



Primary Epithelioid Hemangioendothelioma of the Central Nervous System: A Case Report

원발성 중추신경계 상피모양 혈관내피종: 증례 보고

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Primary epithelioid hemangioendothelioma (EHE) of the central nervous system is an extremely rare sarcoma of vascular origin. Imaging findings have been reported for few cases. Herein, we present a case of intracranial EHE manifesting as spontaneous intracranial hemorrhage. The tumor presented as a well-demarcated hemorrhagic lesion. It had a peripheral location, and showed signs of two-layered target-like mild enhancement in the early phase and gradual fill-in delayed enhancement on MRI.

Index terms Epithelioid Hemangioendothelioma; Primary Brain Neoplasms; Sarcoma

INTRODUCTION

Epithelioid hemangioendothelioma (EHE) is an angiocentric vascular tumor characterized by neoplastic proliferation of epithelioid or histiocytoid endothelial cells (1). EHE may arise in a number of locations, most frequently in the liver, lungs, and bones. It can also arise intracranially. Primary EHE of the central nervous system is extremely rare (< 0.02% of all brain tumors) (2). It may involve the brain parenchyma or its coverings. Because of the rarity of EHE, diagnosis of this entity is not well standardized. Radiological knowledge of EHE is limited. EHE has variable radiological feature, similar to other brain tumors in imaging findings. Thus, it is difficult to diagnose EHE by preoperative imaging alone. We present a case of primary cerebral EHE manifested as acute intracranial hemorrhage with similar imaging patterns to those of a hepatic EHE.

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CASE REPORT

A 72-year-old male presented with left side facial palsy for 3 days before admission. Beside diabetes mellitus, he had no history of malignant or chronic illness. His neurological examination at the time of admission revealed a tongue deviation to left side and left side facial palsy. His general status was good.

An unenhanced CT yielded a 4 cm well-defined hyperattenuating lesion in the right frontal lobe abutting the pial surface of the brain (Fig. 1A). Within this lesion, band like heterogeneous hypoattenuation area was apparent, extending from the pial surface of the brain through the center of the lesion. There was mild to moderate vasogenic edema surrounding the lesion with mass effect. Diagnostic considerations included secondary intracerebral hemorrhage caused by vascular malformations or malignant tumors such as glioblastoma and metastatic tumors.

MRI showed that the lesion had heterogeneous signal intensity, mainly hypointensity on both T2- and T1-weighted images with strongly hypointense “blooming” on susceptibility-weighted images. Immediately after intravenous injection of gadolinium, two-layered target-like mild peripheral enhancements of the lesion were revealed. Time delayed contrast enhanced T1-weighted images (acquired about 5 minutes after injection) showed more increase of peripheral contrast enhancement in area and intensity compared with immediate post contrast study (Fig. 1B). Systemic studies including thoraco-abdominal CT scan were normal. Based on these imaging findings, the possibility of a malignant glioma was considered.

The patient underwent right craniotomy with grossly total resection of the tumor. A macroscopic examination during surgery showed a semi-solid and highly vascular mass. It seemed to be attached to some dura with internal hemorrhage. Histopathologic analysis revealed that capillary-sized vessels formed cords within a myxoid stroma and lined by atypical-appearing endothelial cells with voluminous nuclei and abundant cytoplasm, some of them containing erythrocytes. Immunohistochemical analyses were positive for vimentin (supporting mesenchymal differentiation) and focally positive for factor VIII- related antigen (supporting endothelial differentiation) (Fig. 1C). The tumor cells were negative for cytokeratin and glial fibrillary acidic protein. Ki-67 immunostaining index was less than 5%, meaning the intermediate grade of this tumor. Based on these findings, the pathological diagnosis was EHE. The patient was free of macroscopic recurrence based on follow-up MR at 48 months after the initial diagnosis.

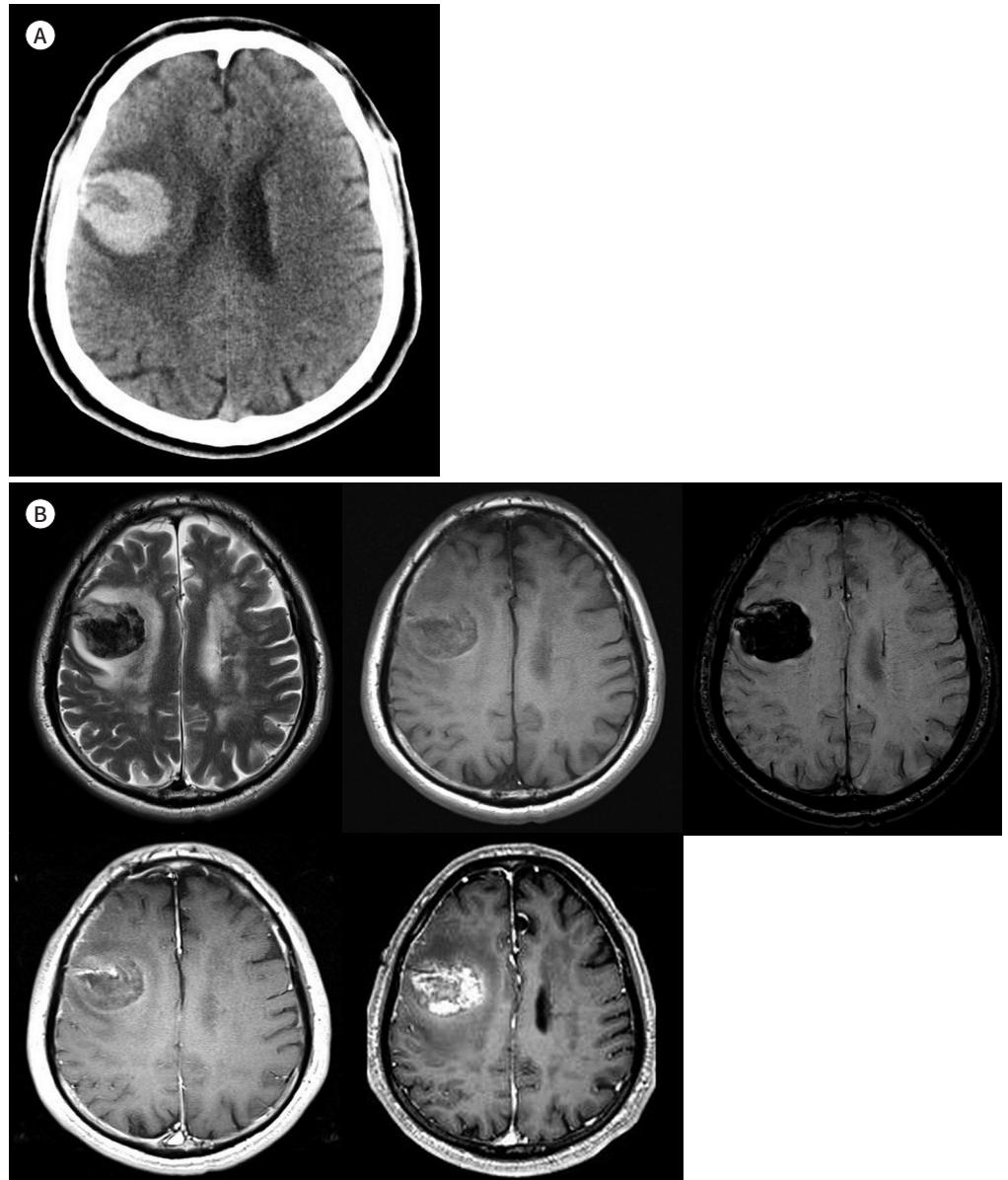
DISCUSSION

EHE is a rare sarcoma of vascular origin which is clinically and histologically intermediate between benign hemangioma and angiosarcoma (1). Microscopically, hemangiomas have well-formed vascular channels while EHE develop intracellular lumina. Angiosarcoma has irregular anastomosing vascular spaces lined by malignant endothelial cells. EHE can be present as either a solitary tumor or in the form of multiple body lesions. It commonly occurs in soft tissues, liver, lung, and bone (3). Therefore, it is important to survey not only the brain, but also the skeleton and visceral organs to determine the full extent of the disease.

Fig. 1. A 72-year-old man with primary epithelioid hemangioendothelioma.

A. Unenhanced axial CT scan shows a well-defined, hyperattenuating lesion in the right frontal lobe abutting the pial surface of the brain. Laterally, a band-like heterogeneous hypoattenuating area can be seen with vasogenic edema surrounding the lesion.

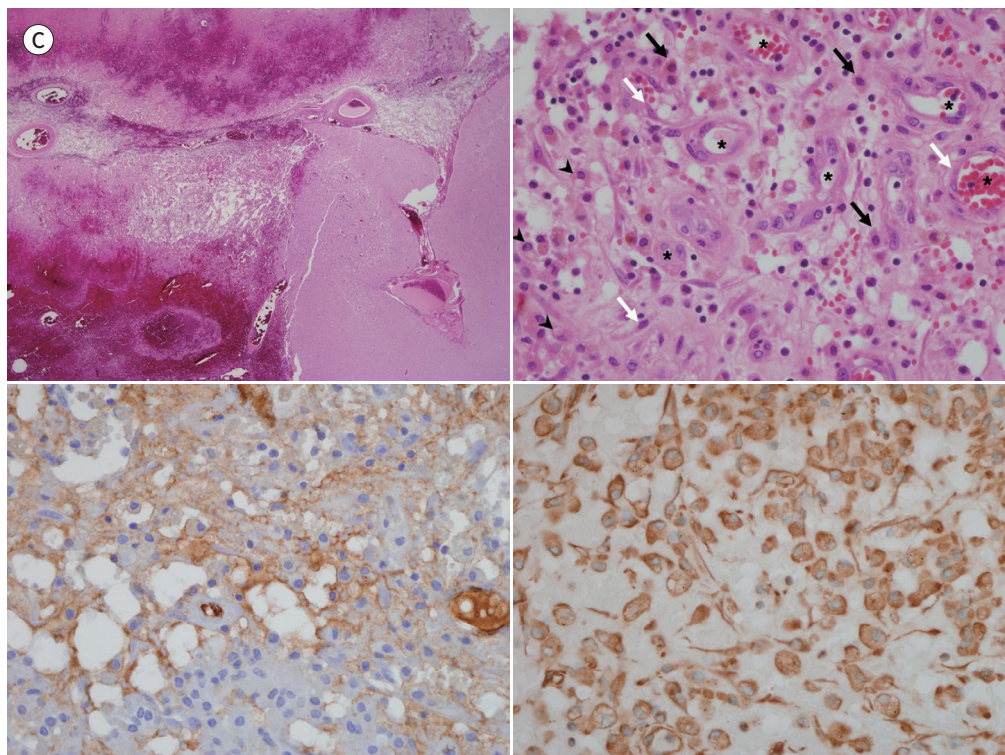
B. The mass exhibits heterogeneous signal intensity, mainly hypointensity, on the axial T2-weighted image (upper left panel) with peripheral edema, heterogeneously isointense with the gray matter on T1-weighted images (upper central panel), and strongly hypointense “blooming” on susceptibility-weighted images (upper right panel). Axial T1-weighted image immediately after contrast injection (lower left panel) demonstrates two-layered target-like, mild peripheral enhancements. Five-minutes delayed postcontrast axial T1-weighted image shows a greater increase of contrast enhancement area and intensity that is pronounced at the periphery (lower right panel).



Primary intracranial EHE is extremely rare. Various clinical, radiological, and pathological features have been sporadically reported. Intracranial EHE may affect individuals of any age, although case reports have demonstrated a bimodal distribution, with a peak in younger children < 1 year of age and another in adults (4). Intracranial EHE display nonspecific imag-

Fig. 1. A 72-year-old man with primary epithelioid hemangioendothelioma.

C. Photomicrograph of hematoxylin and eosin-stained slide (left upper panel, $\times 12$) reveals a relatively well demarcated and hemorrhagic tumor mass. The tumor was composed of epithelioid (black arrows) or spindle shaped cells (white arrows) in nests or cords (asterisks) within a myxoid stroma. Some tumor cells show small intracytoplasmic lumens (“blister cells”) that contain red cells (arrowheads) (right upper panel, $\times 400$). Immunohistochemistry reveals positive factor VIII-related antigen staining (left lower panel, $\times 400$) indicating an endothelial origin. Vimentin stain (right lower panel, $\times 400$) reveals positive staining of part of the tumor, indicating a mesenchymal component.



ing features that correlate with the underlying pathology. Only a few reports have described imaging characteristics of EHE in detail. On non-contrast CT, the lesion is isodense or hyperdense with variable homogeneity. On MR images, it consists of heterogeneous lesions with variable signal intensities on T1- and T2-weighted images. These tumors demonstrate hypervascularity on imaging, with variable pattern of enhancement. The degree of enhancement is usually vivid. Hemorrhage may occur, with subsequent hemosiderin deposits (5, 6).

In our case, EHE manifested as spontaneous intracerebral hemorrhage with superficial location. The high attenuation on CT and strongly hypointense “blooming” on susceptibility-weighted images reflected the presence of acute bleeding in the tumor. Hemorrhage due to EHE can be partially explained by solid endothelial nests or channels merging with capillary-sized vessels. The fine capillaries found histologically in our case are probably the cause of the acute bleeding. The two-layered target like peripheral enhancement in the early phase followed by some progressive peripheral delayed enhancement has not been reported in previous intracranial EHE. These findings are similar to those of hepatic EHE. Although the exact mechanism of this enhancing pattern is unclear, the presence of peripheral proliferating tumor cells with intracytoplasmic blood filled vascular lumina might correlate with a target/ring enhancement pattern in hepatic EHE (7). Thus, the presence of peripheral high tumor cellu-

larity, central myxomatous region associated with abnormal proliferation of blood vessels and sinus-like structures found histologically in our case may be related to this enhancing pattern.

The differential diagnosis is that of a hemorrhagic mass with enhancement, including glioblastoma, metastasis and cavernous malformation. Glioblastoma tends to have typical manifestation with rim enhancement and obvious central necrosis caused by an intrinsic prothrombotic or vaso-occlusive event within the tumor (8). Unlike typical glioblastoma, our case showed double layered target like enhancement with less central necrosis. Although metastatic disease exhibits a wide variety of appearance, the large size of the lesion and lack of multiplicity in this case suggest that a primary tumor is more likely. Cavernous malformation typically shows a mixed signal intensity core, a reticulated “popcorn ball” appearance, and a “T2 blooming sign,” which is due to a low signal intensity hemosiderin rim that completely surrounds the lesion (9). The presence of the surrounding edema and the enhancement are features of a vascular aggressive tumor rather than a cavernous hemangioma.

In conclusion, peripherally located hemorrhagic mass with vasogenic edema, layered target-like mild enhancement in the early phase and gradual fill-in delayed enhancement are new MR imaging findings of intracranial EHE.

Conflicts of Interest

The authors have no potential conflicts of interest to disclose.

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원발성 중추신경계 상피모양 혈관내피종: 증례 보고

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상피모양 혈관내피종은 혈관에서 기원하는 드문 종양으로 원발성으로 중추신경계에서 발생하는 경우는 매우 드물다. 저자들은 자발성 대뇌 피질하 출혈로 발현되었던 원발성 중추신경계 상피모양 혈관내피종의 증례를 경험하여 보고하고자 한다. 자기공명영상에서 이 증례의 상피모양 혈관내피종은 뇌 실질 변연부의 출혈성 종괴로 나타났고 조기 조영영상에서는 이 중 층의 표적 모양으로 약한 조영증강을, 지연 조영영상에서는 변연부에서 중심부로 점차 조영증강되는 양상을 보였다.

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