Differentiation of localization of spinal hemangioblastomas based on imaging and pathological findings

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Received: 13 January 2011 / Accepted: 12 April 2011 / Published online: 29 April 2011
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Abstract Intramedullary + extramedullary hemangioblastomas with largely extramedullary growth are rare and often incorrectly assigned as intradural-extramedullary tumors preoperatively. Preoperative evaluation of the precise tumor location is important for total resection of tumor and improving the surgical outcome. The aim of this study was to provide the first identification of the key differences among of preoperative MR images of hemangioblastomas in different locations and to correlate these with pathological findings. The subjects were 26 patients with surgery for spinal hemangioblastoma in our department, including 6 with an intramedullary tumor who were complicated with von Hippel Lindau disease. Intramedullary, intramedullary + extramedullary, and intradural-

extramedullary tumors were present in 22, 3 and 1 cases, respectively. Sagittal MR images showed that intramedullary and intramedullary + extramedullary tumors gave intramedullary T2 high intensity areas (HIAs) spreading toward the craniocaudal sides of the tumor, whereas such findings were absent for the intradural-extramedullary tumor. All the tumors showed strong contrast on axial images, with focal enhancement of hemangioblastomas limited to the intramedullary region (focal type); smooth boundary lines between the spinal cord and the extramedullary tumor (smooth type); and a snowman sign for intramedullary + extramedullary tumors, which provided a key characteristic for differentiating intramedullary + extramedullary tumors from those limited to the extramedullary region. In pathological findings, the Ki67 activity was less than 1% for intramedullary and intradural-extramedullary tumors, but 18–25% in all cases with an intramedullary + extramedullary tumor. In conclusion, on

This paper is designed and submitted acting on guideline of IRB of Nagoya University Graduate School of Medicine and all patients have signed consent forms for this study.

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preoperative MRI, a change in the intramedullary HIAs spreading the craniocaudal sides of the tumor on sagittal T2 weighted image (T2WI) and a snowman sign on contrast axial T1WI may be important for differentiation among spinal hemangioblastomas in different locations. Pathologically, we found that intramedullary + extramedullary hemangioblastoma has high cell proliferative activity, which may suggest that enlargement of this tumor occurs faster than that of intramedullary hemangioblastoma.

Keywords Spinal hemangioblastoma · Exophytic intramedullary hemangioblastoma · Differentiation of localization · MRI findings · Pathological findings

Introduction

Spinal hemangioblastoma is a rare disease that accounts for 2–10% of intramedullary spinal cord tumors [1–3]; however, the number of patients diagnosed with the disease has increased with more common use of MRI in recent years. Among cases of spinal hemangioblastoma, 20–30% are associated with von Hippel Lindau (VHL) disease [4], but there are sporadic cases that do not show this association. An intramedullary tumor location is most common. Then, regarding hemangioblastoma with exophytic intramedullary, intradural-extramedullary, and extradural locations, the total number of cases of spinal hemangioblastoma is limited to only a few case reports [1, 5–7].

The accuracy of diagnosis of the tumor has been increased by MRI, but hemangioblastomas in unusual locations may be difficult to diagnose preoperatively. Patients with spinal hemangioblastoma often have rapid progression of symptoms and are treated with surgery. Therefore, it is important to diagnose the type and location of the tumor using preoperative imaging for total resection of tumor and improving the surgical outcome. Moreover, caution is needed since exophytic intramedullary hemangioblastomas often progress to extramedullary tumors, and it may be difficult to differentiate these tumors from intradural-extramedullary hemangioblastomas preoperatively. In fact, we experienced some cases of exophytic intramedullary hemangioblastoma that had been diagnosed as an intradural-extramedullary tumor prior to referral to our department.

To our knowledge, classification of the locations of spinal hemangioblastomas using MR images has not been described, and pathological and histological differences in these tumors in different locations have not been examined. Preoperative differentiation of the location of the tumor and prediction of the proliferative properties would be beneficial in treatment. Therefore, the objectives of this study were to examine MR images of spinal hemangioblastoma and intraoperative findings

to obtain an image classification for the location of the tumor preoperatively, and to determine the association of these findings with pathological results.

Subjects and methods

The subjects were 26 patients (15 males, 11 females) with spinal hemangioblastoma who underwent surgery in our department. Data were analyzed after obtaining approval from the Ethics Committee of Nagoya University. The patients had a mean age of 42 years old (21–68 years old). The tumors were in the cervical spine, cervicothoracic spine, thoracic spine, and the conus region in 10, 2, 11 and 3 cases, respectively. Of the 22 cases of intramedullary tumors, 6 (24%) were complicated with VHL disease. All patients were diagnosed using plain and contrast MRI preoperatively. Surgical resection of the tumor was performed under a microscope, and the tumor was pathologically diagnosed postoperatively based on the histological type and Ki67 activity. Preoperative characteristics of MRI findings, intraoperative findings, percentage removal of the tumor, postoperative course, histological and pathological findings, and were examined with respect to the tumor location.

Results

Characteristics of MRI findings

Of the 26 cases, 22 had tumors with intramedullary locations, 3 had intramedullary + extramedullary locations (exophytic intramedullary hemangioblastomas), and one had an intradural-extramedullary location. Sagittal MRI showed that the 25 intramedullary and intramedullary + extramedullary tumors were accompanied by large intramedullary syrinxes or edema spreading toward the craniocaudal sides of the tumors, with a range over 6–19 vertebrae (a mean of 13.9 vertebrae) (Figs. 1a, 2a). In the extramedullary-intradural case, there was no change in intramedullary intensity (Fig. 3a). In all sagittal MR images of all cases of intramedullary + extramedullary tumors, the extramedullary tumor components were so large that they occupied the whole of the spinal canal; therefore, the intramedullary tumor components were not visible and the tumors initially seemed to be mimicking extramedullary only (Fig. 2b). In all cases, the tumors were strongly enhanced. In T1 contrast axial images, the intramedullary hemangioblastomas were focal but strongly enhanced compared with a large range of T2 intramedullary high intensity areas (HIAs) (focal enhancement type) (Fig. 1b). Tumors limited to the

Fig. 1 MRI findings for intramedullary spinal hemangioblastoma. T2WI sagittal plane showed characteristic HIAs in the spinal cord spreading longwise on the craniocaudal sides of the tumor, but the tumor location was not clear (a). On contrast axial T1WI, a focal tumor strongly contrasted with an intramedullary tumor (b)

intradural-extramedullary region showed compression of the spinal cord from the outside, and the boundary lines between the spinal cord and the tumor were smooth (smooth compression type) (Fig. 3b). Intramedullary + extramedullary tumors gave strong signals for both the extramedullary and intramedullary components. This appearance (hereinafter, referred to as the snowman sign) is a characteristic for differentiation of intramedullary + extramedullary tumors from tumors limited to the extramedullary region (Fig. 2c).

Operative findings

In intramedullary + extramedullary cases, an extramedullary tumor that was large enough to cover the whole of the dorsal side of the spinal cord (Fig. 4a). Intraoperative ultrasound revealed the presence of extramedullary tumor components, as well as the intramedullary tumor (Fig. 5a, b). However, the extramedullary tumor highly compressed the spinal cord, and thus intramedullary tumor components might not always be clearly identified. After removal of the extramedullary tumor components (Fig. 4b), ultrasound images revealed the remaining intramedullary tumor components (Fig. 5c), and these might be larger than expected preoperatively. After myelotomy, the intramedullary tumor components were then removed, leading to complete tumor resection (Fig. 4c).

In the 26 cases, tumors were totally removed in 22 patients, and not totally removed in 4 patients with an intramedullary tumor due to deterioration of findings in intraoperative spinal cord monitoring. All four patients experienced worsening of symptoms postoperatively and underwent a reoperation in which the tumors were totally removed.

Pathological findings

Evidence of hemangioblastoma including abundant proliferation of blood vessels and the presence of typical stromal cells was found in all cases (Fig. 6a). The Ki67 activity

Fig. 2 MRI findings for intramedullary + extramedullary spinal hemangioblastoma. On sagittal T2WI, longwise intramedullary HIAs occurred, but a tumor was unclear (a). This image looked like

intradural-extramedullary tumor only (b). On contrast axial images, a clear snowman sign was present, indicating a combination of a large extramedullary tumor and an intramedullary tumor (c)

Fig. 3 MRI findings for intradural-extramedullary spinal hemangioblastoma. On sagittal T2WI, there was no HIA in the spinal cord on the craniocaudal sides of the tumor (a). On contrast axial images, smooth boundary lines were clearly seen due to compression of the spinal cord by the extramedullary tumor (b)

was less than 1% in the 22 intramedullary tumors and the intradural-extramedullary tumor, but as high as 18–25% in all intramedullary + extramedullary tumors (Fig. 6b).

Discussion

Spinal hemangioblastomas often occur as intramedullary tumors that progress from under the pia mater to the intramedullary region. Thus, intramedullary tumor location is relatively common. However, in rare locations, tumors that progressed from the intramedullary to the extramedullary region, intradural-extramedullary tumors derived from nerve roots, and extramedullary tumors have also been described [1, 5–8]. Spinal hemangioblastomas may complicate with VHL disease, and intramedullary + extramedullary cases have been associated with VHL disease in the literature. However, the intramedullary + extramedullary tumors in the present study were sporadic cases. There has been no previous description of MR images in detail in a case in which an intramedullary tumor ruptured the pia mater, progressed into the extramedullary region, occupied the whole of the spinal canal, and displaced the spinal cord from the extramedullary side.

The increased use of MRI has simplified preoperative diagnostic imaging of intramedullary hemangioblastomas. We consider that angiography is no longer necessary, as also suggested previously [9, 10]. This is why the precise MRI evaluation is more important to treat these patients. Hemangioblastoma generally shows an iso-signal intensity on T1WI (T1-weighted image), a high signal intensity on

Fig. 4 Intraoperative tumor findings of intramedullary + extramedullary tumors. Incision of the dura mater revealed an extramedullary tumor that was large enough to cover the whole of the dorsal side of the spinal cord (a). After removing the extramedullary tumor, myelotomy was performed and the tumor was also found to be present in the intramedullary area, as shown on preoperative MRI (b). The tumor was resected, leading to total resection of the tumor (c)

T2WI, and strong contrast [9]. When the tumor is large, the contrast may be uneven [11]. Even if the tumor is small, it may be accompanied by an intramedullary syrinx or edema spreading on the craniocaudal sides of the tumor [9, 12]. The edema may in part be due to venous congestion or arteriovenous shunting. Symptomatic small spinal hemangioblastomas may also have relatively large associated syrinxes, whereas these are often absent for asymptomatic lesions [9, 12].

These characteristic findings are useful for diagnosis, and diagnostic imaging of typical intramedullary

Fig. 5 Intraoperative ultrasound findings of intramedullary + extramedullary tumors. Just after laminectomy, large intradural tumor components were seen (*arrow*). However, the extramedullary tumor highly compressed the spinal cord, and thus intramedullary tumor components were not always clearly identified (*a*). In the axial plane,

the intramedullary tumor might be identifiable as a snowman sign (*b*). After removal of the extramedullary tumor components, the remaining intramedullary tumor components were clearly seen (*arrowhead*), and these might be larger than expected preoperatively (*c*)

Fig. 6 Pathological findings of hemangioblastoma. The tumor composed of a juxtaposition of variable sized vascular spaces and stromal cells (H&E, $\times 200$) (*a*). The Ki67 activity was as high as 25% in intramedullary + extramedullary tumors ($\times 400$) (*b*), but less than 1% in tumors in other locations

hemangioblastomas is relatively easy. However, preoperative differentiation of the location of the tumor is sometimes difficult especially between intramedullary + extramedullary and extramedullary tumors. Why is it important to evaluate the differentiation of the location of this tumor? In the present study, deterioration of spinal cord monitoring findings prevented complete tumor removal in four patients, and this led to worsening of symptoms postoperatively and the requirement for a reoperation in all four patients. For

Fig. 7 Schema of axial MR images for different locations of hemangioblastomas. For intramedullary tumors, limitation of the signal to the intramedullary area is clear (*focal type*). Intramedullary + extramedullary tumors are characterized by a snowman sign. For extramedullary tumors, the pressure of the tumor on the spinal cord produces smooth signals (*smooth type*)

intramedullary + extramedullary tumors, the surgical outcome is worsened if only the extramedullary tumor components are removed and the intramedullary tumor cannot be resected due to problems such as excessive bleeding. Partial removal of a hemangioblastoma results in a failure to treat syrinxes and edema surrounding the tumor, and this inevitably causes worsening of symptoms. Total removal of this tumor is necessary. Therefore, an accurate preoperative imaging evaluation of the tumor location is important for good surgical outcome.

However, for intramedullary + extramedullary tumors with large extramedullary tumor components that compress the spinal cord, as seen in the present study, differentiation from intradural-extramedullary tumors may not be easy using MRI. If the extramedullary tumor components are small, determination of the shape of the spinal cord and whether an intramedullary tumor is present can be

Table 1 Characteristics of MR images of spinal hemangioblastomas in different locations

Tumor location	MRI sagittal HIA (T2 WI) ^a	MRI axial (T1 contrast) ^b
Intramedullary	Present	Positive enhancement only in intramedullary region (focal enhancement type)
Intramedullary + extramedullary	Present	Snowman sign
Intradural-extramedullary	Absent	Smooth and even compression of the spinal cord (smooth compression type)

If both sagittal and axial findings are present, this is useful for differentiation

^a Intramedullary high intensity area (HIA) spreading toward the craniocaudal sides of the tumor

^b Characteristic morphology

performed on contrast axial MR images without much difficulty (Fig. 7). However, if the extramedullary tumor components are large and occupy the whole of the spinal canal, and the spinal cord is highly displaced, it may be difficult to distinguish the intramedullary and extramedullary tumors. A failure to notice the presence of an intramedullary tumor may lead to misdiagnosis of an intradural-extramedullary tumor and subsequent problems in surgery.

In such hemangioblastoma cases, the results of this study indicate that there are two important features on MRI for differentiation of an intramedullary + extramedullary tumor from an extramedullary tumor: a syrinx or edema spreading longwise on the craniocaudal sides of the tumor in the sagittal plane on T2WI; and the tumor appearance on contrast axial MR images (Table 1). If the tumor is limited to the intramedullary region only, the tumor is firmly contrasted, and diagnosis of the tumor location is relatively easy (Focal type). If the spinal cord is displaced only from the extramedullary side, which may occur since hemangioblastoma is relatively a soft tumor, the boundary line between the tumor and the spinal cord is often smooth (smooth type). On contrast MR images in the present study, a “snowman sign” indicates the probable presence of an intramedullary + extramedullary tumor, and this finding is an important point of differentiation in contrast axial images (Fig. 7). The snowman sign seems to be a common

finding for other kinds of tumors that are present in both the intramedullary and extramedullary regions. Therefore, we suggest that an intramedullary + extramedullary hemangioblastoma is highly probable when an intramedullary HIAs on sagittal T2WI and a snowman sign on contrast axial T1WI are both found.

For extramedullary hemangioblastomas, they give no change in intramedullary signal, as shown in the present study and in case reports on intradural-extramedullary hemangioblastomas [8, 13, 14]. This finding is a characteristic for differentiation of tumors limited to the extramedullary region from intramedullary + extramedullary tumors based on appearance on sagittal MR images. However, we had only a few cases of intramedullary + extramedullary and extramedullary tumors, since these tumors are in a rare location for spinal hemangioblastoma. Therefore, we reviewed MRI findings in previous reports, as summarized in Table 2 [8, 9, 13–16]. The results for intramedullary and intradural-extramedullary tumors support the characteristic features found in the present study. Unfortunately, we were unable to find a previous report showing detailed MRI findings for an intramedullary + extramedullary tumor. Preoperative differentiation from other kinds of intradural-extramedullary tumors, such as meningioma, may be difficult. Serpentine flow voids corresponding to large feeding or draining

Table 2 MRI findings in reported cases of spinal hemangioblastoma

Author (year)	Location of tumor	MRI sagittal HIA (T2WI) ^a	MRI axial (T1 contrast) ^b
Lonser (2003)	Intramedullary	Present	Focal
Lonser (2005)	Intramedullary	Present	Focal
Bloomer (2006)	Intramedullary	Present	Focal
Toyoda (2004)	Intradural-extramedullary	Absent	Smooth
Barbosa-Silva (2009)	Intradural-extramedullary	Absent	Smooth
Taniguchi (2009)	Intradural-extramedullary	Absent	Smooth

^a Intramedullary high intensity area (HIA) spreading toward the craniocaudal sides of the tumor

^b Characteristic morphology

vessels on T1WI and T2WI along the dorsal aspect of the spinal cord have been noted [9], and hemangioblastomas with sizes of 25 mm or larger have been found to give vascular flow voids [12]. Definitive preoperative diagnosis of extramedullary hemangioblastomas without such MRI findings is difficult, and angiography may be helpful especially in these cases. However, if surgery for the hemangioblastoma is limited to the extramedullary region only, total removal may be carried out without too much difficulty provided that feeding and draining vessels are treated and bleeding is carefully controlled, since the tumor can be totally removed in the same way as that for other intradural-extramedullary tumors and no myelotomy is required.

Regarding pathological findings, we found that high Ki67 activity in cases with intramedullary + extramedullary (exophytic growth from intramedullary) tumors, whereas the Ki67 activity was less than 1% in all 22 cases of intramedullary hemangioblastoma. In previous reports, high Ki67 activity has only been found in a case of hemangioblastoma complicated with VHL disease [17] and in one case of an intradural-extramedullary hemangioblastoma [8]. To our knowledge, this is the first report showing that the difference in Ki67 activity is correlated with the tumor location in a population including cases without complication with VHL disease. Since cell proliferation is probably active in an hemangioblastoma with exophytic growth from an intramedullary tumor, and mechanical compression from the intramedullary and extramedullary sides is likely to be high, an early operation may be needed after the occurrence of symptoms of spinal disorder.

Conclusion

MR images of intramedullary, intramedullary + extramedullary, and intradural-extramedullary tumors were examined in cases of spinal hemangioblastoma that were treated surgically. The imaging characteristics of the tumors were determined for each location. Preoperative diagnostic MRI is particularly important in cases of intramedullary + extramedullary hemangioblastoma for preparing a surgical plan for total resection, and a change in intramedullary HIAs on the craniocaudal sides of the tumor on sagittal T2WI and a snowman sign on contrast axial T1WI must not be missed for this type of tumor. An intramedullary + large extramedullary hemangioblastoma also has high cell proliferative activity based on pathological evaluation. Enlargement of this tumor probably occurs much more rapidly than that of intramedullary hemangioblastoma, and this may require careful clinical attention and early surgical intervention.

Acknowledgments The authors thank Ms. Saho Horiuchi for her assistance throughout this study.

Conflict of interest None.

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