Acta Med. Okayama, 2023
Vol. 77, No. 3, pp. 335–340

Acta Medica Okayama
http://escholarship.lib.okayama-u.ac.jp/amo/

Case Report

A Case of High-Grade Glioma in an Eloquent Area Treated with Awake Craniotomy in an 85-year-old Patient

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An 85-year-old woman presented with aphasia due to an occupying lesion in the left frontal lobe near the language area. Complete resection of the contrast-enhancing lesion was performed under awake conditions. The pathological diagnosis was anaplastic astrocytoma, and postoperative radiochemotherapy was administered. Awake surgery is a useful technique to reduce postoperative neurological sequelae and to maximize surgical resection. Although the patient was elderly, which is generally considered high risk, she did not have any severe neurological deficits and had a good outcome. Even in the extreme elderly, awake surgery can be useful for gliomas in language cortices.

Key words: awake surgery, high-grade glioma, eloquent area, elderly patient

High-grade gliomas (HGGs), including anaplastic astrocytoma and glioblastoma, are poor prognostic tumors that arise in the brain parenchyma, and the prognosis depends on the rate of surgical removal of the tumor [1-4]. HGGs often occur in or near the eloquent area, which is associated with motor and language functions, and removal of these gliomas is very challenging because of the possibility of critical neurological deficit after surgery. In order to maximize the removal of brain tumors in these eloquent areas and to avoid postoperative complications as much as possible, awake surgery is one of the most useful surgical methods [5-9]. The risk of awake surgery is considered to be higher in the elderly, and there are few reports regarding awake surgery for elderly patients. Here, we present a case of awake surgery for the surgical removal of HGG in an 85-year-old patient that had a good outcome, and we report the results based on literature review.

Received November 23, 2022; accepted January 20, 2023.
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Case Report

An 85-year-old woman visited her primary care physician with a complaint of speech disorder that had been progressing gradually for one month. She had a history of hypertension, appendicitis, and diverticulitis of the colon. She was taking medication for hypertension and had no allergies. She was exhibiting motor aphasia at the time of the first visit. She had many difficulties with verbalization in free speech and some confabulation but had no problems with comprehension. There was no apparent paralysis, and no other neurological dropout symptoms of note. The patient was able to get up, stand up, and walk unaided. Although she had motor aphasia, she was independent in her activities of daily living (ADLs), doing all personal and household chores independently until just before the visit. Her Karnofsky Performance Status score was 80.

On head magnetic resonance imaging (MRI), an

Conflict of Interest Disclosures: No potential conflict of interest relevant to this article was reported.

occupying lesion approximately 4 cm in size was found in the left frontal lobe. T2/FLAIR showed low to equal signal, T1 showed low signal, diffusion weighted imaging (DWI) showed equal signal or slightly high signal, and T1 contrast showed an irregular ring enhancement. Functional MRI showed signal in the left cerebral hemisphere, suggesting that the dominant hemisphere for language was the left side, since the patient already had aphasia (Fig. 1). Blood tests showed no elevation of tumor markers and no other abnormal findings of note. Chest and abdominal computed tomography showed no obvious neoplastic lesions and no other significant findings. Although high-grade glioma (HGG) and metastatic brain tumor were considered as possible differential diagnoses, the results of various tests suggested HGG. It was thought that the patient was symptomatic and tumor removal should be performed at an early stage.

As the lesion was not exposed to the brain surface, it was considered that language mapping under an awake condition was necessary during the tumor removal to develop a good surgical field. Since the patient was very old and tumor removal with language mapping under awake conditions was considered risky, a biopsy was suggested. However, the patient and her family strongly desired tumor removal, so we performed awake surgery to remove the tumor.

The patient underwent total intravenous anesthesia (TIVA) with propofol, and the airway was secured with a laryngeal mask. Adequate regional anesthesia and nerve blocks and a left frontotemporal craniotomy were performed, the induction of TIVA stopped, and the patient was awakened and extubated. At the time of extubation, because this patient was very elderly, they were awakened during an incision in the dura mater to avoid prolonged awake time. On awakening, the patient responded to instructions and was able to answer tasks, and language mapping was performed. Cortical and subcortical mapping were performed with free talk, simple questions, and recitation. We were able to identify the motor cortex and language cortex by language mapping, and the surgical field was developed by open-

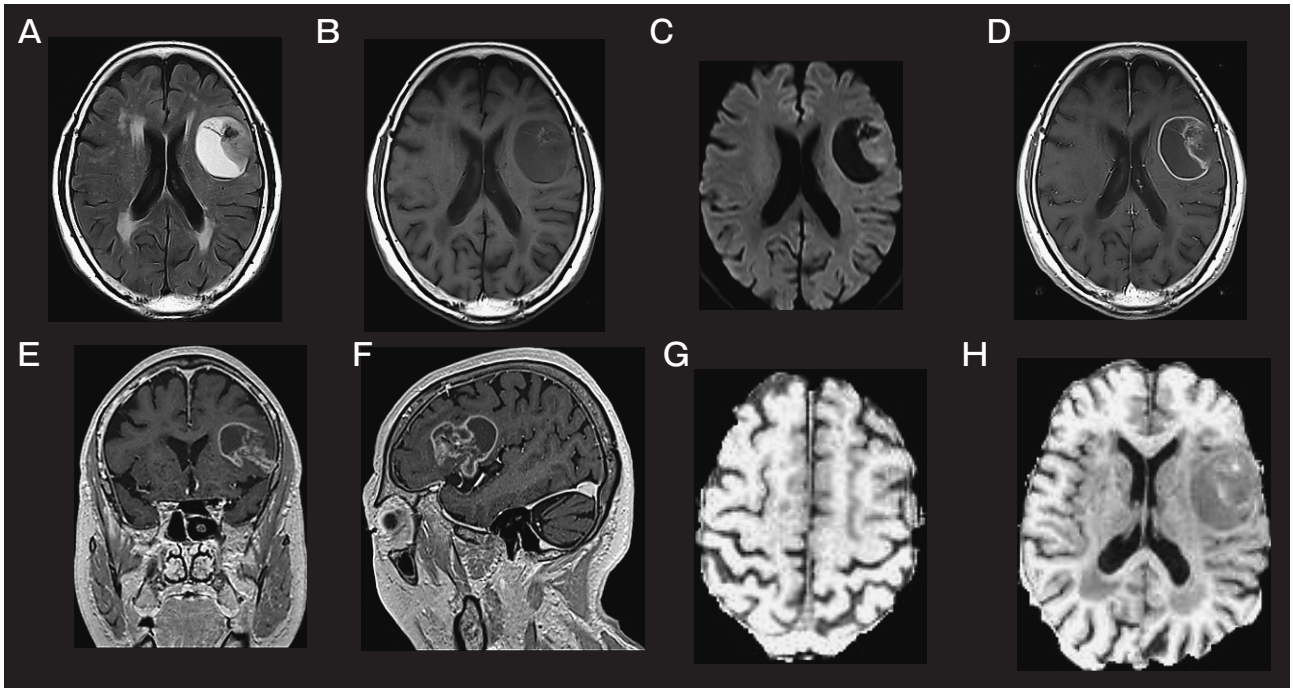

Fig. 1 Brain magnetic resonance imaging (MRI) findings before surgery. **A**, FLAIR presenting a high-intensity lesion in the left frontal lobe. A nodule-like lesion is observed in the cystic lesion; **B**, T1WI (T1-weighted imaging) presenting the cystic lesion as low intensity; **C**, DWI (diffusion-weighted imaging) presenting the cystic lesion as iso intensity; **D**-**F**, Gd (gadolinium)-T1WI presenting distorted ring enhancement with a nodule-like lesion. (**D**, axial; **E**, coronal; **F**, sagittal); **G** and **H**, Functional MRI findings indicate that the dominant hemisphere of language is on the left side although the signal is faint.

ing the sulcus in front of the area considered to be the language cortex (Fig. 2).

Surgery was performed under the awake condition for 1.5 h. During the removal of the tumor, the patient became increasingly fatigued and slow to respond to questions, so she was switched to TIVA again. After the surgery, the patient was in good general condition, but had transiently worsened motor aphasia and developed right mild hemiparesis. Although the lesion with contrast effect was almost completely removed, cerebral infarction was observed near the left supplementary motor cortex on MRI of the head (Fig. 3). The symptoms were transient and gradually improved, and the neurological symptoms recovered to a level similar to the preoperative level in 2 weeks, suggesting that the patient had developed supplementary motor area syndrome due to the cerebral infarction, and no sequelae occurred. The postoperative pathological diagnosis was anaplastic astrocytoma (WHO 2016 classification Grade III), IDH-wild and Ki67 was approximately 40%, and postoperative radiochemotherapy (radiation therapy: 40 Gy/15 Fr, temozoromide 75 mg/m^2) was performed. Two months after the surgery, the patient was able to walk and the motor aphasia remained at the same level as before surgery. She was transferred to a rehabilitation hospital to complete recovery in order to return home. She was discharged from the rehabilitation hospital after 2 months of hospitalization. After discharge home, the patient underwent temozoromide maintenance therapy and imaging follow-up as an outpatient. More than one year after the onset of the disease, there has been no recurrence, and the patient is still receiving imaging follow-up.

Ethics approval. All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee (IRB#1911-023) and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. Written informed consent was obtained from the patient.

Discussion and Conclusions

Gliomas are the most common primary tumors arising in the central nervous system. The Japanese Brain Tumor Registry (2005-2008) reports that gliomas account for approximately 24% of primary brain tumors [1]. The rate of removal of both low- and HGGs is an important factor in determining the prognosis of the patient [2-4]. In the case of glioblastoma, which has the poorest

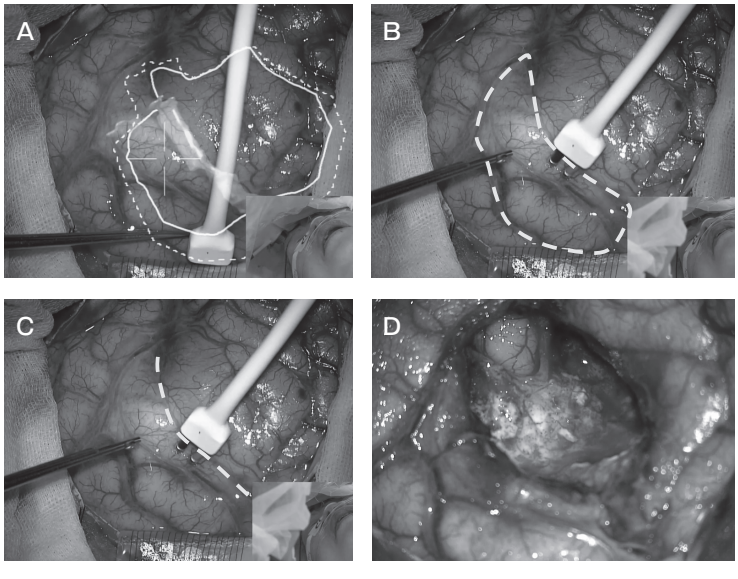

Fig. 2 Intraoperative findings at surgical resection. **A**, Checking lip movement. Both solid and dotted yellow lines are the tumor boundary assumed by neuronavigation (Brainlab navigation system); **B**, The area circled by the yellow dotted line shows arrest of speech when stimulated; **C**, The surgical field was developed by dividing the sulcus (yellow dotted line) anterior to the suspected language field; **D**, Post-extraction surgical field. There was no unforeseen hemorrhage or brain swelling. **A**-**C**. The photograph in the lower right corner shows an intraoperative view of the patient from the caudal side.

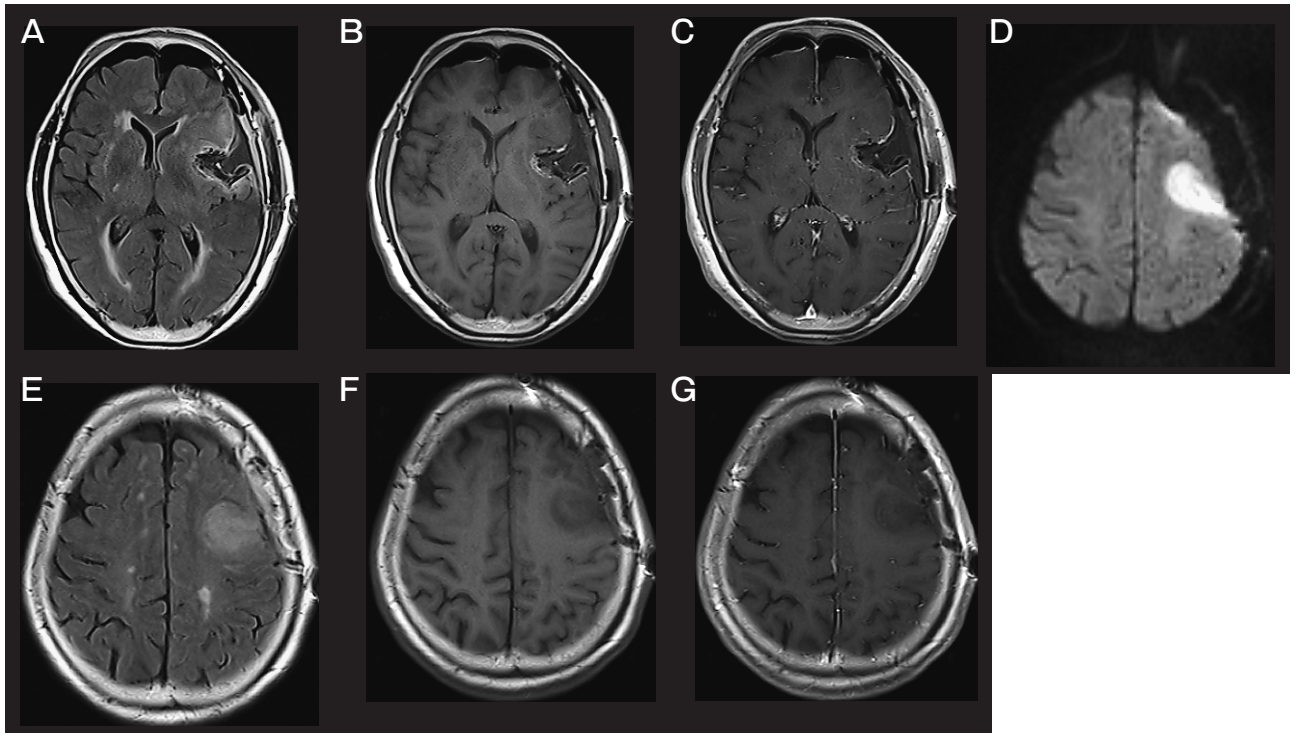

Fig. 3 Brain magnetic resonance imaging findings the day after surgery. **A**-**C**, The preoperative contrast-enhanced lesion was completely removed on magnetic resonance imaging. (**A**, FLAIR; **B**, T1WI; **C**, Gd-T1WI); **D**-**G**, A cerebral infarction appeared in the vicinity of the supplementary motor area. (**D**, DWI; **E**, FLAIR; **F**, T1WI; **G**, Gd-T1WI)

prognosis among HGGs, the higher the percentage of contrast-enhanced lesions removed, the longer overall survival (OS) can be expected. If 78% or more of the lesions are removed, the OS period can be expected to be prolonged [2]. Surgical resection plays a central role in the management of gliomas. A growing body of evidence supports that, in both low- and HGGs, greater resection coverage is associated with better overall survival, progression-free survival, and superior quality of life. Furthermore, higher tumor removal rates are associated with better health-related quality of life [10].

A number of intraoperative techniques are being utilized to safely perform glioma surgery with larger resection margins [11, 12]. However, if the lesion is in an eloquent area, such as the anatomical language area or its vicinity, the lateral parietal lobe centered on the angular gyrus, or near the motor cortex, the risk of severe postoperative neurological symptoms is high and aggressive removal may not be possible, forcing biopsy or partial excision in some cases.

Awake surgical mapping has the potential to maximize removal when gliomas are located within or adjacent to eloquent brain regions. Recent studies have shown that intraoperative awake mapping results in less permanent postoperative neurological damage, better patient condition and quality of life, and better functional outcomes for patients with glioma compared to tumor resection performed under general anesthesia [5-9]. Thus, awake surgery has been reported to be an effective surgical technique for high tumor removal rates and minimizing the risk of poor postoperative functional outcome, as shown in some reviews and analysis [13-15].

Aggressive tumor removal in the treatment of gliomas in the elderly is controversial because aggressive tumor removal may impair the postoperative functional prognosis. Chaichana *et al.*, however, reported that older patients with glioblastoma tolerated aggressive surgery without greater morbidity or mortality than younger patients. They reported 18% new perioperative complications and 0% mortality with aggressive resection, comparable to the approximately 30% new perioperative complications reported by Rahman *et al.* [16, 17]. In a randomized study limited to 30 elderly patients

with HGG, Vuorinen *et al.* reported increased OS for patients who underwent craniotomy and resection compared to biopsy [18]. However, these reports do not mention awake surgery in the elderly. Safe extensive tumor resection was shown to improve survival, functional recovery, and tumor recurrence rates, and did not lead to increased mortality when considered in conjunction with known and established safety measures when treating elderly patients with HGG [19-21]. The management of elderly patients with HGG has evolved in recent years. Perioperative risk factors such as performance status and medical complications are now taken into account, and the maximum safe resection is recommended [22, 23].

In general, awake surgery may be difficult for elderly patients because of the risk of delirium and sudden changes in blood pressure during awakening [24]. Grossman *et al.* reported no significant differences after awake surgery in the incidence of postoperative death, paralysis, or aphasia in younger patients versus patients who are 65 years of age or older [25]. Further, a multicenter cohort study showed significantly fewer neurological deficits in the awake surgery group compared to the asleep group in patients aged 70 years and older at 3 months, with a National Institutes of Health Stroke Scale score of 2 or higher and at 6 months in those with a Karnofsky Performance Status score of 80 or lower. Awake surgery may thus improve functional prognosis in patients aged 70 years or older. In most reports of awake surgery for the elderly, patient age is defined as 70 years or older, but this cohort study included patients up to 90 years of age, which may provide a rationale for adopting a more radical surgical approach for these older glioma patients [26].

Although this patient was very old (85 years old), we believe that she was a good candidate for awake surgery because of her good preoperative performance status and neurological state. After a thorough preoperative consultation and sufficient informed consent from the patient, the patient underwent awake surgery. Although a transient neurological deficit was observed postoperatively, the contrast-enhanced lesion was removed entirely on imaging, the patient did not have any severe neurological symptoms, and she improved to the same level as before surgery in 2 weeks. Despite few reports on awake surgery in elderly patients, here we carried out a tumor resection with awake surgery in an elderly patient with glioma without serious complications. We demonstrated that even elderly patients can be treated with awake surgery if their preoperative ADLs are good, although the indication should be carefully selected in individual patients.

Conclusion

Here, we report a case of awake surgery in an 85-year-old patient. Awake surgery can be considered useful for elderly patients with high ADLs. However, as the elderly are more susceptible to serious illness, adequate preparation and extreme care are necessary.

Acknowledgments. We would like to thank Chris Rowthorn, from Chris Rowthorn Japan, for editing a draft of this manuscript.

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