the exact frequencies and durations of the MEP deterioration in the 2 groups.
In Group A, the deterioration/amelioration score immediately after and 4 weeks after surgery was 0 to −2 (mean, −1.2) and +1 to −2 (mean, −0.6), respectively. In Group B, it was 0 to −2 (mean, −0.8) and +1 to −1 (mean, +0.2), respectively (Table 3). The incidences of scores recorded in the 2 groups immediately after and 4 weeks after surgery are shown in Fig. 2. Immediately after surgery, there was deterioration (−1,−2) or no change (0) in the functional statuses of both groups; 2 patients in Group B and 1 in Group A exhibited no change (score 0), and, in 2 patients in Group A and 1 in Group B, the recorded score was −2. At 4 weeks after surgery, 1 Group A and no Group B patient continued to have a score of −2. Improved scores (+1) were recorded in 2 Group B patients and 1 Group A patient.

The MRI findings are shown in Table 4 and Fig. 3. The thickness of the cord parenchyma ventral to the tumor was 0.9 to 1.5 mm in Group A and 1.5 to 2.0 mm in Group B. The tumor-to-cord ratio on the midsagittal plane was 50–100% in Group A (mean, 82%) and 60–100% (mean, 87.8%) in Group B. Three Group A and 3 Group B patients harbored associated intratumoral cysts, while syringes were observed in 3 Group A and 3 Group B patients.

The pathological diagnoses were well-differentiated ependymoma in all but patient 4 in whom the diagnosis was tanycytic ependymoma. No patient manifested anaplastic changes; the MIB-1 index was less than 1% in 8 patients and less than 5% in 2 (patients 5 and 10).

<table>
<thead>
<tr>
<th>Case no.</th>
<th>Length of tumor (mm)</th>
<th>Thickness of parenchyma (mm)*</th>
<th>Proportion of tumor (%) **</th>
<th>Intratumoral cyst</th>
<th>Syringe</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>20</td>
<td>1.2</td>
<td>75</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>2</td>
<td>10</td>
<td>1.5</td>
<td>50</td>
<td>+</td>
<td>−</td>
</tr>
<tr>
<td>3</td>
<td>63</td>
<td>0.9</td>
<td>85</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>4</td>
<td>40</td>
<td>NA</td>
<td>100</td>
<td>−</td>
<td>−</td>
</tr>
<tr>
<td>5</td>
<td>55</td>
<td>NA</td>
<td>100</td>
<td>−</td>
<td>+</td>
</tr>
<tr>
<td>6</td>
<td>18</td>
<td>NA</td>
<td>100</td>
<td>−</td>
<td>−</td>
</tr>
<tr>
<td>7</td>
<td>38</td>
<td>1.5</td>
<td>79</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>8</td>
<td>58</td>
<td>NA</td>
<td>100</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>9</td>
<td>17</td>
<td>NA</td>
<td>100</td>
<td>−</td>
<td>+</td>
</tr>
<tr>
<td>10</td>
<td>25</td>
<td>2.0</td>
<td>60</td>
<td>+</td>
<td>−</td>
</tr>
</tbody>
</table>

*ventral to the tumor, **to the cord on the mid-sagittal plane, NA: not applicable, +: present, −: absent.

Table 4 Findings of magnetic resonance imaging

The MRI findings are shown in Table 4 and Fig. 3. T1-weighted gadolinium-enhanced magnetic resonance images, sagittal and axial views (insets), that were obtained from patients with ependymomas with (case 2: a, case 3: b) and without attachment to the anterior median septum (case 6: c, case 7: d). In patients with and without tumor attachment, the tumor-to-cord ratio on the midsagittal plane can be large or small. An intratumoral cyst (arrow) or syringe (arrowhead) may or may not be present. Thus, there are no specific findings that suggest attachment of the tumor to the septum.
Our study showed that patients whose tumors were attached to the AMS, a part of the pia that contains the central vessels, experienced delayed post-operative functional recovery. The pia covering the spinal cord is comprised of 2 layers. The inner thin layer, which consists of reticular tissue, is the intima pia, or the so-called true pia. The outer thick layer, which consists of collagenous fibers, is the epipial layer (Figs. 4~6). The intima pia is also found on the brain surface, while the epipial layer exists only on the medulla oblongata and
spinal cord. The intima pia continues from the ventral surface of the spinal cord to the bottom of the anterior median fissure (AMF). The epipial layer, which thickens ventral to the AMF, is known as the linea splendens. From there, collagenous tissue continues into the AMF and forms the AMS. The anterior spinal artery and vein run along the AMF that is covered with linea splendens and then branch off to form the central arteries and collect blood from the central veins, respectively\(^9\),\(^10\),\(^15\). These neighboring central vascular systems run sagittally within the AMS and enter the ventral white commissure after forming vascular bundles. The AMS covering the central vessels terminates immediately before the entrance to the white commissure\(^11\). This anatomical relationship between the pial and vascular structures is commonly seen from the cervical to the sacral cord. There are 5–9 central arteries and 4–9 veins within each centimeter length in the cervical cord; 3–6 and 3–6, respectively, in the thoracic cord; 7–12 and 7–11, respectively, in the lumbar cord; and 8–14 and 8–12, respectively, in the sacral cord\(^15\). On the basis of the branching pattern and the course direction, the central arteries and veins are classified into the following 3 supply types: undivided unilateral (type 1), branched bilateral (type 2), and branched unilateral (type 3). Type 1 is common in the central arteries, whereas types 2 and 3 are dominant in the central veins\(^15\). In the presence of ependymomas, the central vessels are usually displaced ventrally by the tumor expanding around the central canal (Fig. 1a, c).

The goal of spinal ependymoma surgery may not be total curative removal, but rather the preservation of cord function. Therefore, although patients who undergo subtotal removal tend to experience a benign postoperative course\(^2\)–\(^5\),\(^12\),\(^16\)–\(^18\), aggressive manipulations that risk damaging normal tissues, including the central vessels, should be avoided. When the tumor is not attached to the AMS (Group B in the present study), lifting it facilitates the identification of the stretched tumor–feeding vessels that can then be coagulated and separated very close to the tumor. This maneuver helps to preserve the central vessels. However, if the tumor is tightly attached to the AMS (Group A), it cannot be moved safely and tumor feeders and central vessels cannot be differentiated. In addition, tumor feeders that are covered by thick adhered AMS usually require meticulous bipolar coagulation, which increases the risk of iatrogenic injury to adjacent central vessels. Considering these issues, initial dissections that leave small tumor fragments on the tip of the AMS (Fig. 1a, c) may be justified. The residual tumor on the AMS can be identified and addressed by subsequent meticulous piecemeal removal with the help of photodynamic techniques. This technique uses protoporphyrin IX, a metabolic product of 5-aminolevulinic acid that accumulates specifically in tumor tissue\(^19\).

The ventral cord parenchyma in an area adjacent to the AMS must be considered as a bed of the central vessels. If it is preserved below the dissection plane, the central vessels can be expected to be preserved as well. While vessels coursing in the dissection plane can often be seen, exposure of the ventral pia may result in the unintentional dissection of vessels with a thin gliotic parenchyma (Fig. 1b, c).

Decreases in the MEP amplitude during tumor dissection in the ventral part, which were predominantly observed in Group A, were attributable to impairment of the microvascular circulation in the cord, which is supplied by the central vasculature.

Tumor attachment to the AMS and damage to central vessels of the cord upon exposure of the ventral pia may result in the postoperative deterioration of patients with spinal intramedullary tumors. Other risk factors are a poor preoperative functional status\(^2\)–\(^5\),\(^12\),\(^17\),\(^20\), a prolonged duration of preoperative symptoms\(^4\), a large tumor size\(^20\), tumor location in the thoracic cord\(^16\), cord atrophy\(^4\),\(^21\), arachnoid scarring\(^21\), postoperative posterior tethering of the spinal cord\(^14\), and postoperative spinal deformity\(^16\).

While preoperative information on the type of tumor attachment is important for the development of appropriate surgical strategies, we found that a thin cord parenchyma ventral to the tumor and a large tumor-to-cord ratio on MRI scans were not always predictors of tumor attachment to the AMS. In addition, the presence of associated intratumoral cysts or syringes was not helpful (Table 4, Fig. 3).

Because none of our 10 patients manifested specific radiological, intraoperative, or pathological findings indicative of tumor adhesion to the adjacent tissue, such as prior hemorrhage (presenting as intratumoral cysts or hemosiderin deposits) or anaplastic changes of the tumor,
the pathological mechanisms leading to tumor attachment to the AMS remain unknown.

Our study showed that patients with spinal intramedullary ependymomas that attached to the AMS tended to suffer postoperative deterioration. This may be attributed to iatrogenic damage to the central vasculature supplying normal cord tissue through entering into the cord at the tip of the AMS and running in the ventral parenchyma adjacent to the tumor. Careful dissection, based on an understanding of the anatomical relationship between the AMS and the central vessels and the tumor-feeding arteries, is necessary to improve the treatment outcome in patients undergoing surgery for spinal ependymomas.

**Acknowledgment**
The authors thank Professor Emeritus Isao Yamamoto, Department of Neurosurgery, Yokohama City University, Yokohama, Japan, for reviewing the manuscript. They also thank Dr. Satoshi Utsuki, Department of Neurosurgery, Higashi Totsuka Memorial Hospital, for providing Fig. 5.

**References**