

## 소뇌의 세포충실성 혈관모세포종의 압착도말 세포소견

성균관대학교 의과대학 삼성서울병원 병리과

오 영 루 · 서 연 림

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= Abstract =

### The Cytology of a Cellular Variant of Cerebellar Hemangioblastoma in Squash Preparation: Pitfalls in Diagnosis

Young Lyun Oh and Yeon-Lim Suh

Department of Pathology, Samsung Medical Center,  
Sungkyunkwan University School of Medicine, Seoul, Korea

Due to its nuclear pleomorphism, knowledge regarding the cytological findings of cerebellar hemangioblastoma can lead to misdiagnosis when using squash specimens, which in other circumstances serves as a useful adjunct in the diagnosis of brain tumors on frozen section. We recently experienced the cytological findings of a cellular variant of cerebellar hemangioblastoma in a 51-year-old man. Squash specimens revealed scattered single tumor cells, with pleomorphic nuclei and cytoplasmic vacuoles, on a hemorrhagic background. The cellular clusters were composed of spindle-shaped endothelial cells in addition to densely clustered stromal cells. Intranuclear inclusions were frequently seen. The nuclear pleomorphism, bubbly cytoplasmic vacuoles and presence of intranuclear inclusions, seen in the squash specimen, may increase the difficulty of frozen section diagnosis of cerebellar hemangioblastoma. Awareness of the cytological findings of hemangioblastoma is needed to avoid the pitfalls in the intraoperative diagnosis of cerebellar hemangioblastomas.

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**Key words:** Cerebellar hemangioblastoma, Cellular, Cytology, Pitfall, Squash preparation

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책임저자 : 오 영 루  
주 소 : (135-710) 서울시 강남구 일원동, 성균관대학교 의과대학 삼성서울병원 병리과  
전 화 : 82-2-3410-2805  
팩 스 : 82-2-3410-0025  
E-mail address: yloh@smc.samsung.co.kr

## INTRODUCTION

Hemangioblastomas are highly vascular tumors of uncertain origin and are frequently associated with cystic degeneration. They develop preferentially in the cerebellum, medulla and spinal cord. Histologically, the tumor is composed of capillary networks and intervascular stromal cells.<sup>1,2</sup> Although the histological features of hemangioblastoma are well described, its frozen section diagnosis is often difficult due to artifact.<sup>1</sup> The cytological features obtained by squash preparation are valuable as an adjunct to frozen section diagnosis of brain tumors.<sup>3</sup> However, there are few reports describing the cytological findings of hemangioblastomas, especially the cellular variant.<sup>4,5</sup> This paper reports the cytological features of a hemangioblastoma evaluated by a squash preparation.

## CASE

### Clinical Presentation

A 51-year-old man had a history of headache and dizziness for a two month duration and complained of a weight loss of 22 lbs. The neurological examination showed a positive Romberg sign and difficulty with tandem gait. A brain magnetic resonance imaging (MRI) scan revealed a contrast-enhancing solid mass with a central cystic portion in the left cerebellum (Fig. 1). Radiologically, either a metastatic tumor or a glioblastoma was suspected. In addition to the cerebellar mass, two discrete nodules of about 4 mm diameter were identified in both upper lobes of the lung by the computerized tomography (CT) of the chest. Abdominal and pelvic CT showed a simple cyst in the left kidney. There was no evidence of bone metastasis by bone scan (Tc-99m MDP) evaluation. Serum levels of alpha-fetoprotein, carcinoembryonic antigen and prostate specific antigen were within normal limits. At surgery, a relatively well-demarcated, solid and hemorrhagic mass was observed in the cerebellar vermis. Both squash preparation and cryostat sections were per-

formed for intraoperative evaluation and diagnosis.

### Cytological Findings

The smeared slides were fixed immediately in 95% alcohol for 2 minutes, followed by rapid hematoxylin-eosin stain. The cytological smears revealed many single cells, as well as clusters, on a hemorrhagic background (Fig. 2A and 2B). Most cells had large, oval-to-reniform or pleomorphic nuclei with that were hyperchromatic (Fig. 3). Nucleoli and mitosis were rarely observed. Intranuclear inclusions of variable size were occasionally seen (Fig. 4). Cytoplasm was abundant and granular, often containing small cytoplasmic vacuoles (Fig. 5). Spindle-shaped cells were observed in a few tight cellular clusters (Fig. 6). The frozen sections also revealed large cellular lobules with nuclear pleomorphism. The initial frozen section diagnoses included malignant glioma or metastatic carcinoma, such as the sarcomatoid variant of renal cell carcinoma. However, the characteristic reddish coloration that reflected a rich vasculature led us to note a delicate vascular network that was obscured by frozen artifact. In addition, the absence of a known renal tumor, the nuclear features with chromatin smudging, and the lack of mitotic activity favored the possibility of a hemangioblastoma.

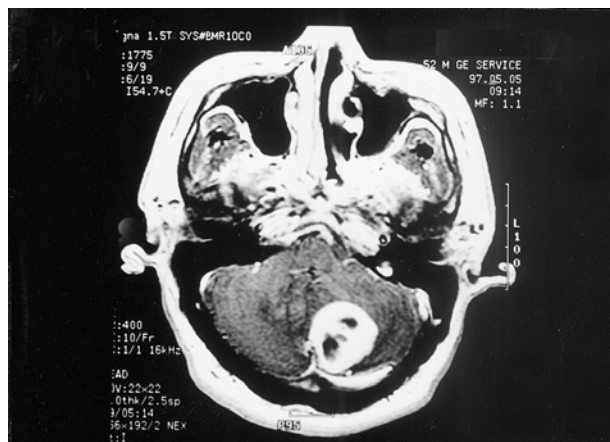


Fig. 1. A brain MRI scan showing a highly enhanced solid lesion in the cerebellum.

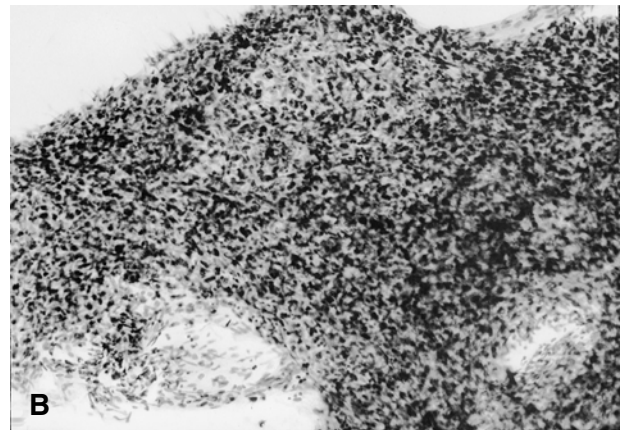
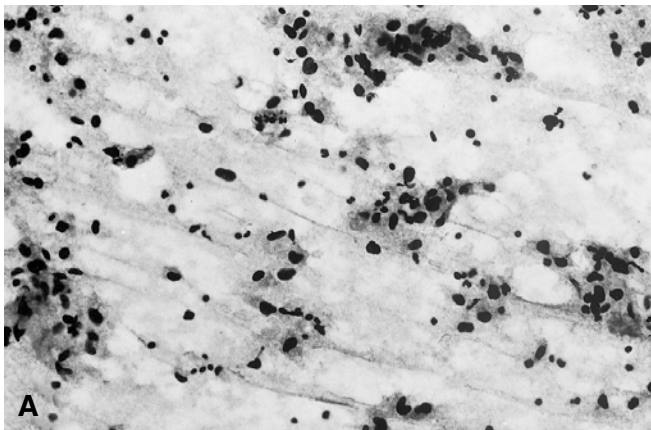


Fig. 2. Low power view of cytology showing many single cells (A) and cellular clusters (B) on a hemorrhagic background. (H-E)

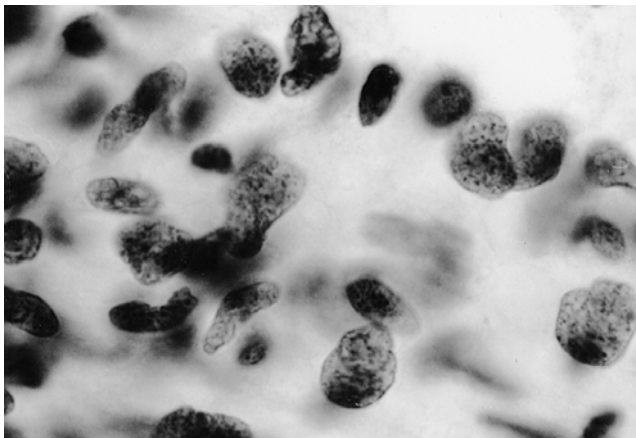


Fig. 3. Single stromal cells with hyperchromatic, pleomorphic nuclei and indistinct nucleoli. (H-E)

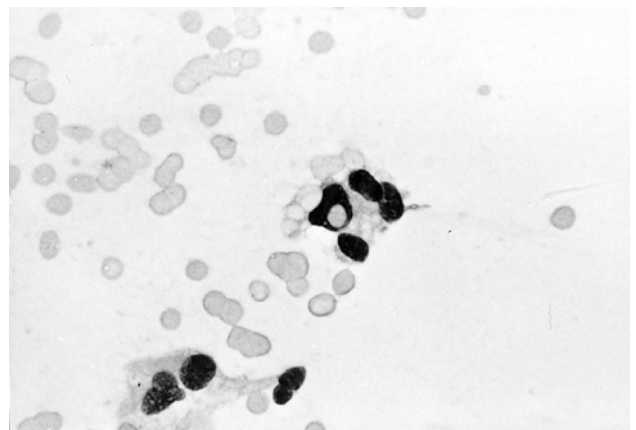


Fig. 4. Tumor cells frequently show intranuclear inclusions. (H-E)

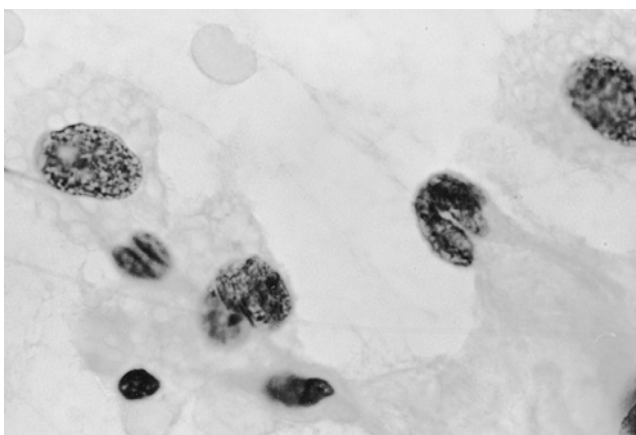


Fig. 5. Most of the tumor cells have abundant cytoplasmic vacuoles. (H-E)

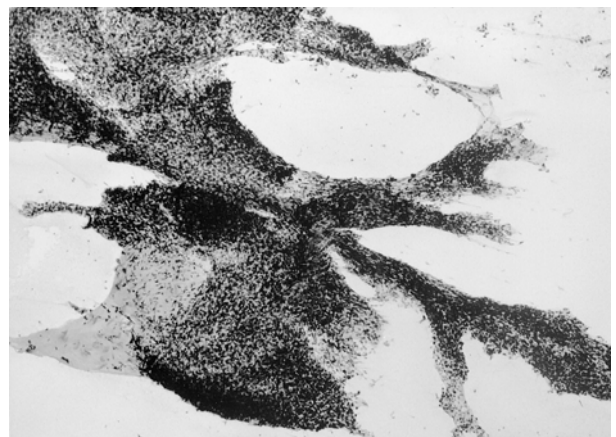


Fig. 6. Tight cellular clusters of spindle cells with hyperchromatic nuclei. (H-E)

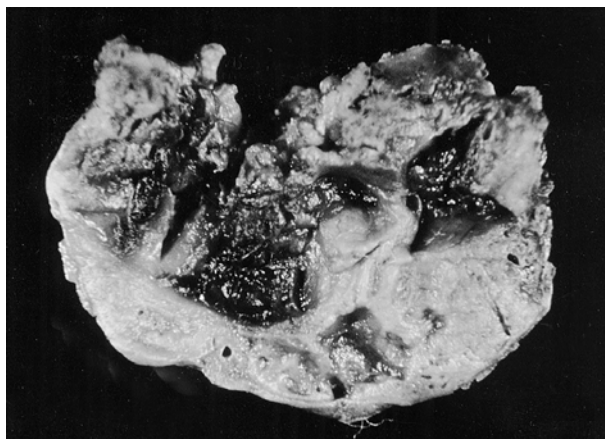


Fig. 7. Solid and partly cystic mass with yellow to dark red color.

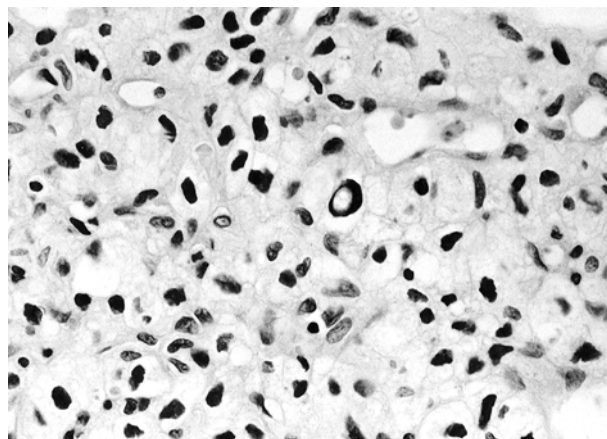


Fig. 9. Tumor cells frequently containing intranuclear inclusions. (H-E)

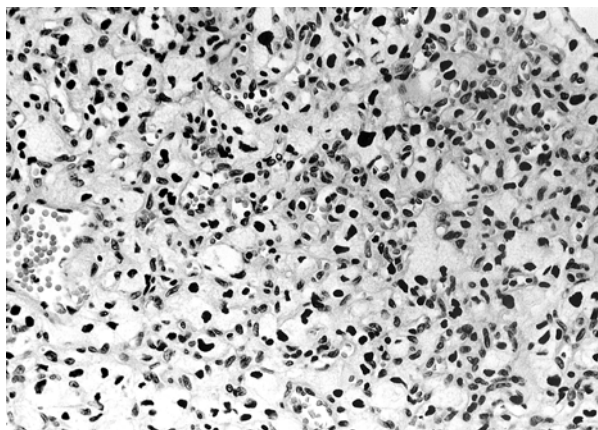


Fig. 8. Histology of solid area showing highly cellular stromal cells with abundant vasculature. (H-E)

### Histological Findings

Complete excision of the mass was carried out. The removed specimen measured  $2.5 \times 2.0 \times 1.8$  cm. Its cut surface appeared solid and partly cystic (Fig. 7). The solid area had a yellow to dark red color. Histologically, the solid area was highly cellular with a rich capillary network (Fig. 8). Stromal cells had large, round, reniform or pleomorphic nuclei. The nuclei were often quite hyperchromatic, but mitoses were rare. However, intranuclear inclusions were frequently seen (Fig. 9). The cytoplasm of stromal cells was vacuolated and oil red O stain demonstrated intracytoplasmic lipid.

### DISCUSSION

Hemangioblastomas usually present in the young adult or middle age as a cerebellar mass they develop more often in men.<sup>1</sup> They appear to be cystic, partly cystic or solid lesions based on the cell density.<sup>1</sup> Hemangioblastomas may resemble malignant gliomas on frozen section because of the obscured distinction between stromal cells, and the vasculature and accentuated nuclear pleomorphism.<sup>1</sup> However, the characteristic radiological and intraoperative findings such as a cystic cerebellar mass with a contrast-enhancing mural nodule may aid pathologists in making the correct diagnosis of a cystic lesion.<sup>1,2</sup> By contrast, the cellular variant usually presents as a solid tumor, and the stromal cells are usually more abundant than the vascular elements.<sup>1</sup> These stromal cells are large, round, pleomorphic and often quite hyperchromatic.<sup>1</sup>

Clinically, a malignancy was highly suspected in our case because of the patient's age, and the predominantly solid nature of the tumor showing postcontrast enhancement on the brain MRI. The cytological smear showed both components of round pleomorphic epithelioid cells and spindle cells which were misinterpreted as features of a malignant tumor, in particular a metastatic sarcomatoid carcinoma. High-grade astrocytoma, which is characteristically hypercellular and rich in large fragments of thick-walled blood vessels

surrounded by numerous malignant pleomorphic tumor cells, was also considered in the differential diagnosis. However, the absence of a fibrillary background and mitotic activity was not consistent with the diagnosis of a high-grade glioma. In Yamamoto's case, most stromal cells were singularly scattered due to degeneration.<sup>5</sup> However, the cytological findings of stromal cells around capillaries was considered characteristic of hemangioblastoma.<sup>5</sup> The cellular details can be seen better in scattered single cells the overemphasis of cellular clusters should be avoided. The clear cells of renal cell carcinoma have abundant and finely vacuolated cytoplasm. In addition, abundant capillary vessels and erythrocytes are found in the cytological smear. Occasionally, intranuclear cytoplasmic inclusions may also occur in renal cell carcinoma.<sup>6</sup> Thus, the overall cytological findings, in our case, may be compatible with those of metastatic renal cell carcinoma, which is the second most common central nervous system manifestation of the von Hippel-Lindau syndrome. However, the awareness of the presence of cellular clusters, which may be frequently found in squash specimens of cellular hemangioblastoma, can help avoid the misdiagnosis of metastatic carcinoma with sarcomatoid features, especially those of renal origin. Intranuclear cytoplasmic inclusions, corresponding to cytoplasmic invaginations, have not been described in previous reports of hemangioblastomas. Intranuclear cytoplasmic inclusions are frequently found in the diagnosis of meningioma and have been helpful in the differential diagnosis of astrocytoma.<sup>1</sup> The knowledge of their presence in hemangioblastoma may also be helpful in differentiating it from a high-grade glioma and in avoiding the diagnosis of metastatic renal cell carcinoma.

In the present report we described the cytological features of a cellular hemangioblastoma by squash preparation of the specimen with emphasis on the intranuclear cytoplasmic inclusions, not previously described. Therefore, the cytodiagnosis of hemangioblastoma may be aided by a detailed knowledge of the cytology of hemangioblastomas and be a useful adjunct in the diagnosis by frozen section during surgery.

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