福岡大医紀（*Med. Bull. Fukuoka Univ.*）：41(1)，25–29，2014

Fatal Hemorrhage of a Supratentorial Extraventricular Anaplastic Ependymoma in an Elderly Patient

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Abstract

Introduction: Intracranial ependymomas are less common in adults, and supratentorial extraventricular anaplastic ependymomas requiring emergency surgery are extremely rare. In addition, effective adjuvant chemotherapy for anaplastic ependymoma has not been defined, especially in adults. We herein describe a rare case of supratentorial extraventricular anaplastic ependymoma with fatal intratumoral hemorrhage and discuss the adjuvant therapy in malignant glioma patients with a poor cognitive function.

Case report: A 69-year-old female presented with a large area of intratumoral hemorrhage manifesting as a sudden coma. A cauliflower-like tumor was found primarily in the left inferior frontal gyrus unattached to the lateral ventricle. The histologic features were consistent with those of anaplastic ependymoma. Due to the patient's age and impaired cognitive function, we administered only temozolomide chemotherapy as adjuvant therapy.

Conclusion: Maximal surgical resection is a valuable treatment option for anaplastic ependymoma.

Key words：**Anaplastic ependymoma, Supratentorial, Extraventricular, Hemorrhage, Temozolomide**

Introduction

Anaplastic ependymoma is a malignant glioma that exhibits ependymal differentiation characterized by increased cellularity and a brisk mitotic activity often accompanied by microvascular proliferation and pseudopalisading necrosis. It corresponds histologically to grade III disease according to the World Health Organization (WHO) classification of brain tumors.[(1)] Intracranial ependymomas in a broad sense are less common in adults,[(2)] and reports of supratentorial extraventricular anaplastic variants are rare.[(3-10)] Furthermore, the occurrence of these variants in association with sudden coma requiring emergency surgery is extremely rare. We herein report our experience with a rare case of supratentorial extraventricular anaplastic ependymoma with fatal intratumoral hemorrhage and discuss the use of adjuvant therapy in such cases.

Case Report

A 69-year-old female was hospitalized due to a sudden coma with a decorticate posture and dilation of the left pupil. Computed tomography revealed uncal transtentorial herniation associated with a large mass in the left frontal lobe. A large area of intratumoral hemorrhage with a small amount of calcification was also observed (Fig. 1). We immediately performed craniotomy and removed the cauliflower-like, reddish-gray tumor with an intratumoral hematoma. The tumor was found to be well demarcated and was resected approximately 5 mm from its macroscopic circumference. The lesion,

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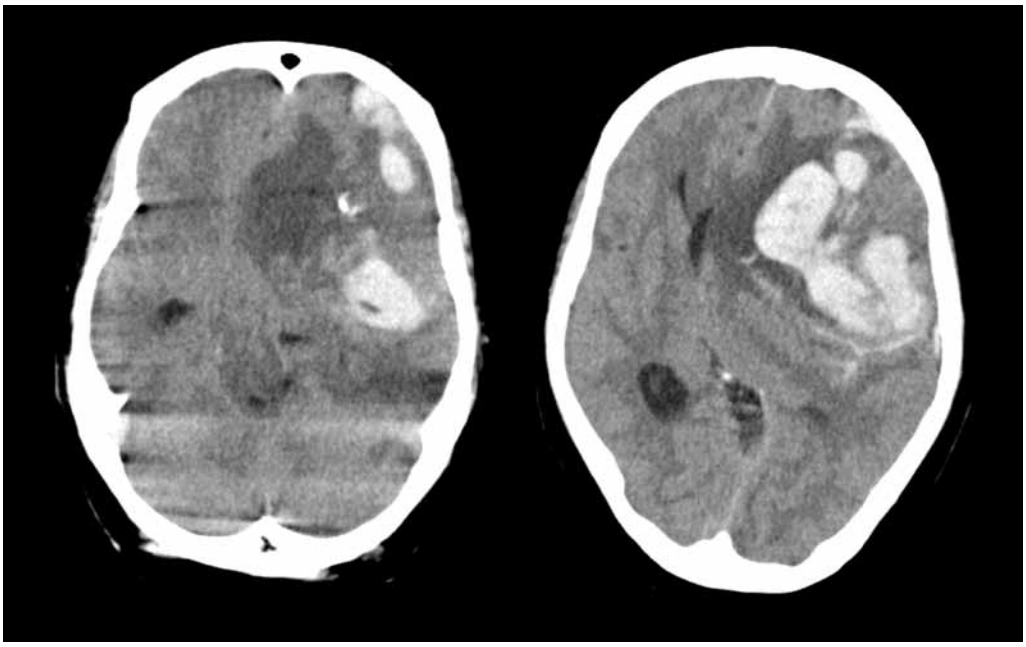

Fig. 1 Computed tomography revealed a mass with a large hematoma and focal calcification in the left frontal lobe. Both the frontal and temporal lobes were herniated and the brainstem was compressed.

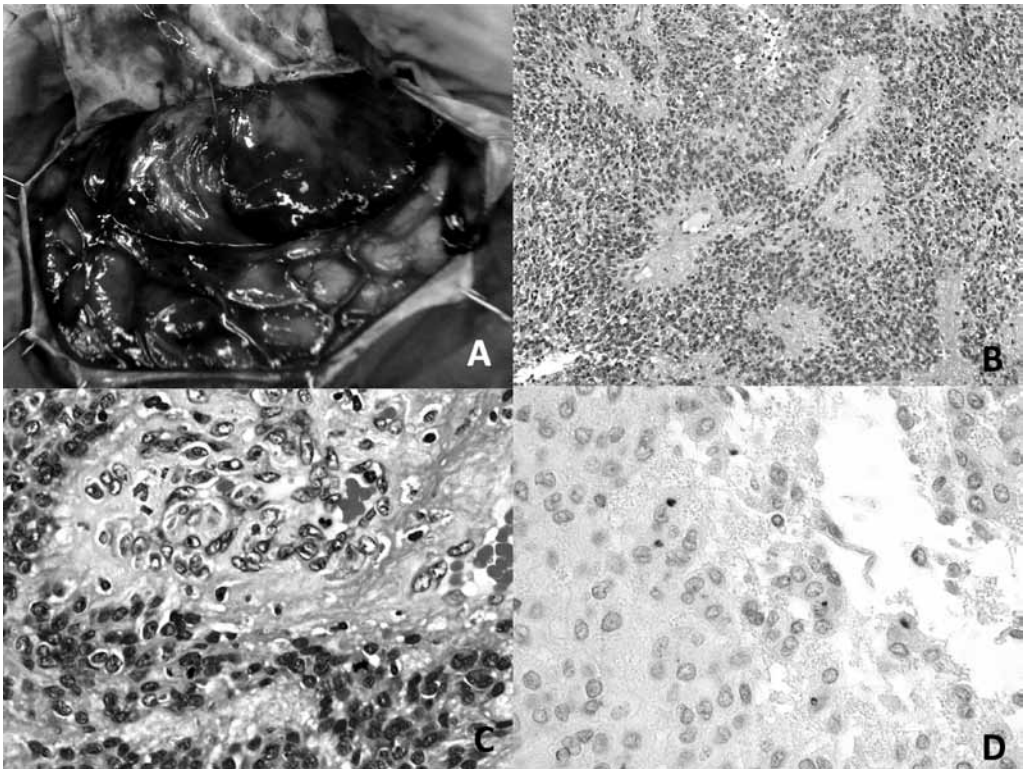

Fig. 2 The cauliflower-like tumor was reddish-gray in color. The tumor was located in the cortex and subcortical regions of the left frontal lobe and grew exophytically (A: intraoperative photograph). Microscopic images of the tumor showed proliferation of atypical cells forming a diffuse pattern. Perivascular pseudorosettes were found (B: hematoxylin and eosin [H&E] stain, original magnification ×100). Increased cellularity and microvascular proliferation were observed. The mitotic activity was eight mitotic figures/10 high-power fields (C: H&E stain, original magnification ×400). Epithelial membrane antigen immunoreactivity showed a dot-like pattern (D: original magnification ×400).

which originated primarily from the left inferior frontal gyrus, grew rather exophytically and was not deeply invasive（Fig. 2A）. It was not attached to the anterior horn of the lateral ventricle. Histopathologically, the tumor exhibited proliferation of atypical and polygonal cells arranged in a diffuse pattern with perivascular pseudorosettes（Fig. 2B）. Increased cellularity, a high mitotic activity（eight mitotic figures/10 high-power fields）and microvascular proliferation were present（Fig. 2C）. There were also some regions of hemorrhage and calcification within the tumor. Immunohistochemically, the tumor was focally positive for glial fibrillary acidic proteins. Epithelial membrane antigen staining showed a dot-like pattern（Fig. 2D）. The tumor was negative for Olig2, NKX2-2, epidermal growth factor receptor and isocitrate dehydrogenase-1. The MIB-1 labelling index was 9.1%. Positive staining for O6-methylguanine-DNA-methyltransferase（MGMT）was also observed. These pathological findings corresponded to a diagnosis of anaplastic ependymoma. No contrast-enhanced lesions were present in the brain or spine on postoperative magnetic resonance imaging（MRI）（Fig. 3）. Two weeks postoperatively, the patient remained bedridden, and we worried that radiotherapy would cause her cognitive function to deteriorate further. Therefore, we treated her with temozolomide chemotherapy and rehabilitation only, and she gradually recovered. However, six weeks after tumor resection, MRI revealed an enhanced mass lesion in the wall of the cavity. We considered this finding to indicate tumor recurrence and performed a second operation. Gliosis was found during the second surgery, and there were no tumor cells in the specimen; hence, we discontinued the chemotherapy. Although the patient continued to require help, she was discharged from the hospital.

Discussion

Anaplastic ependymomas are malignant gliomas with ependymal differentiation. Hemorrhage, calcification and the presence of microcysts are seen more frequently in patients with the anaplastic variant,[11] while intracranial anaplastic ependymomas are more frequent in children.[1] Supratentorial extraventricular anaplastic ependymomas are rarely reported,[3-11] and supratentorial extraventricular anaplastic ependymomas requiring emergency surgery are extremely rare. Of the extraventricular types of ependymoma, cellular

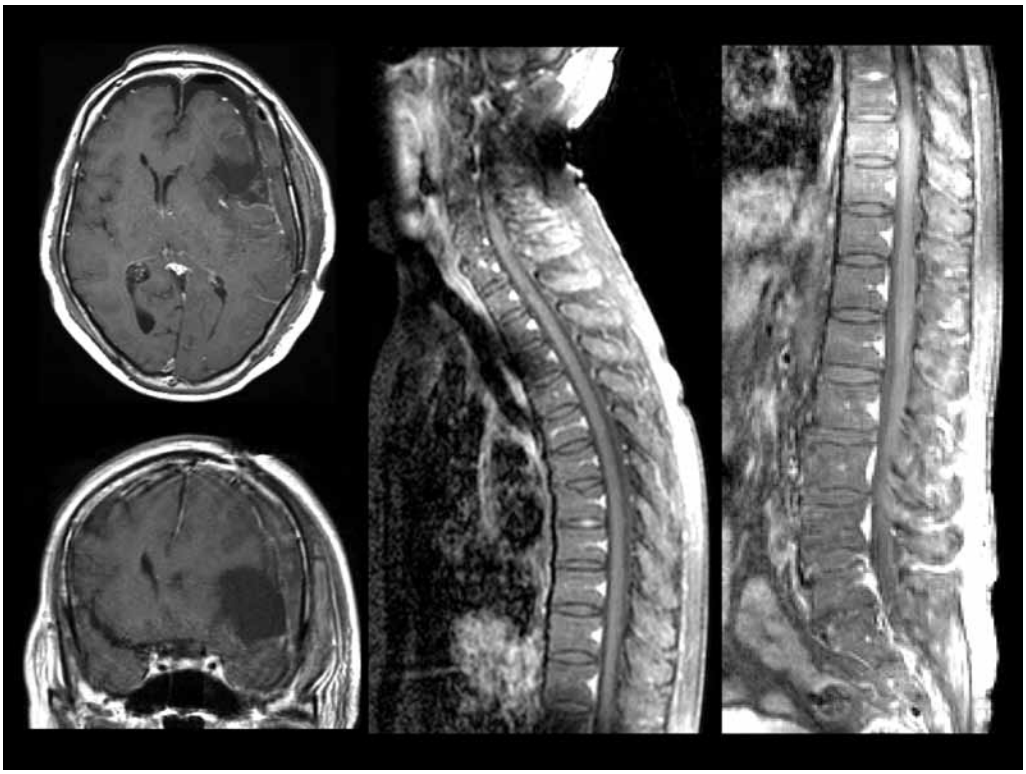

Fig. 3 Postoperative magnetic resonance images showed no masses in the brain or spine.

ependymomas are more common, with perivascular pseudorosettes and true ependymal rosettes being less frequent in this variant.[2,11] In the present case, the tumor was located in the frontal lobe unattached to the lateral ventricle, and true ependymal rosettes were absent. This case may therefore be related to anaplastic changes of cellular ependymoma. Although the preoperative diagnosis includes oligodendroglioma or glioblastoma, anaplastic ependymoma should be considered as a differential diagnosis when extraventricular tumors with hemorrhage are detected.

The standard therapy for anaplastic ependymomas consists of maximal surgical resection followed by focal irradiation.[12] Effective adjuvant chemotherapy for anaplastic ependymomas has not been defined, especially in adults.[6] However, although almost all previously reported patients underwent maximal resection and radiotherapy, we did not administer radiation therapy due to the patient's poor cognitive function. Although ependymomas in a broad sense are not considered to be infiltrative and are usually distinct from neighboring tissue,[13,14] the tumor in the present case was malignant, and we thus considered the administration of adjuvant chemotherapy to be necessary.

There are some reports of the use of temozolomide chemotherapy for anaplastic ependymoma.[15-17] Chamberlain et al. reported 25 cases involving temozolomide chemotherapy for recurrent platinum-resistant benign ependymoma. One patient (4%) showed a partial radiographic response, and nine (36%) achieved stable disease.[15] Freyschlag et al. also treated multifocal recurrence of anaplastic ependymoma with temozolomide and reported no radiographic progression for five months.[16] In contrast, Kim et al. lost their patient with spinal cord anaplastic ependymoma due to uncontrollable progression of the tumor despite the administration of temozolomide chemotherapy.[17] Because positive staining for MGMT was observed in the present case, we considered that temozolomide chemotherapy was not effective. However, there were no tumor cells in the specimen of the resection stump obtained at the second surgery, and there has been no recurrence of the tumor for eight months since the last round of chemotherapy. We considered that maximal surgical resection may have been the most valuable treatment in this case. Recently, some reports have addressed the problems of MGMT. For example, Bobstuc et al. reported that the anticonvulsant levetiracetam decreased the MGMT expression in four glioblastoma samples.[18] In addition, Motomura et al. reported that combination therapy with interferon-β and temozolomide prolongs survival, even in patients with tumors exhibiting an unmethylated MGMT promoter.[19]

Conclusion

Maximal surgical resection is a valuable treatment for adult malignant ependymoma in patients with a poor cognitive function. The role of adjuvant chemotherapy in cases of adult anaplastic ependymoma remains uncertain; however, it may be effective if temozolomide chemotherapy can overcome tumors with an MGMT expression.

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（平成 25. 10. 30 受付，平成 26. 1. 20 受理）