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Case report

DE NOVO FORMATION OF HIGH-GRADE GLIOMA AFTER TOTAL REMOVAL OF HEMANGIOBLASTOMA

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Abstract

Hemangioblastomas are the most common adult primary intra-axial tumors located in the posterior fossa. They may occur sporadically, or in combination with tumors of internal organs, which is typical for von Hippel-Lindau disease. Hemangioblastomas are histologically benign tumors. The most common location of hemangioblastomas is the posterior fossa. The supratentorial location is very rare. These tumors may also occur in the spinal cord (1.5-2.5% of spinal cord tumors). However, 20-38% of hemangioblastomas occur as a part of von Hippel-Lindau disease. The reported cases about recurrence of totally removed hemangioblastomas are rare and there are no reported cases about its malignant transformation.

This report presents a case of a patient treatment who initially presented with a posterior fossa hemangioblastoma. The patient underwent surgery, and the tumor was completely removed. One year after the initial surgery, the patient presented again with a recurrent hemangioblastoma in the area of the previous surgical site. The surgery was repeated, and the tumor was totally resected. Two years after the second surgery, follow-up studies did not reveal any tumor recurrence. However, three years after total resection of the recurrent hemangioblastoma, the patient presented with similar symptoms. At this time, the final histological diagnosis from the third surgery was consistent with high-grade glioma. The patient was referred to radiation therapy to receive whole brain radiation. A two-year follow-up revealed a small recurrent tumor in the right cerebellar hemisphere, which did not require additional resection.

Keywords: *hemangioblastoma, recurrence, malignant transformation, high-grade glioma.*

Hemangioblastomas are histologically benign tumors, which are most commonly located in the posterior cranial fossa and spinal cord. They may occur sporadically, or as a part of von Hippel-Lindau disease [*Boström A et al., 2008; Takeuchi H et al., 2008*].

The reported cases about recurrence of totally removed hemangioblastomas are rare. The recurrence rates after resection of central nervous system hemangioblastoma is estimated to be between 20 to 33%. Partially removed tumors usually recur in all cases. The risk factors of recurrence of completely removed hemangioblastomas include young age (<30 years) at diagnosis and an association with von Hippel-Lindau disease [*Conway J et al., 2001; Sumida M et al., 2004; Cavaliere R, 2006; Jarrell S et al., 2006; Jagannathan J et al., 2008*]. There are only a few reports about recurrence of hemangioblastomas even in patients after 20 years from the initial total removal of the tumor [*Sumida M et al., 2004; Hanse M et al., 2007; Zilidis G, Cadoux-Hudson T, 2007; Boström A et al., 2008*].

There are no reports in the literature about malignant transformation of hemangioblastoma to high-grade glioma. However, it is well established that hemangioblastomas are an early and preferred site for tumor-to-tumor metastases in von Hippel-Lindau disease from other visceral malignancies. This occurs quite often in this disease. Metastasis to

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the central nervous system hemangioblastoma was found in 8% of resected hemangioblastomas from patients with von Hippel-Lindau disease [*Jarrell S et al., 2006*]. The explanation for this phenomenon may be due to the high vascularity of these lesions compared to other primary brain neoplasms.

In regards to high-grade gliomas, the cerebellar hemisphere appears to be a relatively uncommon location particularly for patients of advanced age. The combination of prior totally resected hemangioblastomas and "de novo" glioblastoma seems to be quite unusual. This is of particular interest especially in patients without prior radiation therapy. Moreover, both hemangioblastomas and glioblastomas have a high-level expression of vascular endothelial growth factor-A, which is suggestive of some histological similarities of these tumors [*Jenny B et al., 2006*].

Some authors affirm that radiosurgery of benign tumors can potentially cause malignant transformation of the tumor, especially in young patients [*Evans D et al., 2006*]. However, long term follow-up of a large group of patients treated with radiosurgery showed no difference of malignant transformation of benign tumors compared with those treated without radiation therapy [*Wang E et al., 2004; 2005; Kubo O et al., 2005; Rowe J et al., 2007*].

This report presents a case of a patient treatment who initially presented with a posterior fossa hemangioblastoma.

CASE REPORT

A 75-year-old woman was admitted to the Georgia Neurosurgical Institute complaining of difficulties with balance that began 2-3 months before her admission to the hospital. She also complained of headaches, but did not have associated nausea or vomiting. In addition, according to the relatives, she started having difficulties with concentration and memory. Neurological examination on admission revealed bilateral cerebellar ataxia. The MRI of brain with contrast revealed a 3.1×3.8×3.9 *cm* mass lesion in the right cerebellar hemisphere with perifocal edema, partial compression and displacement of the fourth ventricle. The patient underwent a suboccipital craniotomy and microscopic resection of the cerebellar tumor. The tumor was brownish and very hemorrhagic. Good margins were obtained at least laterally and inferiorly. The tumor

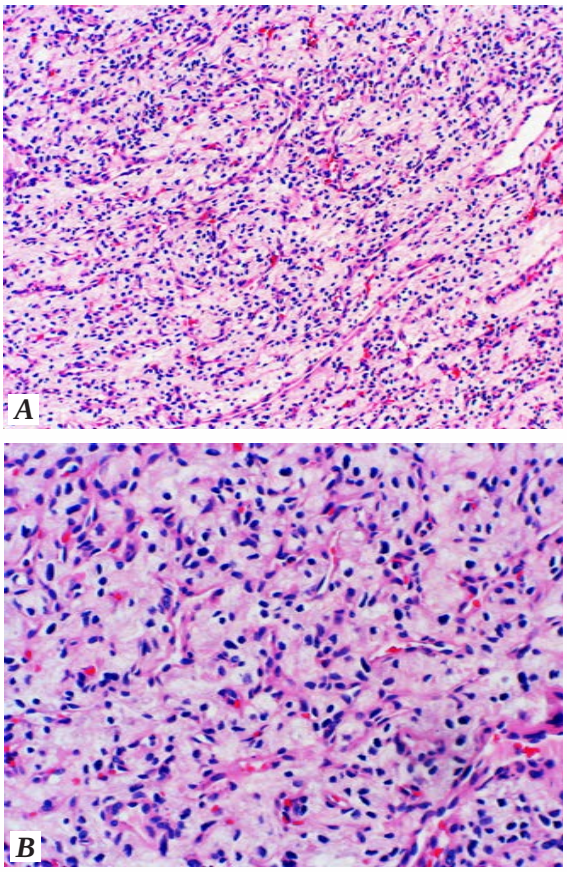

FIGURE 1. *Histological analysis of the intraoperative tumor taken during the first operation*
*Note: Increased by 10 (**A**) and 20 (**B**) times*

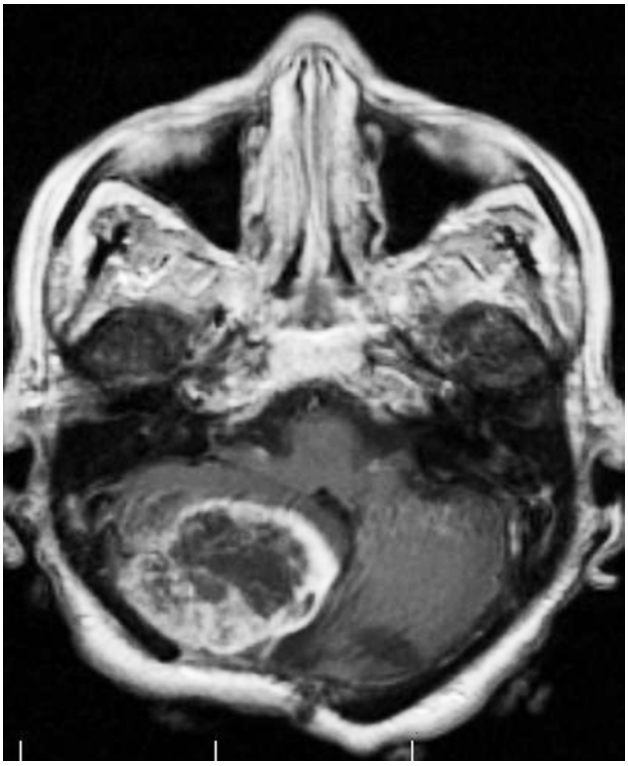

FIGURE 2. *MRI of the brain demonstrates recurrent tumor of posterior fossa*

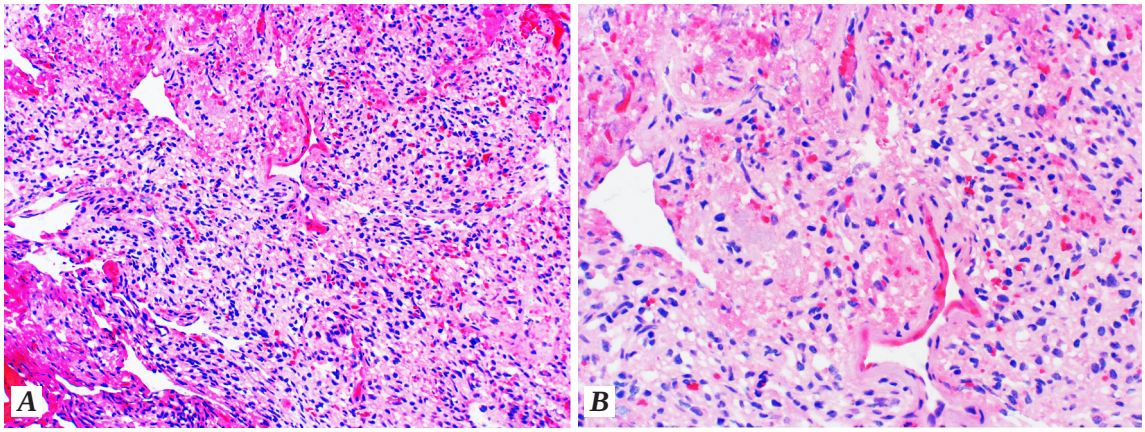

Figure 3. *Histological analysis of the intraoperative tumor taken during the second operation Note: Increased by 10 (**A**) and 20 (**B**) times*

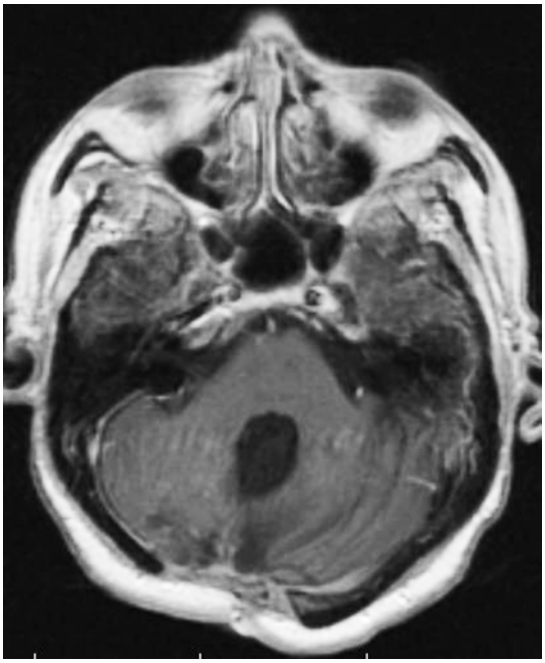

Figure 4. *Postoperative MRI shows no residual tumor*

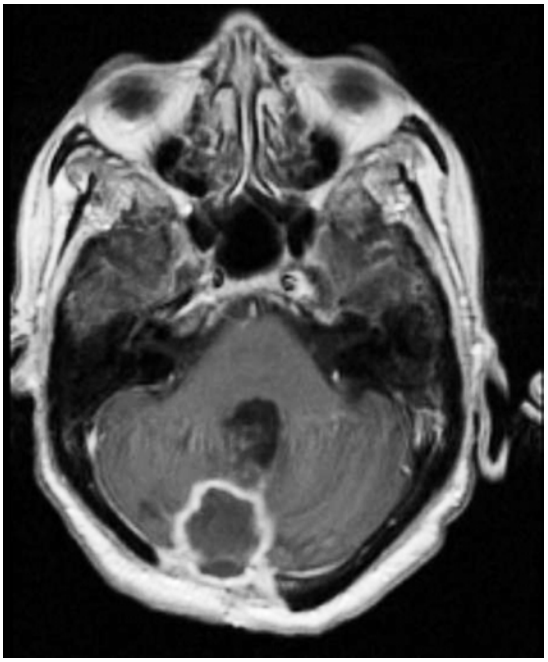

Figure 5. *MRI of the brain two years after the removal of recurrent hemangioblastoma*

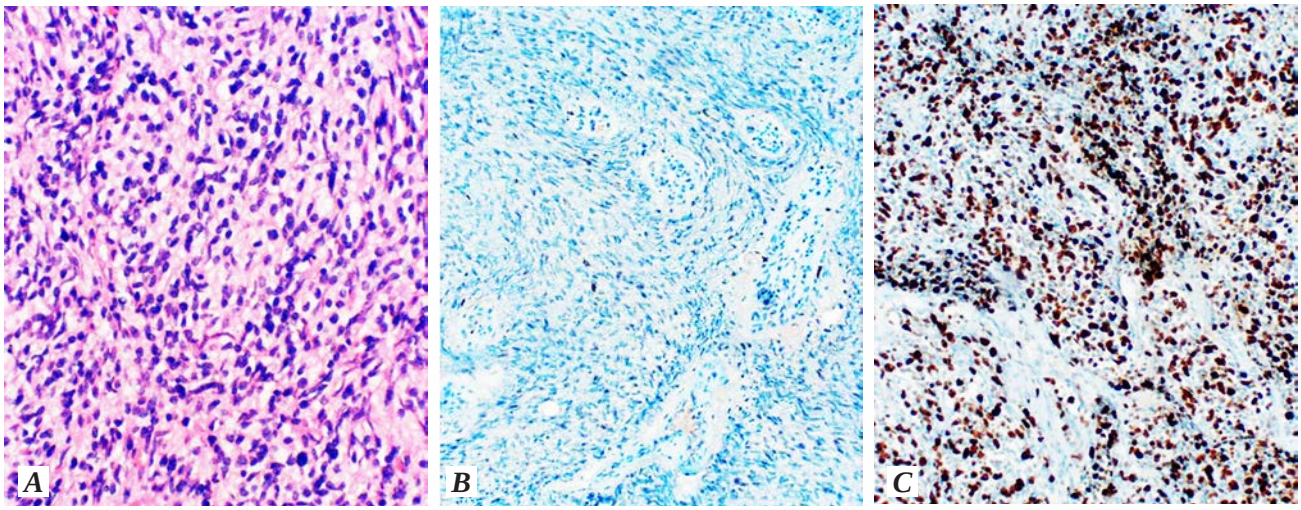

Figure 6. *Histological analysis of the intraoperative tumor taken during the third operation, (**A**) increased by 20 times, (**B**) - P53 and (**C**) - inhibin, increased by 10 times*

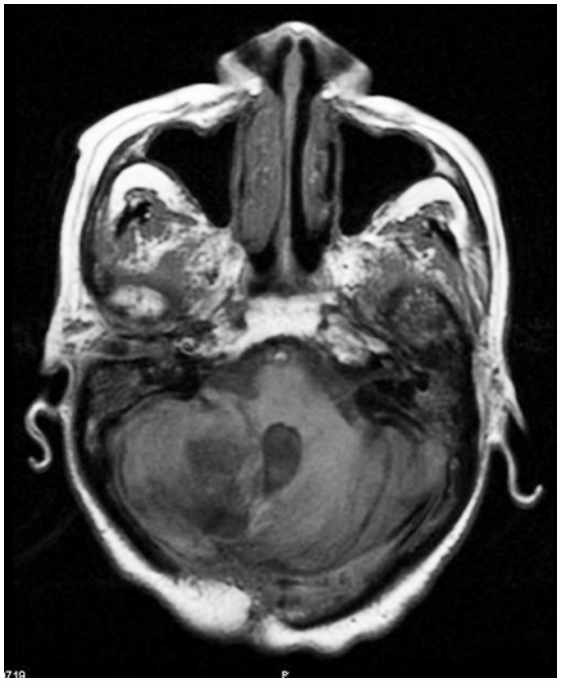

FIGURE 7. MRI of the brain, which shows a small recurrent tumor

was completely resected. There were no postoperative complications. The final pathology report was consistent with hemangioblastoma (Fig. 1). The patient experienced progressive neurological improvement after surgery. Postoperative imaging studies showed no residual lesion.

One year later, the patient presented with similar complaints. The MRI of brain with and without contrast showed a large mass measuring up to 4.3 *cm* in the area of the previous craniotomy with worsening mass effect, midline shift, and compression of fourth ventricle causing secondary hydrocephalus (Fig. 2). The neurological examination revealed bilateral cerebellar signs with a very ataxic gait. Re-exploration of occipital area using microscopic technique was performed. The entire neoplasm was again separated from surrounding tissue and removed. Final histological diagnosis was again consistent with hemangioblastoma (Fig. 3). Postoperative MRI did not reveal residual tumor (Fig. 4). On her postoperative follow-up visits, the patient improved from a neurosurgical standpoint. Her headaches and cerebellar signs improved significantly. A two year follow-up MRI showed only postoperative findings.

On December 2013, two years after the previous surgery, the patient presented once again with complaints of headaches, some tremors in her right arm, and occasionally slurred speech. Brain MRI with contrast enhancement revealed 42×58 *mm* heterogeneously enhancing right cerebellar hemisphere with mass effect on the brainstem and fourth ventricle (Fig. 5). In January 2014, she underwent a re-exploration of the previous posterior craniotomy sites with microscopic dissection and resection of a large neoplasm. At this time, subtotal resection of neoplasm was performed. The final histological diagnosis was grade IV astrocytoma (glioblastoma) (Fig. 6).

After the surgery the patient was referred to radiation therapy to begin whole brain radiation therapy. She denied complaints of headaches, but did complain of some blurry vision. Two years following her third surgery, a postoperative MRI revealed a small recurrent tumor in the right cerebellar hemisphere, which did not require additional resection (Fig. 7). Currently, the patient uses a wheelchair. The neurological examination reveals a significant tremor in the right arm with cerebellar ataxia.

REFERENCES

1. *Boström A, Hans FJ, Reinacher PC, Krings T, Bürgel U., et al.* Intramedullary hemangioblastomas: timing of surgery, microsurgical technique and follow-up in 23 patients. Eur Spine J. 2008; 17(6): 882-886.
2. *Cavaliere R.* Central nervous system disseminated hemangioblastoma treated with thalidomide. Abstracts for the Eleventh Annual Meeting of the Society for Neuro-Oncology: TA-07. November 16-19, 2006.
3. *Conway JE, Chou D, Clatterbuck RE, Brem H, Long DM, Rigamonti D.* Hemangioblastomas of the central nervous system in von Hippel-lindau syndrome and sporadic disease. Neurosurgery. 2001; 48(1): 55-62.
4. *Evans DG, Birch JM, Ramsden RT, Sharif S, Baser ME.* Malignant transformation and new primary tumors after therapeutic radiation for benign disease: substantial risks in certain tumor prone syndromes. J Med Genet. 2006; 43(4): 289-294.

5. *Hanse MC, Vincent A, van den Bent MJ.* Hemangioblastomatosis in a patient with von Hippel-Lindau disease. J Neurooncol. 2007; 82(2): 163-164.

6. *Jagannathan J, Lonser RR, Smith R, DeVroom HL, Oldfield EH.* Surgical management of cerebellar hemangioblastomas in patients with von Hippel-Lindau disease. J Neurosurg. 2008; 108(2): 210-222.

7. *Jarrell ST, Vortmeyer AO, Linehan WM, Oldfield EH, Lonser RR.* Metastases to hemangioblastomas in von Hippel-Lindau disease. J Neurosurg. 2006; 105(2): 256-263.

8. *Jenny B, Harrison JA, Baetens D, Tille JC, Burkhardt K., et al.* Expression and localization of VEGF-C and VEGFR-3 in glioblastomas and hemangioblastomas. J Pathol. 2006; 209(1): 34-43.

9. *Kubo O, Chernov M, Izawa M, Hayashi M, Muragaki Y., et al.* Malignant progression of benign brain tumors after gamma knife radiosurgery: is it really caused by irradiation? Minim Invas Neurosurg. 2005; 48(6): 334-339.

10. *Rowe J, Grainger A, Walton L, Silcocks P, Radatz M, Kemeny A.* Risk of malignancy after gamma knife stereotactic radiosurgery. Neurosurgery. 2007; 60(1): 60-65.

11. *Shin DA, Kim SH, Kim KN, Shin HC, Yoon DH.* Surgical management of spinal cord haemangioblastoma. Acta Neurochir (Wien). 2008; 150(3): 215-220.

12. *Sumida M, Taguchi H, Eguchi K, Kuroki K, Murakami T, Akimitsu T.* [Multiple recurrences of cerebellar hemangioblastoma after 20 years from initial total removal of the tumor] [Published in Japanese]. No Shinkei Geka. 2004; 32(3): 263-268.

13. *Takeuchi H, Hashimoto N, Kitai R, Kubota T.* A report of supratentorial leptomeningeal hemangioblastoma and a literature review. Neuropathology. 2008; 28(1): 98-102.

14. *Wang EM, Pan L, Wang BJ, Zhang N, Zhou LF., et al.* The long-term results of gamma knife radiosurgery for hemangioblastomas of the brain. J Neurosurg. 2005; 102: 225-229.

15. *Wang EM, Wang BJ, Zhang N, Pan L, Dong YF., et al.* [Analysis of the results of gamma knife radiosurgery for hemangioblastomas of the brain and the factors related to the tumor recurrence] [Published in Chinese]. Zhonghua Yi Xue Za Zhi. 2004; 84(10): 813-817.

16. *Zilidis G, Cadoux-Hudson TA.* Recurrent dural based cystic cerebellar haemangioblastoma in a patient with von Hippel-Lindau disease. Acta Neurochir (Wien). 2007; 149(4): 433-436.