Brain Tumor Pathol (2007) 24:35–40
DOI 10.1007/s10014-007-0215-3

CASE REPORT

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Supratentorial ectopic cortical ependymoma occurring with intratumoral hemorrhage

Received: February 5, 2007 / Accepted: March 1, 2007

Abstract We report here a rare case of supratentorial ectopic cortical ependymoma. This tumor was localized in the left angular gyrus, occurred with intratumoral hemorrhage, was attached to the dura mater, exhibited no continuity with the ventricular system, showed distinctive pathological features (perivascular pseudo-rosette formations and firework-like giant rosette formations), and finally transformed to a glioblastoma-like high-grade lesion. A cortical ependymoma should be considered in the differential diagnosis of supratentorial cortical tumors with intraparenchymal hemorrhage and high vascularity, even if not in contact with the ventricular system. Although malignant transformation is unusual in cortical ependymoma, close observation and adjunctive radiotherapy are strongly recommended after the excision.

Key words Ectopic ependymoma · Cortical ependymoma · Anaplastic ependymoma · Supratentorial ependymoma · Hemorrhage

Introduction

A minority of ependymomas can arise in the supratentorial parenchyma with no attachment to the ventricular system. Such an ependymoma variant is called an ectopic ependymoma. Among these ependymomas are some rare pathological entities that are difficult to differentiate from other brain tumors.[1] Only 14 cases of supratentorial ectopic *cortical* ependymomas with no attachment to the ventricular system, including the present case, have been reported.[1,2] We report here the fourth case of a surface-located *anaplastic* ependymoma occurring with intratumoral hemorrhage that was localized in the left angular gyrus and rapidly transformed to a glioblastoma-like high-grade lesion postoperatively. We discuss the clinical features and pathological aspects of supratentorial ectopic cortical ependymomas.

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Clinical summary

A 33-year-old man presented with sudden headache, vomiting, and transient motor aphasia on February 2, 2005. Computed tomography (CT) scanning demonstrated subcortical hemorrhage, approximately 20 mm in diameter, in the left parietal region (Fig. 1a). Postictal motor dysphasia rapidly improved for several days. To clarify the radiologic diagnosis, we waited until complete absorption of the hematoma had occurred. Cerebral angiography showed a thick angular branch of the middle cerebral artery that mainly fed the anterior part of the tumor (Fig. 2).

Approximately 2 months later, plain CT scanning revealed stick-shaped calcification and complete absorption of the hemorrhage (Fig. 1b). Magnetic resonance imaging (MRI) performed on April 12 showed the lesion was strongly enhanced heterogeneously on intravenous administration of gadolinium-diethylenetriaminepentaacetic acid (Gd-DTPA) (Fig. 1d,e). The lesion was surrounded by perifocal cerebral edema (Fig. 1c). In some parts, a thick flow-void appearance could be seen. These findings suggested the possibility of hemorrhage from the brain tumor. A part of the enhanced tumor seemed to protrude from the surface of the cerebral cortex. The tumor did not show any anatomical connection with the wall of the lateral ventricle. Preoperative neurological examination was normal.

On April 18, left parietal craniotomy was performed. During opening of the dura mater, we observed a light brown-colored tumor adhering to the dura mater. The tumor was located immediately subpially on the angular gyrus and was well demarcated from surrounding gyri (Fig.

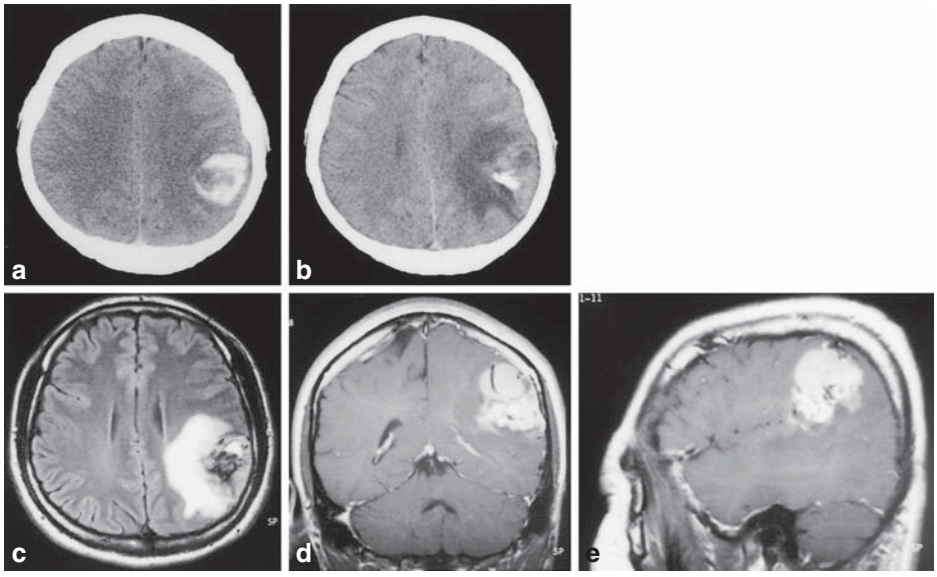

Fig. 1. **a** Axial image of a plain computed tomography (CT) scan obtained at admission. Subcortical hemorrhage can be observed in the left parietal cortex. **b** Axial image of a plain CT scan obtained 2 months after admission demonstrates complete absorption of the hemorrhage and stick-shaped calcification. **c** Axial fluid-attenuated inverse recovery (FLAIR) magnetic resonance imaging (MRI) demonstrates a subcortical tumor with heterogeneous intensity, concomitant with perifocal brain edema (high-intensity area). **d** Coronal view of a T_1-weighted image with contrast enhancement. In some parts, a thick flow-void appearance (main feeding artery) can be seen. A part of the enhanced tumor seems to protrude from the surface of the cerebral cortex. The tumor does not show any anatomical connection with the wall of the lateral ventricle. **e** Sagittal T_1-weighted image with contrast enhancement. The tumor occupies the left angular gyrus

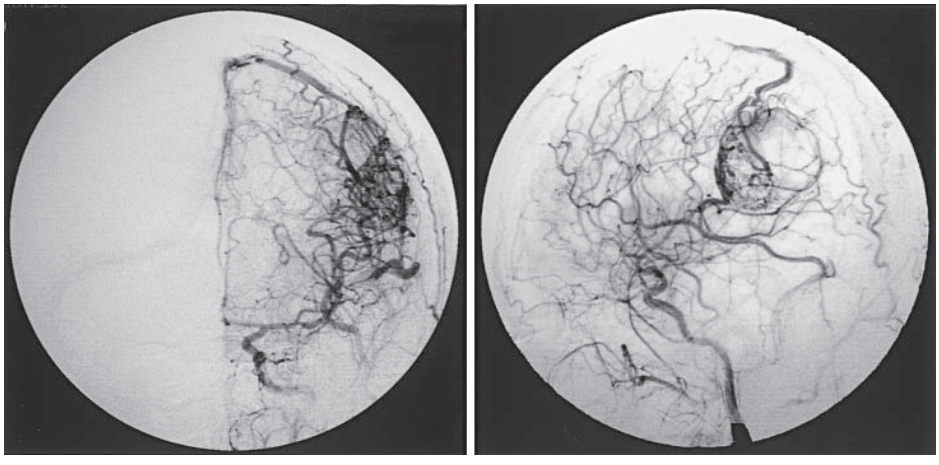

Fig. 2. Anteroposterior (*left*) and lateral (*right*) views of left internal carotid cerebral angiography performed on March 9, 2005. Marked tumor staining and early venous filling can be observed. The thick angular branch of the left middle cerebral artery mainly feeds the anterior part of the tumor

3). The intraoperative pathological diagnosis was a malignant glioma. Intergyral dissection was able to reduce the amount of bleeding without dissection of the tumor itself. The main feeder of the tumor, the angular branch of the middle cerebral artery, was easily detected and cut safely. This tumor exhibited no continuity with the ventricular system. We confirmed gross total removal of the tumor. Finally, the lateral ventricle was opened.

Postoperatively, there was no neurological deterioration. According to the pathological diagnosis of an anaplastic ependymoma, IAR therapy (combination therapy including intravenous administration of interferon-β and ACNU, and conventional local irradiation, 60 Gy) has been performed.

On follow-up MRI on October 11, obvious tumor recurrence could be seen, without a neurological deficit. On October 17, the recurrent tumor, including the angular gyrus, was radically removed. Postoperative MRI on November 16 showed total removal of the recurrent tumor and the angular gyrus. Although the patient showed Gerstmann's syndrome (right-left disorientation, acalculia, finger agnosia, and agraphia) postoperatively, such neurological deficits are rapidly improving with rigorous speech therapy.

Pathological findings

Histological sections of the first specimen revealed that the lesion was very cellular and well vascularized. The hyperchromatic nuclei showed mild polymorphism. Small areas of necrosis and mitotic figures were rarely seen. There were

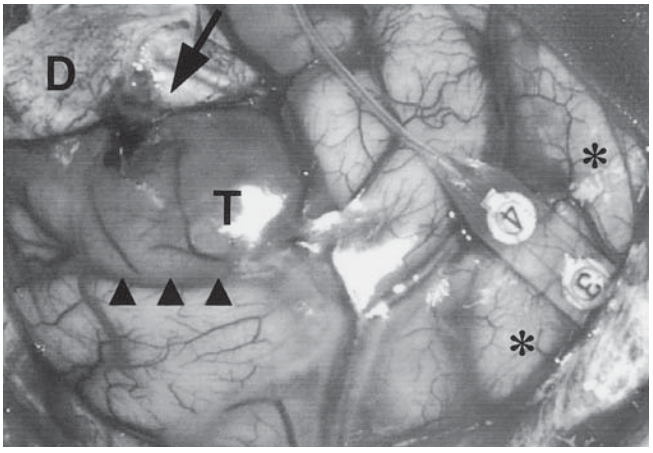

Fig. 3. Intraoperative photograph on April 18, 2005. Left parietal craniotomy was performed. The dura mater (*D*) was tightly adhered to the light brown-colored tumor (*T*) (*single arrow*). The tumor was located on the surface of the parietal lobe, mainly in the region of the angular gyrus, and is well demarcated from surrounding gyri (*arrowheads*). The intraoperative pathological diagnosis was a malignant glioma. To clarify the location of the central sulcus, a 4-channel-electrode was inserted toward the central sulcus to monitor the phase reversal of the somatosensory evoked potential (Numbers 3 and 4 indicate the number of electrode). We confirmed that the gyrus indicated by *asterisks* was a postcentral gyrus (namely, the sensory cortex). The central sulcus is hidden by the dura mater

numerous perivascular pseudo-rosette formations (Fig. 4a). The nuclei of the cells in these formations were aligned around the central vessel, with the eosinophilic cytoplasmic processes directed toward the vessel. In addition, as a specific pathological finding in the present case, firework-like giant rosette formations formed several clusters limited to only a few foci (Fig. 4b). An immunohistochemical study revealed that the tumor cells were positively stained for glial fibrillary acidic protein (GFAP), S-100 protein, and epithelial membrane antigen (EMA). Synaptophysin, a marker of synaptic proteins, was negative. The MIB-1 labeling index was about 15%.

An electron microscopic study of the first specimen revealed that tumor cells with irregularly shaped nuclei contained variable amounts of rough endoplasmic reticulum, mitochondria, lysosomes, and intermediate filaments. Cell surfaces were covered with microvilli-like cell projections, and the opposite side facing the stroma with a basal lamina (Fig. 4c). Rudimentary cell junctions were occasionally noted between tumor cells. No cilia was identified.

The pathological specimen of the recurrent tumor showed anaplastic features corresponding to glioblastoma (Fig. 4d,e).

Discussion

Ependymomas usually arise from the cells lining the ventricular system and the central canal of the spinal cord. With the advent of MRI, with which accurate evaluation of the exact relationship between a tumor and the ventricular wall is possible, it has been recognized that *real* ectopic localization of an ependymoma is extremely rare.[1] In particular, supratentorial cortical ependymomas without attachment to the ventricular system are extremely rare. Such an ependymoma variant was termed with several names: "supratentorial ectopic ependymoma,"[5,6,11] "brain surface ependymoma,"[1,3,7] "extraventricular ependymoma,"[8] "parenchymal ependymoma,"[2] "extraaxial ependymoma,"[4] and "cortical ependymoma."[9,10]

To our knowledge, only 14 cases of supratentorial ectopic cortical ependymomas, including the present case, have been reported (Table 1).[1–11] The mean age of these 14 cases was 33 years (only 6 were pediatric cases), which was higher than that of patients with general supratentorial ependymomas (18.4 years).[12] The male-to-female ratio was 6:8. The location of the tumor was the frontal lobe in 6,[1,3,5,9–11] the parietal lobe in 3,[6,10] the temporal lobe in 2,[8,10] the frontoparietal lobe in 1,[7] the temporoparietal lobe in 1,[2] and the parietooccipital lobe in 1.[4] In 8 cases, the tumor was located immediately subpially on the brain surface.[1,3,4,9,10] Interestingly, because 9 of the 14 cases have been reported from Japan, some racial specialization may exist.[1–8] In 7 of the 14 cases, remarkable calcification could be seen on CT scanning.[2–5,10] Furthermore, only 4 cases of supratentorial ectopic cortical *anaplastic* ependymomas, including our case, have been reported.[1,2,8] In 3 of these cases, intratumoral hemorrhage was observed.[1,2]

Vernet et al.[11] hypothesized the following pathogenesis for supratentorial ectopic ependymomas. (1) The tumors develop from intraparenchymal or subarachnoid ependymal cysts resulting from disorders of migration from the germinal matrix. (2) The tumors represent primitive neuroectodermal tumors that have differentiated extensively along the ependymal lineage. (3) The tumors might be the result of neoplastic growth within an ectopic ependymal cell and are, therefore, at least in part, the consequence of a migrational error.[1,2,11]

Site-related differences in the molecular biology of intracranial anaplastic ependymomas have been observed recently.[13] Tumors at infratentorial sites showed gene expression patterns similar to those found in their low-grade counterparts, suggesting the likelihood of "secondary" multistep malignant transformation. In contrast, the genetic signatures of low-grade and high-grade supratentorially located tumors clearly differed, raising the question of whether these neoplasms represent molecularly distinct ependymoma entities.[14]

Ho et al. proposed criteria with a better correlation with the clinical outcome; namely, anaplastic ependymomas are defined by the presence of any two factors of four or more: 4 mitoses per 10 high-power fields (1.7/mm^2), hypercellularity, endothelial proliferation, and necrosis.[15] The present case fulfils these criteria, and can be classified as an anaplastic ependymoma and WHO grade III. This tumor also showed distinctive pathological features: namely, pseudo-rosette formations and firework-like giant rosette formations. However, in the present case, in spite of gross total removal of the tumor and postoperative focal irradiation, the tumor recurred rapidly and transformed to a glioblastoma-like high-grade lesion. Although Roncaroli et al.[10] denied the

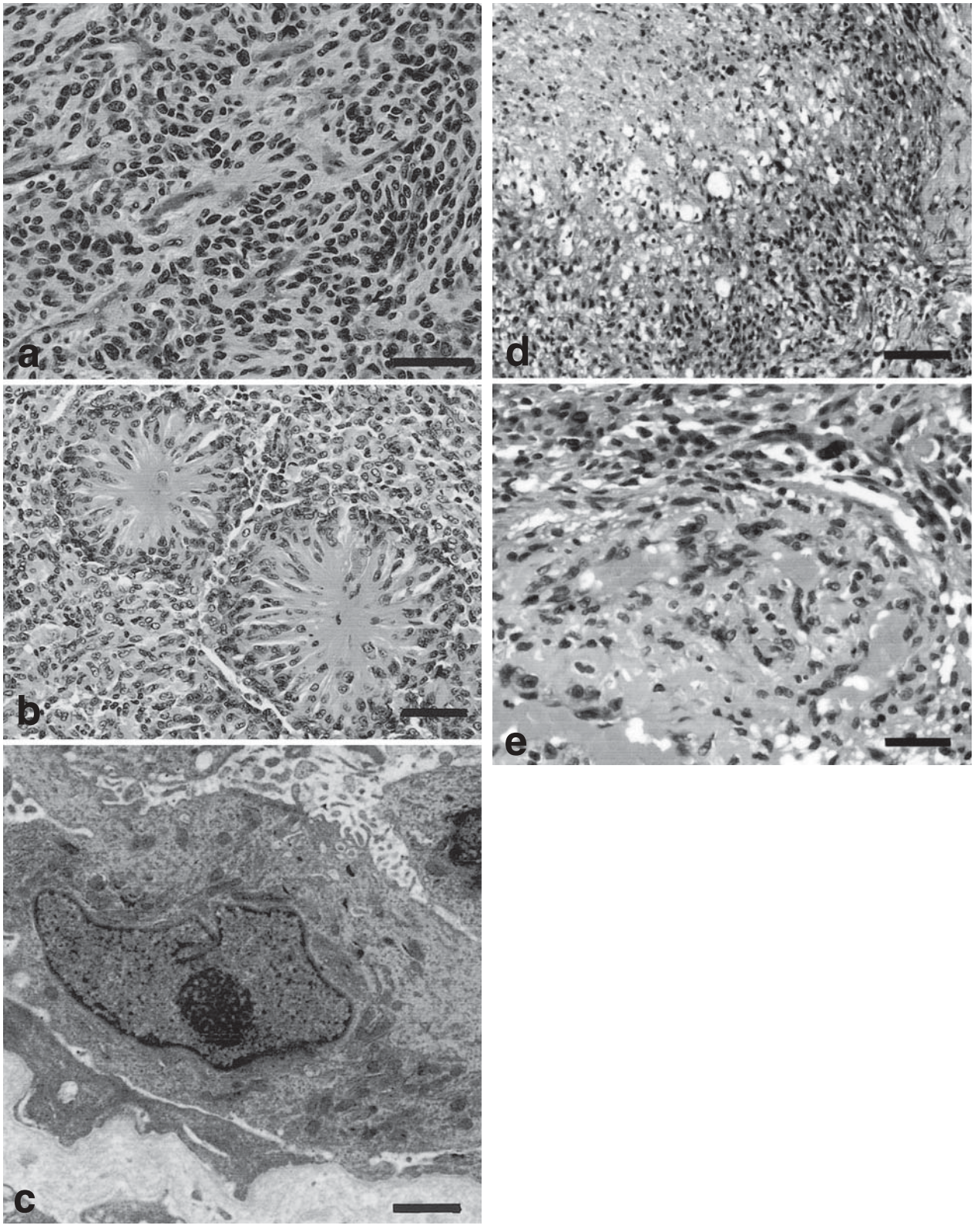

Fig. 4. Pathological micrographs (**a**, **b**) and an electron micrograph (**c**) from the first surgical specimen and pathological micrographs (**d**, **e**) from the second surgical specimen. **a** This micrograph shows the cellular and well-vascularized tumor. The hyperchromatic nuclei showed mild polymorphism. There were numerous perivascular pseudo-rosette formations. The nuclei of the cells in these formations were aligned around the central vessel, with the eosinophilic cytoplasmic processes directed toward the vessel. Hematoxylin and eosin (H&E) stain. **b** As a specific pathological finding in the present case, firework-like giant rosette formations formed several clusters limited to only a few foci. H&E. **c** Tumor cells possessing irregular nuclei and abundant cytoplasm containing mitochondria and rough endoplasmic reticulum. Note irregular microvilli-like cell projections (*upper*) and a basal lamina (*bottom*) on the cell surface. **d**, **e** Micrographs of surgical specimen of recurrent tumor show anaplastic features corresponding to glioblastoma. Note necrosis with surrounding pseudo-palisading (**d**), and cellular pleomorphism and endothelial proliferation (**e**). H&E. *Bars* **a**, **b**, **d**, **e** 50 μm; **c** 1 μm

Table 1. A list of reported cases with supratentorial ectopic ependymomas without attachment to the ventricular system

No.	Author, year	Age/ sex	Initial symptom	Pathology/ location	Continuity with surface	Calcification	Hemorrhage	Cyst formation	Enhancement effect on MRI	Staining on angiography	Therapy	Recurrence
1	Hayashi (1994)[4]	13/M	Headache Vomiting	Clear cell/ parietooccipital	+ (adhered to the dura mater)	+	–	+	+	+ (fed by MMA)	Operation	–
2	Vernet (1995)[11]	11/F	Vomiting Headache	Ependymoma/ frontal	–	–	–	–	+ (CT)	No study	Operation	–
3	Fujimoto (1997)[3]	13/M	Transient dysarthria (seizure?) Headache Hypesthesia	Clear cell/ frontal	+ (adhere to the dura mater)	+	–	+	+	+	Operation	–
4	Saito (1999)[6]	63/F	Consciousness disorder (seizure?)	Cellular/ parietal	–	–	–	–	+	+	Operation	–
5	Sato (2000)[7]	41/F	Dysesthesia, weakness in right upper limb	Ependymoma/ frontoparietal	–	–	–	+	+	No study	Operation Irradiation	–
6	Takeshima (2002)[1]	70/F	Consciousness disorder Dementia	Anaplastic/ frontal	+	–	+	+	+	No study	Operation	–
7	Kojima (2003)[2]	56/F	Transient mild vertigo Seizure	Anaplastic temporoparietal	–	+	+	–	+	No study	Operation Irradiation	– Residual lesion
8	Lehman (2003)[9]	10/F	Seizure	Ependymoma/ frontal	+	–	–	+	+	No study	Operation	–
9	Moritani (2003)[8]	50/F	Headache	Anaplastic/ temporal	–	–	–	+	No description	Hypovascular	Operation Irradiation Chemotherapy	+
10	Ono (2004)[5]	6/M	Seizure Hemiparesis	Ependymoma/ frontal	–	+	–	+	+	+	Operation	–
11	Roncaroli (1) (2005)[10]	52/M	Seizure	Ependymoma/ frontal	+	–	–	–	+	No study	Operation Irradiation	–
12	Roncaroli (2) (2005)[10]	34/M	Seizure	Ependymoma/ temporal	+	+	–	–	+	No study	Operation	–
13	Roncaroli (3) (2005)[10]	11/F	Seizure	Ependymoma/ parietal	+	+	–	–	+	No study	Operation	–
14	Present case (2007)	32/M	Seizure	Anaplastic/ parietal	+ (adhered to the dura mater)	+	+	–	+	+	Operation Irradiation Chemotherapy	+

MMA, middle meningeal artery

possibility of local recurrence and malignant transformation in supratentorial cortical ependymomas, our case indicates that adjuvant radiotherapy and close MRI follow-up of patients with supratentorial ectopic cortical anaplastic ependymomas is mandatory, even after gross total removal of the tumor.

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