Case Report

Recurrence of Cystic Part of Cerebellar Hemangioblastoma at Early Postoperative Period and its Spontaneous Resolution: A Pregnant Patient With Serial Magnetic Resonance Imaging Findings

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Summary

We report a patient with cerebellar hemangioblastoma who was operated during her seventh month of pregnancy. The patient underwent operation during which the mural nodule was removed and cyst aspirated but the cyst wall was not. At 17th day after operation, the cystic part of the mass recurred. She was not reoperated and a conservative approach was adopted. During follow-up, magnetic resonance imaging showed spontaneous resolution of the cerebellar cystic lesion. The mechanism for recurrence and spontaneous resolution of the cystic part of the tumor is discussed.

Key words: Cerebellum, hemangioblastoma, magnetic resonance imaging, pregnancy, spontaneous resolution

Erken Postoperatif Dönemde Serebellar Hemanjioblastomun Kistik Bölümünün Tekrarlaması ve Onun Kendiliğinden Kaybolması: Gebe Bir Hastada Seri Manyetik Rezonans Görüntüleme Bulguları

Özet


Anahtar Kelimeler: Serebellum, hemanjioblastoma, manyetik rezonans görüntüleme, gebelik, kendiliğinden kaybolma

INTRODUCTION

Pregnancy has been found to be an aggravating factor for hemangioblastoma. Possible reasons for the increase in size of the hemangioblastoma during pregnancy are expansion of the tumor vascular bed due to increased maternal blood volume, hormonal influence of the tumor and finding of progesterone receptor protein in the tumor.¹¹,¹⁶,²¹ Our pregnant patient with cerebellar hemangioblastoma underwent total removal of solid nodule and aspiration of cyst and then the cyst and symptoms rapidly recurred. She was neither reoperated nor antiedema drugs were given. The cyst resolved at follow-up. Recurrence and spontaneous resolution of
the cystic part of the tumor was shown by serial magnetic resonance imaging (MRI), and the mechanism of this condition is discussed.

**CASE PRESENTATION**

A 28-year-old woman on her seventh month of pregnancy presented with vomiting and vertigo. On examination she was fully orientated, and had no neurological abnormalities other than papilla edema. MRI of the brain demonstrated a 5x5 cm cystic lesion in the left cerebellar hemisphere and vermis with a 1 cm enhancing nodule at the superior-posterior wall. The fourth ventricle was compressed by the mass and obstructive hydrocephalus was evident. In addition, MRI showed several intensely enhancing nodular lesions in the right cerebellum, the largest was approximately 1 cm in size (Figure 1A, B, C, D). A left suboccipital craniectomy was performed at sitting position. A Y-shaped dural incision is made. The posteriorly and superiorly located mural nodule was totally excised. A peritumoral cyst, containing yellow serous fluid, was aspirated. Cyst wall was not excised. Dura mater is water-tight sutured closed. The wound is closed in layers. Pathologic examination of the tumor revealed thin-walled capillary vessels mixed with stromal cells, consistent with hemangioblastoma. She had no family history or clinical stigmata to suggest the presence of von Hippel-Lindau (VHL) disease. Ocular examination showed no other VHL-associated lesion. Obstetricians consulted the patient and no problem was found in her pregnancy. Postoperative MRI of the brain, on day four, revealed postsurgical changes of the cerebellar tissues including a small hematoma and complete excision of the cyst and mural nodule (Figure 2A, B). Cerebrospinal fluid leaks and pseudomeningocele formation did not occur after operation. On the eight day after surgery, she was discharged with good condition. Nine days later (at postoperative 17th day) she presented again with headache and vomiting. On examination, there was no neurological deficit. Cranial MRI showed that the cyst in the left cerebellar hemisphere had recurred, measuring 4x4 cm. A small hematoma, due to operation, was also noted in the anterior wall of the cyst. There was no increase in ventricular size. (Figure 3A, B, C). She was then admitted to our department, where a conservative approach was adopted. No surgery was applied, she was only observed clinically. At 24th day after operation, repeat cranial MRI revealed that left cerebellar cystic lesion had increased in size. This lesion had surrounding edema with mass effect and compression of the fourth ventricle. There was no hydrocephalus (Figure 4A, B, C). Since she had no neurological deficit, surgery was not performed. Antiedema drugs (steroid and/or mannitol) were not given because of continuing pregnancy. Symptoms disappeared ten days later and she was discharged. Patient after discharge from frequent communication and change whether a case has been checked. She subsequently delivered a healthy child at term. After the delivery (seventy days after the operation), a computed tomography (CT) of the brain and abdomen were performed. CT of the brain revealed a significant decrease in the size of the lesion (Figure 5). CT of the abdomen showed no abnormal findings for VHL-disease. MRI obtained 3 months after the operation showed a decrease in the size of the left cerebellar cystic lesion (Figure 6A, B, C). It continued to decrease in size, as demonstrated by MRI obtained 3 months later MRI, obtained 10 months and 2 years (Figure 7A, B, C, D) after operation, showed small residual cyst at the operation site without any enhancing mural nodule. Enhancing nodular hemangioblastomas in the right cerebellum remained unchanged during follow up.
Figure 1: Cerebellar hemangioblastomas at presentation. T1-weighted axial (A) and T2-weighted axial (B) MR images show a 5x5 cm cystic lesion in the left cerebellar hemisphere and vermis. Contrast-enhanced T1-weighted sagittal (C) and T1-weighted axial (D) images demonstrate a 1 cm enhancing mural nodule of the superior-posterior wall of the left cerebellar cystic lesion. Contrast-enhanced axial image shows several additional solid hemangioblastomas as enhancing small nodules in the right cerebellar hemisphere. The fourth ventricle is compressed by the tumor.

Figure 2: Four days after operation. T1-weighted (A) and T2-weighted (B) axial images show total removal of the mural nodule and cyst aspiration as well as postsurgical changes. The cyst wall was not removed during surgery.
**Figure 3:** Seventeen days after operation. T1-weighted sagittal (A), axial (B) and T2-weighted axial (C) images show that the cyst has recurred, measuring 4x4 cm. A small hematoma due to operation is also noted in the anterior wall of the cyst.

**Figure 4:** Twentyfour days after operation. T1-weighted sagittal (A), axial (B) and T2-weighted axial (C) images show that the left cerebellar cystic lesion has increased in size. This lesion has surrounding edema with mass effect and compression of the fourth ventricle.

**Figure 5:** Seventy days after operation (after the delivery). CT of the brain showing a significant decrease in the size of the lesion.
DISCUSSION

Hemangioblastomas are 2007 World Health Organization Working Group grade 1 tumors of borderline or uncertain behaviour that occur most commonly in the posterior fossa. These tumors were categorised "other neoplasms related to the meninges"(14). Hemangioblastomas are benign vascular lesions and account for 1 to 2% of primary intracranial tumors. They are approximately make up 5-15% of all posterior fossa tumors in adults. It may occur sporadically (66% of cases) or in association with VHL disease (33% cases). Solitary hemangioblastomas occur sporadically in the absence of family history, whereas VHL-associated hemangioblastomas are usually multiple and associated with additional retinal, brain stem, spinal cord, and/or lumbosacral nerve root hemangioblastomas as well as visceral neoplasms and benign lesions(9,12). The average age at onset of symptoms in VHL cases is 33 years(9,23). Sporadic cases of hemangioblastoma tend to present later, with a mean age at presentation of 42 years(1). These tumors are more common in men(12). Our patient is likely to represent sporadic case, as there was no relevant family history and none of the other features seen in VHL was noted. The mean age of sporadic disease is 42 years and this patient presented when she was 28 years old.

When associated with pregnancy, these tumors can grow quickly and symptoms may occur. Many theories have been proposed to explain neurological deterioration seen in hemangioblastoma patients. However, pathophysiologic

Figure 6: Three months after operation. Contrast-enhanced T1-weighted sagittal (A), T1-weighted axial (B) and T2-weighted axial (C) images show a decrease in the size of the cyst. Compression of the fourth ventricle is also decreased.

Figure 7: Two years after operation. T1-weighted axial (A), T2-weighted axial (B), contrast enhanced sagittal (C), and axial (D) images show a small residual cyst without mural nodule. Additional hemangioblastomas in the right cerebellar hemisphere remained unchanged during follow up.
behavior and histogenesis of this disease is still not adequately understood. Plasma volume and cardiac output increases during pregnancy. These changes depend on increased production of oestrogen and progesterone by the trophoblast. Possible theories for the increase in size of the hemangioblastoma during pregnancy are: expansion of the tumor vascular bed due to increased maternal blood volume, hormonal influence of the tumor and finding of progesterone receptor protein in the tumor. Some patients spontaneously improve after delivery in the literature. We speculated that a critical size of the tumor was present before pregnancy in our patient and then rapidly became symptomatic due to vascular engorgement or hormonal influences of the tumor itself in gestation.

Hemangioblastomas may be purely cystic (5%), purely solid (26%), cyst with a mural nodule (60%) and solid tumor with internal cysts (9%) [17]. In our patient, there was a cyst with a mural nodule. Pathogenesis of the cysts is still not well understood. The cyst fluid contains amino acid, nitrogen, mucoprotein and alkaline phosphate levels similar to that of blood, suggesting that the cyst fluid arises by diffusion from the vascular component of the mural nodule [18]. Lonser et al. demonstrated with study of 16 VHL patients with 22 hemangioblastomas the protein profiles of peritumoral cyst fluid and serum were similar [13]. Also, the mean vascular endothelial growth factor levels determined in peritumoral cysts was 1.5 ng/ml (range, 0.5-4 ng/ml). These authors showed that histological analysis of the cyst walls was consistent with reactive gliosis devoid tumor cells. Peritumoral cysts develop as a result of a tumor interstitial process that begins with generation of edema. Increased tumor vascular permeability, increased interstitial pressure in the tumor and/or hydrodynamic forces within tumor vasculature promotes plasma extravasation. When these forces overcome the ability of adjacent tissue to resorb fluid, edema and subsequent cyst formation occur [3,13]. Van Velthoven et al. hypothesized that transudation of fluid from the tumor capillaries and tubular dissection along the gray matter near the central canal are the main pathophysiological mechanisms for brain stem and spinal cord hemangioblastomas [20]. The cyst wall generally does not enhance on contrast administration and the enhancement indicates neoplastic extension along the cyst wall [15]. Bishop et al. presented the case of a VHL patient with a cystic cerebellar hemangioblastoma that recurred twice after removal of the nodule and drainage of the cyst. The cyst wall was excised in the third operation. The cyst wall contained tumor with the same histopathological pattern observed in the nodule. Besides, the enhancing cyst wall contained vascular endothelial growth factor-expressing hemangioblastoma cells intermixed with gliosis [3]. Our patient’s MRI scans did not demonstrate nodular enhancement of the cyst wall.

Symptoms of cerebellar hemangioblastomas depend on the tumor’s size and location [2,22]. Serial MRI studies of patients with hemangioblastomas have shown that cyst formation can arise from solid tumor [13,17]. Solid cerebellar nodules are well tolerated and the onset of symptoms heralds the development of such cysts [17,23]. The rate of cyst growth is typically much greater than the rate of tumor growth [25]. Ammerman et al. analyzed that the serial clinical and MRI findings in 19 patients with VHL disease (total 143 hemangioblastomas; 68 hemangioblastomas were located in the cerebellum) who were followed up for more than 10 years. The combined tumor and cyst growth rates and the combined tumor and cyst sizes are the significant predictors of symptoms development for hemangioblastomas in the cerebellum [3]. Simple cyst drainage is an inadequate therapy. Total removal of the solid nodule...
is mandatory to avoid tumor recurrence. The cyst may be entered during tumor resection, but additional removal of the cyst wall is not necessary\(^{(8,9,22)}\).

Jagannathan et al. in serial MRI studies (60 patients; 126 operations for 164 cerebellar hemangioblastomas; 91 hemangioblastoma-associated peritumoral cysts) demonstrated that tumor resection produced collapse or complete disappearance of the associated peritumoral cyst. Cyst wall removal was not performed in any case. Because the tumor is the source of the cyst, simply removing the tumor elicits cyst collapse. Significant reduction in cyst size within 24 hours of tumor removal and maximal or complete collapse within 24 weeks of removal was noted in all cases. Also, these authors announced that there was no case fluid reaccumulation in peritumoral cysts after resection of the hemangioblastoma associated with the cyst\(^{(9)}\). Vougioukas et al. recommended the surgical removal of symptomatic and asymptomatic tumors with validated radiological size progression\(^{(22)}\). Nearly all of the tumors (Ammermann’s above-mentioned article) studied showed radiographic progression but only half went on to require therapy. Thus, neither presence of tumor nor radiographic progression is an indication for therapy. Asymptomatic tumors should be followed with serial imaging at regular intervals\(^{(22)}\). In the second admission to hospital we did not recommend surgery to our patient. Cyst had grown but there was no mural nodule. There were no clinical and neurological signs of raised intracranial pressure. Antiedema drugs (steroid and/or mannitol) were not given because of continuing pregnancy. Symptoms such as headache and vomiting quickly disappeared. The patient remained neurological intact during hospitalization and discharge home.

In the literature, recurrence has ranged from 20-33\%\(^{(5-7,10,19)}\). De la Monte and Horowitz documented that an age of less than 30 years on initial diagnosis, the presence of VHL disease, and a multicentric involvement of the central nervous system are independent predictors of hemangioblastoma recurrence\(^{(7)}\).

Our patient underwent total removal of the solid nodule and aspiration of cyst without cyst wall excision, but unfortunately, the cyst and symptoms rapidly recurred. We believe that recurrence of the cyst was due to transudation of fluid from the cyst wall capsule during pregnancy. Cyst collapse may be result of the absence of cystic wall fluid excretion because of changes in the hormonal system after birth. In the surgery of cystic cerebellar hemangioblastoma, excision of the cyst capsule together with cyst drainage and excision of the mural nodule may be necessary. When a cyst is seen to be developing and enlarging right after surgery, repeat surgery should be avoided, since spontaneous resolution is possible for pregnancy, as demonstrated by our case report. Also, because of the spontaneous resolution of the cyst for pregnant patient mentioned above, in the patients who do not have neurological deficit or are asymptomatic, the first preference should be a conservative approach.

**CONCLUSION**

We report the recurrence of the cystic part of cerebellar hemangioblastoma in a pregnant patient after cyst aspiration and mural nodule excision. Serial MRI has convincingly demonstrated the recurrence and spontaneous resolution of the cyst. Reoperation should be avoided when the cyst recurs, because spontaneous resolution is possible for pregnant patient, as demonstrated by our case report. Excision of the cyst capsule together with cyst drainage and excision of the mural nodule may be necessary.

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REFERENCES


