Possible Delayed Recurrence of Sporadic Spinal Hemangioblastoma after Complete Surgical Resection: A Case Report

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INTRODUCTION

Spinal cord hemangioblastoma (HBL) is a benign, slow-growing tumor that consists of stromal cells and small blood vessels. HBL accounts for 2% to 15% of primary tumors in the spinal cord, and it arises either sporadically or in relation to von Hippel-Lindau disease (VHL). VHL is a familial neoplastic condition caused by germline mutations of the tumor suppressor gene VHL (3p25) in most cases. VHL could occur via de novo mutation of the VHL gene in approximately 20% of the cases. In VHL patients, tumors can occur in the kidneys, adrenal glands, pancreas, reproductive organs, retina and central nervous system (CNS) including spinal cord. Approximately two-thirds of spinal HBLs are sporadic, and 80% of HBLs are solitary. VHL syndrome is suspected in the presence of multiple lesions.

Surgical treatment should be considered for patients with neurologic symptoms. Complete surgical resection is usually curative, sometimes with the aid of preoperative embolization for large tumors. Recurrence has been reported in up to 25% of patients with CNS HBLs, and recurrence of sporadic HBL after gross total resection (GTR) is rare. Recurrences of sporadic HBLs have been associated with prior incomplete resection. In this study, we describe a case of multiple recurrent spinal HBLs 10 years after GTR in a patient, despite the absence of evidence of residual tumor 1 year after the operation.

CASE REPORT

A 54-year-old male patient visited the outpatient department complaining of bilateral buttock pain that had been present for 5 months. Magnetic resonance (MR) images revealed a 2.6-cm hypervascular intrathecal tumor at the L3 level, with tortuous venous engorgement from T10 to the sacrum. A spot-like lesion within the venous engorgement was observed above the tumor at L2-3 level. The tumor characteristics appeared consistent with spinal cord HBL on the basis of findings from imaging studies (Fig. 1). A spot-like lesion was noted and it was thought to be either cross section of venous engorgement or a daughter nodule.

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Fig. 1. (A) Magnetic resonance image showed a homogenous 2.6 cm sized well enhancing mass at L3 level and (B) tortuous vascular structure from T10 to sacrum is observed.
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Fig. 3. Tumor tissue obtained from the operation. Microscopic study of the tumor tissue showed stromal cells with clear foamy cytoplasm (×400 magnification, middle), and CD56 stained stromal cells (×400 magnification, right). The pathological study was consistent with a hemangioblastoma.

Fig. 4. Magnetic resonance image of 1 year from the surgery did not show any evidence of residual or recurrent tumor. The pain of the patient disappeared and he was also neurologically free.

Fig. 2. Microscopic view of the spinal hemangioblastoma. The tumor was highly vascularized and had solid multiloculated pattern. The tumor adhered to the filum terminale, showed no infiltration to surrounding tissues. The tumor was completely removed by en bloc pattern.

Upon dura incision, a 2.6-cm hard and well-demarcated mass was observed (Fig. 2). A reddish and hypervascular tumor was located in the subpial layer of the filum terminale, and total en bloc resection of the mass was performed with a clear resection margin (Fig. 3). The operative field was carefully inspected, and tumor seeding and daughter nodules were not observed. Histological examination confirmed a benign stromal tumor consistent with spinal cord HBL (Fig. 3).

The patient’s clinical symptoms improved markedly after surgery. MR images obtained on postoperative day 1 as well as 1 year after the surgery showed total resection of the tumor with no evidence of residual or recurrent tumors (Fig. 4). The spot-like lesion shown at preoperative MRI imaging around the venous engorgement was disappeared as well as solid tumor, so we could conclude that the spot lesion meant a part of venous engorgement rather than a daughter nodule.

The patient returned to our clinic complaining of pain in the right leg ten years after the surgery. An MR study of the lumbar spine showed an extraforaminal ruptured disc at L4-5 on the right side (Fig. 5), consistent with the patient’s symptoms. In addition, four well-enhancing round nodules around the L3-4 level were noted (largest, 7.8 mm; Fig. 5). The nodules were homogeneously enhanced and located along the cauda equina. Even though the mass was not pathologically confirmed, the diagnosis of delayed recurrence of HBL could be made with characteristic findings of image study. The patient underwent L4-5 discectomy by a paraspinal approach because of persistent, radiating pain despite the root block. The pain immediately alleviated after surgery. The recurrent tumors did not evoke any neurological symptoms requiring treatment. Considering associated tumors such as retinal or CNS HBL, renal cell carcinoma, pancreatic cysts, and neuroendocrine tumors. Genetic study of VHL gene could be supplemented to confirm the diagnosis. The patient had no family history of VHL syndrome; hence, possibility of VHL could be excluded.

The patient underwent laminectomy, and the tumor was exposed.
the benign nature of spinal cord HBLs, observation of the tumors through repeated follow-up imaging studies was planned. If tumor growth is noted, surgical resection or adjunctive radiotherapy can be considered as treatment options.

**DISCUSSION**

Spinal HBL is a benign, highly vascularized tumor that can occur sporadically or in relation to VHL. GTR is the treatment of choice for patients presenting with neurological symptoms. Preoperative embolization of the tumor may be considered to reduce intraoperative blood loss and shrink the tumor to facilitate surgical resection. Radiosurgery is an option for treatment in unresectable locations and remnant tumors after surgery.

VHL-related spinal HBL tends to develop multiple lesions and recurs frequently after surgery. In contrast, sporadic-type spinal HBL is a benign tumor, which is thought to rarely recur after GTR. In general, recurrence after surgery is associated with subtotal or incomplete resection.

There have been previous reports of relapsed HBL after complete surgical resection. Lee et al. reported that microscopic remnants during surgical resection or the presence of tumor cells in the cystic wall could be related to recurrence in cases of recurrent cerebellar HBL without VHL. In posterior fossa HBLs with mural nodules, remnant cystic walls from a previous operation may regrow because of diffusion of cerebrospinal fluid. In addition, the presence of multiple satellite lesions that cannot be detected in the operative field can become a cause of recurrence. The HBLs are usually hypervascular, and excessive bleeding may interfere with complete surgical excision.

Efforts to minimize residual tumors can prevent or reduce tumor recurrence. According to Gläsker et al., dissection of the tumor from the nerve sheath alone is insufficient in avoiding recurrence. Surgeons should try to identify and resect the fascicles of origin. Intraoperative fluorescence imaging, such as indocyanine green, could be useful in preventing subtotal resection of the tumor. Li et al. reported intraoperative fluorescence as helpful for effective GTR of spinal HBL, with their results showing no postoperative recurrence. Fluorescence angiography could help identify subtle lesions located in the intramedullary space.

Stereotactic radiosurgery (SRS) is also available for treating spinal HBLs. Gamma knife surgery or CyberKnife radiosurgery has been reported as a successful treatment option for remnant, inoperable, and multiple lesions in cranial and spinal HBLs. SRS for recurrent cranial HBLs has proven beneficial in both the sporadic and VHL-related types. There have been a few studies on the effects of SRS in recurrent spinal HBL cases. In a study by Ryu et al., SRS was effective in three recurrent spinal HBL cases. For patients who are not candidates for surgery, SRS can be regarded as an effective and safe treatment option to control disease and improve survival and is an attractive alternative to multiple surgical procedures.

Although surgical resection is the treatment of choice for spinal HBL, radiotherapy also plays a role. Fractionated radiotherapy could be useful in eloquent areas of the brain, intradural spinal cord lesions, or multiple tumors with extensive lesions. However, radio-
rapy has limitations such as radiotoxicity. Dose-response relationships have to be closely monitored to prevent radiotoxicity. Moreover, in multiple lesions, the effective radiation dose differs according to the histopathologic characteristics of each tumor. Therefore, radiotherapy is considered in cases of VHL-related spinal HBLs rather than in sporadic types.

Complete surgical resection of the spinal HBL is the most effective treatment to prevent a recurrence. However, tumors can still recur after GTR even in sporadic cases. Shin et al.\textsuperscript{13} reported five recurrent sporadic spinal HBL tumors in 16 patients who had undergone prior surgery. Among the five patients with recurrent tumors, three patients had undergone total resection and the others had undergone subtotal resection. The average period of recurrence from surgery was 6.4 years and ranged from 1 to 13.1 years. Sun et al.\textsuperscript{14} reported subtotal resection. The average period of recurrence from surgery prior surgery. Among the five patients with recurrent tumors, three patients had undergone total resection and the others had undergone subtotal resection. The average period of recurrence from surgery was 6.4 years and ranged from 1 to 13.1 years. Sun et al.\textsuperscript{14} reported subtotal resection. The average period of recurrence from surgery was 6.4 years and ranged from 1 to 13.1 years. Sun et al.\textsuperscript{14} reported subtotal resection. The average period of recurrence from surgery was 6.4 years and ranged from 1 to 13.1 years.

In our case, we achieved GTR of the tumor using a microscope without any evidence of residual mass in the operative field. Residual tumor masses were not observed at tumor one year after the surgery but incidentally multiple-well enhancing masses were found around the previous tumor lesion and along the cauda equina, ten years thereafter. The lesions showed vivid contrast enhancement which suggests that HBLs are recurrent. HBLs usually arise as solitary expansive masses; however, in our case, the tumor had a multilobular appearance and intermingled with multiple lumbar roots, which made surgical removal significantly more complex. In total, this delayed recurrence might be related to the subtle microscopic remnant tumor or tumor seeding that could not be identified in the operative field slowly growing over the years. Therefore, meticulous observation of the origin and remnants or satellite lesions of the tumor is necessary, especially when surgeons resected multilobular mass, to decrease the possibility of recurrence.

According to the reported articles and our case review, delayed recurrent tumors were often discovered several years after surgery. Because of the low recurrence rate and slow growth, recurrence may be described as having a delayed pattern. Therefore, after total resection of HBLs, even in sporadic cases, follow-up imaging studies should be continued for a long time. In particular, if preoperative HBLs consist of high-risk factors for recurrences, such as VHL syndrome, cysts, and a multilobular shape, careful long-term follow-up is necessary. Considering the reported cases, follow-up could be conducted for up to 10 to 15 years after the surgical excision.

The limitation of this study is that there were few long-term follow-up studies on spinal cord HBL surgery to suggest guidelines for the imaging study follow-up. More cases need to be supplemented. Also, the recurrence was found ten years after the surgery in our case. The only prior imaging study was performed one year after the surgery; due to the time gap of the imaging studies, we cannot specify the exact time of recurrence. In addition, since the patient did not show any neurologic symptoms related to recurrent lesions, we did not perform a second operation to confirm the pathologic diagnosis. The diagnosis of recurrence HBLs was made based on consistent radiological findings. We could not completely rule out newly developing VHL syndrome because we did not check VHL gene study. Longer follow-up and additional imaging studies are planned to surveil the tumor growth. We plan to conduct a genetic study to exclude VHL syndrome if the tumor grows as large as the need for surgery in the future.

**CONCLUSION**

Complete surgical excision is the treatment of choice for spinal cord HBL. Delayed recurrence may be observed even after GTR in sporadic cases. Long-term follow-up should be performed, and resection surgery or radiosurgery can be considered in cases of symptomatic recurrence.

**CONFLICTS OF INTEREST**

No potential conflict of interest relevant to this article was reported.

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