Case Report
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Rapidly Growing Anaplastic Ganglioglioma Mimicking Brain Metastasis in a Middle-Aged Woman: A Case Report
중년여성에서 뇌전이암으로 오인되었던 역형성 신경절교종: 증례보고

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Anaplastic gangliogliomas (AGGs), the malignant counterpart of gangliogliomas, are classified as grade III tumors by the World Health Organization. Although, the clinical course and optimal treatment of AGGs are not well understood, they often result in worse local control rate and shorter survival. The authors describe the magnetic resonance imaging findings of a middle-aged woman with supratentorial AGG, that manifested as a rapidly growing cystic mass which mimicked metastasis. The authors suggest that AGG may be considered as a possible diagnosis for a rapidly growing peripheral enhancing mass in the brain, especially when it is superficially located.

Index terms
Ganglioglioma, Malignant
Magnetic Resonance Imaging
Metastasis
Brain

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INTRODUCTION

Gangliogliomas are uncommon tumors in the central nervous system (CNS) that account for 1.3% of CNS neoplasms in adults and 0.4% to 7.6% of those in the pediatric group (1). They consist of two components: differentiated ganglial cells and neoplastic glial cells. They are categorized as mixed neuronal-glial tumors in accordance with the World Health Organization (WHO) classification system for brain tumors, and most of them have indolent behaviors and are categorized as WHO grade I tumors (2). They are most frequently observed in children and young adults, and frequently located in the temporal lobe. The WHO grade III variant or anaplastic gangliogliomas (AGGs) are extremely rare, accounting for only 1–8% of gangliogliomas (3). Only 10 articles have been published so far, including 12 cases of brain AGGs between 2007 and 2016 (Table 1). AGGs are known to have worse local control rate and shorter survival (4). We herein describe an adult case of supratentorial AGG that manifested as a rapidly growing cystic mass in a middle-aged woman.

CASE REPORT

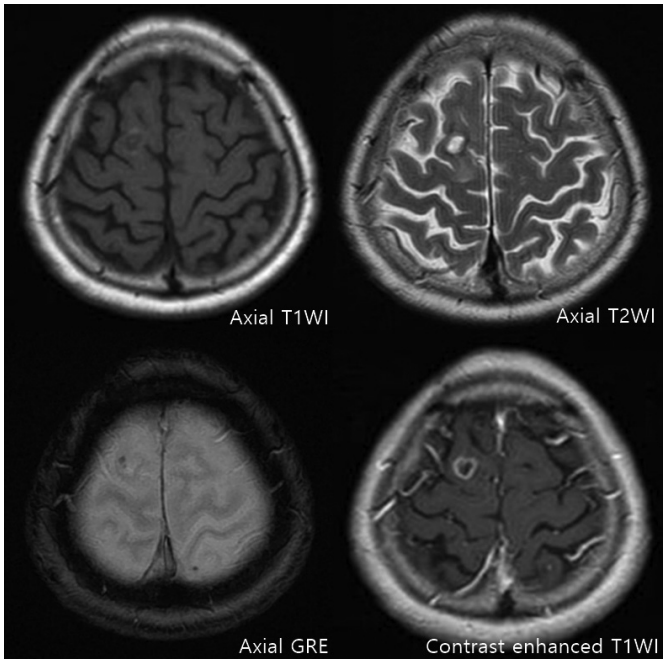
A 68-year-old woman visited the outpatient clinic of the department of neurology with a complaint of rotatory type dizziness for a month. She had postmenopausal osteoporosis with medication and denied any other history of previous disease.

A neurological examination revealed nothing remarkable. Magnetic resonance imaging (MRI) revealed a cystic mass with a mild surrounding edema in the right superior frontal gyrus, which appeared hypointense on T1-weighted imaging and hyperintense on T2-weighted imaging. Combined hemorrhage

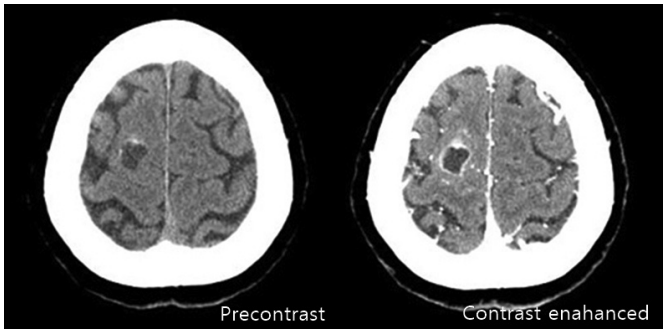
appeared hyperintense on T1-weighted imaging and as a dark signal intensity on gradient-echo imaging. Peripheral ring enhancement was observed after the intravenous administration of gadolinium (Fig. 1A). It was reported as a brain metastasis or infectious condition such as cysticercosis or tuberculosis, and the patient was referred to the oncology department. Abdomi-

Table 1. Reported Cases of Brain Anaplastic Ganglioglioma between 2007 and 2016 in the English Literature

Authors	Year of Publication	Sex/Age	Clinical Manifestation	Location of Lesion	Management	Follow-Up Periods	Follow-Up Results
Kang et al.	2007	F/45	Headache	Left frontal lobe	Total resection, adjuvant chemo- and radiotherapy	35 months	Recovery
Mittelbronn et al.	2007	F/47	None	Left frontal lobe	Surgical resection	60 months	Recovery
Kawataki et al.	2010	M/34	Seizure	Left temporal lobe	Subtotal resection	6 months	Death
DeMarchi et al.	2011	M/61	Headache	Left temporal lobe	Total resection	29 months	Death
Reis et al.	2012	M/9	Seizure	Right cingulate gyrus	Biopsy	48 months	Local recur and alive
Gonzalez et al.	2012	M/33	Right side weakness	Pons and midbrain	Biopsy	16 months	Death
Scoccianti et al.	2012	M/14	Seizure	Left frontoparietal lobe	Tumor resection	72 months	Recovery
Lucas et al.	2015	M/12	Headache	Left temporoparietal lobe	Surgical resection	23 months	Death
		M/11	Seizure	Left medial temporal lobe and hypothalamus	Radiotherapy and resection	16 months	Death
		M/34	Headache	Right medial temporal lobe	Surgical resection	22 months	Death
Costa et al.	2016	F/32	Headache	Pineal gland	Gross total resection	4 days	Recovery
Martinez et al.	2016	M/21	Headache	Left temporal lobe	Surgical resection	24 months	Death



A

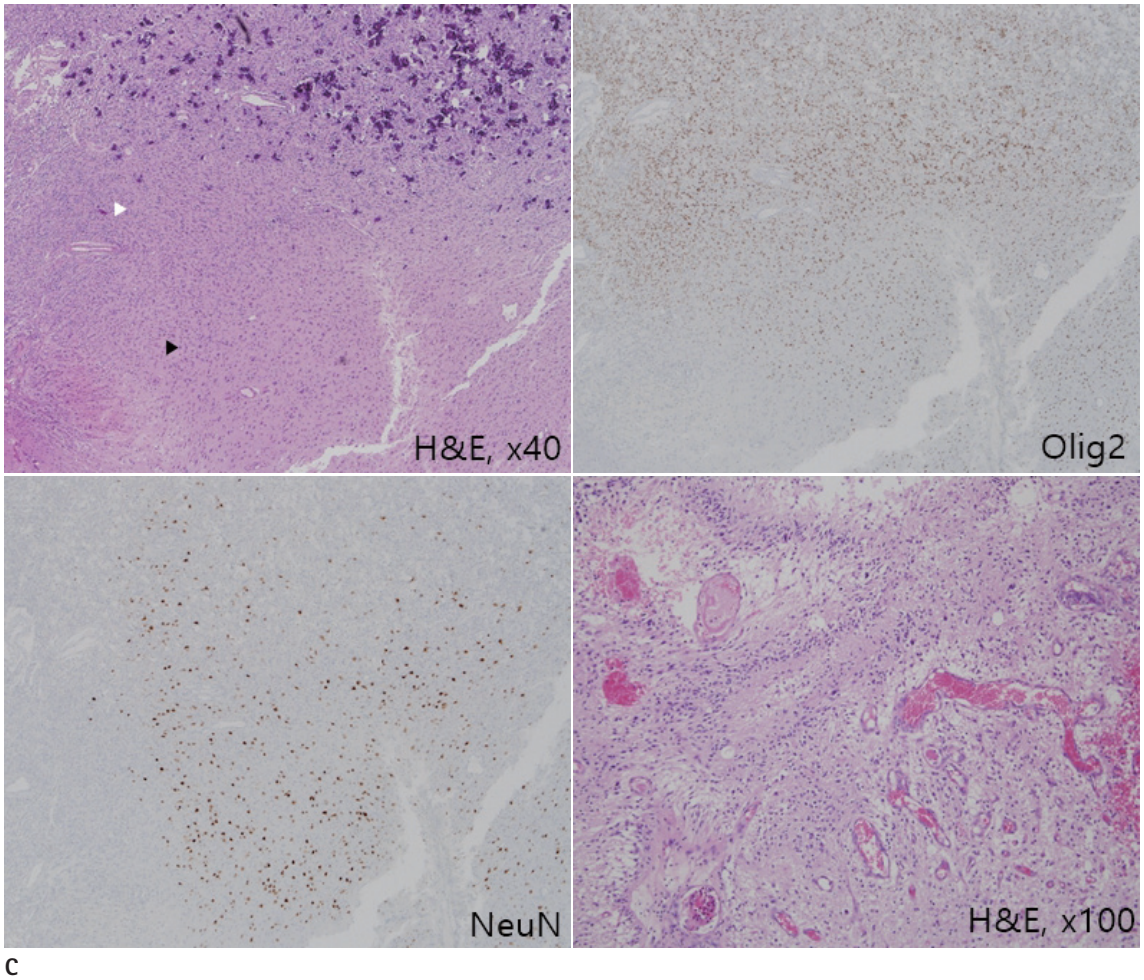


B

Fig. 1. Anaplastic ganglioglioma with rapid tumor growth in a 68-year-old woman.
A. Axial T1 (left upper panel) and T2 (right upper panel) magnetic resonance images showing a cystic mass with a mild surrounding edema in the right superior frontal gyrus. The gradient echo image (left under panel) shows a dark signal intensity within the mass, suggesting calcification or hemorrhage. The contrast-enhanced T1WI (right under panel) shows a peripheral ring enhancement.
B. Approximately 2 months after the initial magnetic resonance scan, follow-up precontrast- (left panel) and contrast-enhanced (right panel) brain computed tomography images showing a rapidly growing peripheral enhancing cystic mass with septation and peripheral calcification in the right superior frontal gyrus, with a maximum diameter of 1.6 cm.
GRE = gradient echo sequence, T1WI = T1-weighted image, T2WI = T2-weighted image

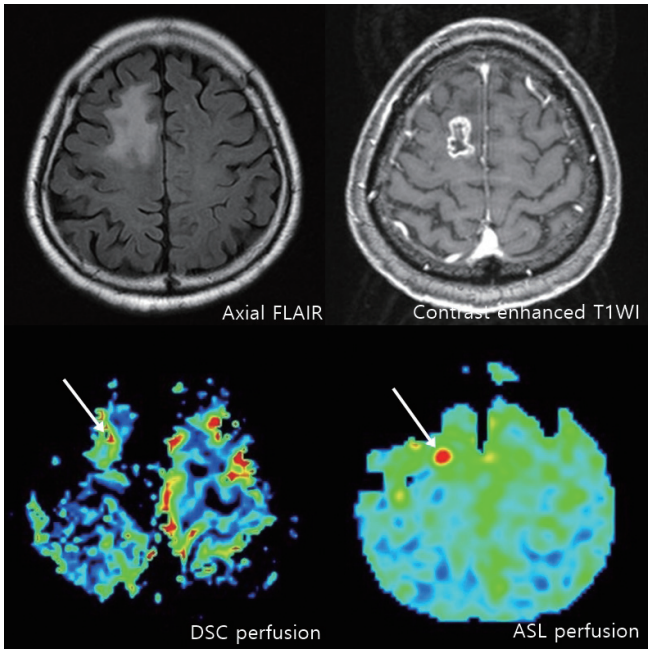
nal and thoracic computed tomography (CT) revealed no evidence of malignancy. The cerebrospinal fluid analysis results were within the normal limits. Antibodies against cysticercosis and Cryptococcus antigen were all negative. After approximately 2 months after the initial magnetic resonance scan, seizure-like movement developed, and she visited our emergency center. She was hospitalized in the department of neurosurgery. Follow-up contrast-enhanced brain CT revealed a rapidly growing peripheral enhancing cystic mass with septation and peripheral calcification in the right superior frontal gyrus, with a maximum diameter of 1.6 cm (Fig. 1B). These findings were attributed to a rapidly progressing brain metastasis or other cortical brain tumors, including ganglioglioma or pleomorphic xanthoastrocytoma or lymphoma with unusual presentation. The patient underwent surgery, and the tumor was excised.

Microscopic examination revealed that the tumor had a biphasic histological architecture characterized by neuronal and astrocytic components (Fig. 1C). Malignant features were evident in both neuronal and astrocytic components with increased cellularity, nuclear pleomorphism, and high proliferative index (Ki-67 index, approximately 2%). Evidence that show focal necrosis, endothelial proliferation, and calcifications was found. Immunohistochemical analysis revealed that the ganglion cells were positive for Olig 2 and NeuN. The patient was di-



C

Fig. 1. Anaplastic ganglioglioma with rapid tumor growth in a 68-year-old woman.
C. Microscopic finding showing the histopathological features of anaplastic ganglioglioma in our case. Biphasic neoplasm with calcification. Neuronal (black arrowhead) and astrocytic components (white arrowhead; H&E, original magnification, × 40, left upper panel). The immunostaining features are suggestive of ganglioglioma. The neoplastic glial components are positive for Olig2 (anti-Olig2 immunohistochemistry, × 40, right upper panel), and the ganglion cells are positive for NeuN (anti-NeuN immunohistochemistry, × 40, left under panel). Anaplastic pathological features include focal necrosis and endothelial proliferation (H&E, original magnification, × 100, right under panel).
H&E = hematoxylin-eosin stain



D

Fig. 1. Anaplastic ganglioglioma with rapid tumor growth in a 68-year-old woman.
D. Postoperative evaluation was performed 3 months after the surgical resection. FLAIR (left upper panel) and contrast-enhanced (right upper panel) magnetic resonance images showing an irregular peripheral enhancing lesion with a maximum diameter of 1.9 cm and a surrounding edema along the resection margin. DSC perfusion image (left under panel) shows increased cerebral blood volume (white arrow), and ASL perfusion image (right under panel) shows increased cerebral blood flow (white arrow). These findings suggest tumor recurrence.
ASL = arterial spin labelling, DSC = dynamic susceptibility contrast, FLAIR = fluid-attenuated inversion recovery, T1WI = T1-weighted image

agnosed as having an AGG (WHO grade III).

The patient recovered postoperatively without any neurological deficits. External radiotherapy was subsequently administered for a total dose of 5400 cGy in 30 fractions for 2 weeks.

Postoperative evaluation was performed 3 months after the end of the treatment, and a brain MRI revealed an irregular peripheral enhancing lesion with a maximum diameter of 1.9 cm and a surrounding edema along the resection margin. Cerebral blood volume and cerebral blood flow were increased on dynamic susceptibility contrast and arterial spin labelling perfusion studies, respectively. These finding suggested tumor recurrence (Fig. 1D). Additional chemotherapy was performed with the procarbazine, lomustine (CCNU), and vincristine (PCV) regimen. The treatment was well tolerated. She was scheduled for periodic clinical and radiological evaluation every 4 months. The final follow-up MRI obtained 8 months after the treatment revealed no evidence of recurrent disease. Currently, she has an intact neurological status and manages a normal life.

DISCUSSION

AGGs, similarly to low-grade gangliogliomas, histopathologically contain a mixture of neoplastic glial cells such as astrocytes and neuronal cells but have malignant features such as increased cellularity, mitotic activity, atypia, microvascular proliferation, and necrosis, which are similarly observed in other high-grade gliomas (2). The glial components are confirmed by using immunohistochemical staining, including glial fibrillary acidic protein and S-100 protein. The neuronal components are positive for synaptophysin and neuron-specific enolase (2). The malignant characteristics are more frequently featured by glial components, (5) however, both neuronal and astrocytic components showed malignant features in our case.

Imaging findings and clinical courses of AGGs have been poorly understood because their incidence is extremely rare and published case series are mostly case reports. In a recent case series of 18 patients with AGG, the clinical and imaging features of AGGs were different from those of their benign counter forms. Most tumors showed single enhancing lesions, the temporal lobe was not the main location, and tumor hemorrhage was not common. Midline and posterior fossa locations were relatively common in children. Irregular strong enhancing tumors in the left frontal lobe extend to the cingulate gyrus, and large heterogeneous enhancing lesions with central necrosis in the right parietal lobe were reported. In our case, the tumor was initially a small cystic lesion with ring enhancement and hemorrhage, located in the right frontal cortex. The tumor grew rapidly over 2 months to 1.5 times larger than its initial long diameter.

Traditionally, differential diagnoses for single small cystic lesions with peripheral enhancement in brain parenchyma were metastasis, cerebral abscess, glioblastoma, and other infectious conditions such as tuberculoma and neurocysticercosis. These lesions are difficult to discriminate from each other based on imaging features because they have similar imaging findings. Clinical setting and incidence are the keys for the differentiation of these lesions. In our case, the initial imaging feature was a small ring-enhancing lesion with superficial hemorrhage, which

led to several differential diagnoses such as metastasis and several infectious conditions. However, rapid growth on short-term follow-up made the diagnostic process more challenging. Rapid tumor progression with hemorrhage and necrosis is occasionally found in hemorrhagic brain metastasis (6), and acquired immune deficiency syndrome- or *Ebstein-Barr virus*-related CNS lymphomas (7), or anaplastic pleomorphic xanthogranuloma (8). Although the incidence of AGG is extremely rare, it can be included as a differential diagnosis for superficial cystic tumors with rapid progression.

Unlike WHO grade I gangliogliomas, AGGs have a relatively poor prognosis. The tumor recurrence interval after initial resection ranges from 2 to 15 months, in spite of adjuvant chemotherapy and radiotherapy performed after surgical resection. Management strategies are not well established, but total tumor resection provides better prognosis (9). The usefulness of radiotherapy and chemotherapy for AGG is controversial (10).

We report a case of an AGG that appeared as a rapidly growing ring-enhancing cystic mass mimicking brain metastasis in a middle-aged woman. We suggest that AGG may be considered as a differential diagnosis for a rapidly growing peripheral enhancing mass in the brain, especially when it is superficially located.

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중년여성에서 뇌전이암으로 오인되었던 역형성 신경절교종: 증례보고

박주용[1] · 이하영[1]* · 박인서[2] · 김은영[3] · 임명관[1] · 강영혜[1] · 김준호[1] · 조순구[1]

역형성 신경절교종은 매우 드문 악성종양으로 주로 소아나 젊은 성인에서 발생하는 것으로 알려져 있으나, 치료방법이나 임상경과에 대한 연구가 많이 이루어지지 않았다. 이에, 저자들은 고리모양 조영증강을 보이고 2개월 동안 빠른 크기 증가를 보여 뇌전이암으로 오인되었던 표재성 전두엽 병변으로 나타난 68세 여자환자의 천막상부 역형성 신경절교종의 증례를 보고하고자 한다.

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