Research Square

Preprints are preliminary reports that have not undergone peer review.
They should not be considered conclusive, used to inform clinical practice,
or referenced by the media as validated information.

A Bilateral, Mirror-Like Multifocal/Multicentric Glioblastoma: A Case Report and Literature Review

Mulin Xie
Shenzhen University
Guiliang Liu
Shenzhen University
Zhong Deng
The First Affiliated Hospital of Shenzhen University
Shuai Xiao
The First Affiliated Hospital of Shenzhen University
Guodong Huang
huangguodong@email.szu.edu.cn

The First Affiliated Hospital of Shenzhen University

Case Report

Keywords: Glioblastoma, IDH-wildtype, Multicentric GBM, Multifocal GBM, Survival, Cerebral edema, Maximal safe resection, Chemoradiotherapy delay, Case report

Posted Date: February 27th, 2026

DOI: https://doi.org/10.21203/rs.3.rs-8923634/v1

License: This work is licensed under a Creative Commons Attribution 4.0 International License.
Read Full License

Additional Declarations: No competing interests reported.

Abstract

Background

Multifocal or multicentric glioblastoma (mGBM) generally carries an unfavorable prognosis. Tumor burden, choice of surgical approach, and perioperative management of cerebral edema directly determine whether adjuvant chemoradiotherapy can commence on schedule. We report a patient with bilateral, symmetric supratentorial lesions without callosal continuity who developed diffuse postoperative cerebral edema with cardio-respiratory instability and died 4 months after surgery.

Case presentation:

A 60-year-old woman presented with a 2-week history of progressive limb weakness (GCS 15; KPS 60; limb power grade 3). MRI suggested bilateral frontal tumors. She underwent simultaneous bilateral frontal craniotomies for tumor resection under general anesthesia. Final pathology confirmed GBM, WHO grade 4, IDH-wildtype. Although initially arousable, her consciousness worsened on postoperative days 3–6, followed by cardio-respiratory instability and lower respiratory tract infection/ventilation-related complications. She alternated between the general ward and neurointensive care unit (NICU). Unable to tolerate adjuvant chemoradiotherapy because of poor performance status, she died approximately 4 months postoperatively after the family elected to cease treatment.

Conclusions

For mGBM, the primary surgical objective is to debulk within functional tolerability and secure the 2–6-week postoperative window for chemoradiotherapy to extend overall survival. Operative strategies should be individualized according to tumor burden, particularly in patients with large, bilaterally balanced hemispheric disease. Prognosis depends more on achieving an adequate extent of resection within functional limits, rigorous postoperative edema/ICP control, and on-schedule completion of the Stupp regimen than on the multifocal/multicentric phenotype per se. These observations are hypothesis-generating and should be interpreted in the context of a single case.

Background

Glioblastoma (GBM) is the most common and most aggressive primary brain tumor in adults. Current guidelines recommend maximal safe resection (MSR) followed by concurrent chemoradiotherapy and adjuvant chemotherapy, with a median overall survival of about 15 months. Clinically, GBM usually presents as a solitary lesion; multiple lesions are uncommon and should be differentiated from intracranial metastases (1–3). Multifocal/multicentric GBM (mGBM) with large, bilaterally balanced tumor burden is relatively rare and presented poor outcome, compared with solitary GBM. Balancing tumor-burden control and postoperative management including edema and intracranial pressure

remains challenging in mGBM, especially in those with large tumor burden. We retrospectively report a patient admitted to our neurosurgical department in February 2022 with symmetric, isolated contrast-enhancing masses in both frontal lobes. Both lesions were resected in a single session and confirmed as GBM histologically. Postoperatively, the patient developed progressive cerebral edema with cardio-respiratory instability, was unable to tolerate chemoradiotherapy due to poor physiological reserve, and died 4 months after surgery.

Case Presentation

A 60-year-old woman was admitted with a 2-week history of progressively worsening limb weakness. Over the same period, she developed gait difficulty, memory decline, and blunted affect, without dizziness, headache, nausea, vomiting, or seizures. CT at an outside hospital showed bilateral frontal masses with intra-tumoral hemorrhage highly suspicious for metastases. Past history included hypertension (irregularly treated), hyperlipidemia/hypercholesterolemia, multiple pulmonary nodules, and focal bronchiectasis; she denied the use of anticoagulants or antiplatelet agents. On examination, she was alert but affectively blunted (GCS 15; KPS 60) with marked memory impairment. Cranial nerves were intact. Motor strength was 1/5 in the right upper limb and 3/5 in the remaining limbs, with normal tone. Preoperative MRI revealed bilateral frontal lesions suspicious for malignancy (metastasis?) (Fig. 1–2). She underwent simultaneous bilateral frontal craniotomies for tumor resection. Intraoperative frozen section suggested glioma, and final pathology confirmed glioblastoma according to the 5th World Health Organization classification of tumors of central nervous system (Fig. 3–4: H&E showed necrosis and MVP; IDH1 R132H was negative on immunohistochemistry.).

Postoperatively, the patient remained intubated with spontaneous respiration and stable vital signs. Immediate CT showed large bilateral pericavitary hypodensities with mass effect and a midline centered position (Fig. 5). Post-surgery day 1 (D1): shallow coma (GCS 4T; E2VTM2); intensified dehydration therapy, sedation/analgesia, antiepileptics, and antibiotics were administered. D3: mental status improved (GCS 8; E2V2M4); dehydration was maintained and she was transferred to the general ward. Imaging showed finger-like hypodensities around the cavities on CT; MRI suggested gross resection of both lesions (Fig. 5). D4–D6: apathetic (GCS 9; E3V2M4) with intermittent hypertension and tachycardia that improved after symptomatic treatment; dehydration therapy was tapered. D9: episodic hypertonia with elevated blood pressure and heart rate, relieved with symptomatic therapy. D12: palpitations and dyspnea with suprasternal/intercostal retractions and tongue-base collapse; despite suction and oropharyngeal airway, endotracheal intubation was required. She was transferred to the NICU for tracheotomy and advanced airway care. D13–D16: stabilized and returned to the general ward. D17 to discharge: hemodynamically stable; consciousness improved from shallow coma to minimally conscious state; limb strength 0/5; tracheostomy in situ. Intermittent arrhythmias and frequent ventricular ectopy improved with symptomatic management and fluid restriction. In summary, the postoperative course featured fluctuating consciousness and severe peritumoral edema necessitating prolonged airway management. Despite intensive dehydration and ICP control, the patient’s poor

physiological reserve precluded chemoradiotherapy; her condition deteriorated, and she died about 4 months after surgery at the family's request.

Discussion

This report describes a patient with bilaterally balanced, heavy-burden multifocal/multicentric IDH-wildtype glioblastoma (mGBM) and the treatments administered over the disease course. Overall survival (OS) in mGBM is generally reported to be inferior to that in solitary GBM. Prior studies have described median OS of approximately 6–13 months, compared with ~ 12–16 months in solitary GBM (4–7). In retrospective series, improved survival in mGBM has been associated with better performance status, greater extent of resection (EOR), MGMT promoter methylation, and completion of radiotherapy plus temozolomide (RT + TMZ), whereas multifocality itself may be less predictive when these factors are accounted for (4, 7, 8).

Surgical decision-making for mGBM remains individualized because high-quality prospective evidence is limited. Within strict functional boundaries, maximal safe resection (MSR) may reduce tumor burden, alleviate mass effect, and facilitate timely initiation of adjuvant therapy. In a retrospective cohort including patients with mGBM and solitary GBM, Krenzlin et al. reported that active multimodal therapy (MSR + RT + TMZ) was associated with improved survival outcomes, and that resection of multiple lesions was not clearly inferior to resection of a dominant lesion in selected patients (8). These observations suggest that aggressive treatment may be considered when feasible, while carefully balancing anatomical/functional risk.

Across available retrospective studies, outcomes in mGBM appear to be influenced by both the degree of cytoreduction achievable within functional tolerability and whether chemoradiation can commence on schedule. Krenzlin et al. described a stepwise association between EOR and survival, and reported that both conventional and hypofractionated radiotherapy were associated with prolonged PFS/OS; the addition of TMZ was associated with further benefit, such that survival in multifocal disease may approach that of solitary GBM under comparable treatment intensity in selected cohorts (8). A weighted survival analysis suggested that cytoreductive resection may provide a survival advantage over biopsy in multifocal glioblastoma when feasible (9). Similarly, Friso et al. reported an EOR gradient (GTR ~ 17 months, STR ~ 11 months, PR ~ 7 months, biopsy ~ 5 months), with complications more closely related to anatomy/functional risk than to multifocality itself, supporting the principle of MSR when safely achievable (10). For deep or diffusely infiltrative disease, stereotactic biopsy followed by prompt chemoradiotherapy is a reasonable option; overall, available evidence supports prioritizing function-preserving cytoreduction when appropriate and minimizing delays to adjuvant therapy (12, 13). When multiple targets are present, Hassaneen et al. observed no statistically significant survival difference compared with matched single-lesion surgery and did not report clearly higher perioperative morbidity, although selection bias is likely in such series (6). Phenotype may still matter: Patil et al. reported shorter OS in multifocal GBM, which they attributed largely to lower EOR, reduced KPS, and incomplete adjuvant therapy (14). In another retrospective analysis, Guerrini et al. reported survival associations favoring

GTR/STR over biopsy and suggested that maintaining postoperative KPS ≥ 70 may be important for realizing any benefit of surgery (11). Baro et al. also identified RT + TMZ as an independent predictor of OS in their cohort (4).

In the present case, the unfavorable outcome likely reflects a combination of high-risk disease burden and a complicated perioperative course that prevented timely delivery of standard adjuvant therapy. Postoperative CT demonstrating extensive pericavitary hypodensity (Fig. 5) is consistent with severe vasogenic edema and blood–brain barrier disruption, which may contribute to intracranial hypertension, neurological deterioration, and increased susceptibility to systemic complications. In this context, poor physiological reserve and fluctuating neurological status made it difficult to initiate and sustain the Stupp regimen within the typical postoperative window, potentially diminishing the overall effectiveness of surgery. Therefore, the early death in this case should be interpreted as the combined effect of tumor biology/burden, perioperative complications, and treatment interruption, rather than as evidence for or against simultaneous bilateral resection as a strategy per se. Practically, a key surgical aim in selected mGBM patients may be to achieve meaningful cytoreduction within functional limits while also protecting the postoperative window for multimodal therapy through rigorous edema/ICP management and systemic supportive care (15, 16). If adjuvant therapy cannot proceed on schedule, any incremental survival benefit of surgery may be substantially reduced.

Overall, this case suggests that imaging-defined “maximal resection” may be undermined by postoperative cerebral swelling and systemic instability; thus, functional recovery and timely initiation/completion of multimodal therapy may be critical determinants of outcome in selected patients. However, because bilaterally balanced, heavy-burden supratentorial mGBM is uncommon, available evidence remains largely retrospective and prone to selection bias, and optimal surgical strategies lack prospective validation. These observations are hypothesis-generating and should be interpreted in the context of a single case.

Limitations

This report is limited by its single-patient design and retrospective nature, which precludes causal inference and limits generalizability. Treatment decisions and outcomes may have been influenced by patient-specific factors, perioperative course, and the inability to complete standard adjuvant therapy. In addition, molecular profiling was limited to routine clinical testing, and advanced genomic characterization was not available. Larger cohorts are needed to validate whether the observations described here apply to broader populations of multifocal/multicentric glioblastoma.

Conclusions

In multifocal/multicentric glioblastoma, surgical management should be individualized. When conditions allow, the primary surgical goal may be to achieve maximal safe cytoreduction within functional tolerability while, as far as possible, preserving the critical early postoperative window for initiating and

completing multimodal therapy. This case suggests that outcomes in bilaterally balanced, high-burden disease may be strongly influenced by perioperative complications, postoperative edema/intracranial pressure control, and the ability to initiate chemoradiotherapy on schedule. However, these observations are hypothesis-generating and should be interpreted cautiously in the context of a single case; larger studies are needed to clarify the optimal surgical strategy and perioperative management for this population.

Abbreviations

ATRX, alpha-thalassemia/mental retardation syndrome X-linked;
BBB, blood–brain barrier;
CBF, cerebral blood flow;
Cho, choline;
Cr, creatine;
CT, computed tomography;
D1 (etc.), postoperative day 1 (etc.);
DSC-PWI, dynamic susceptibility contrast perfusion-weighted imaging;
EOR, extent of resection;
GFAP, glial fibrillary acidic protein;
GBM, glioblastoma;
GCS, Glasgow Coma Scale;
GTR, gross total resection;
H&E, hematoxylin and eosin;
HR, hazard ratio;
ICP, intracranial pressure;
IDH, isocitrate dehydrogenase;
IDH1 R132H, isocitrate dehydrogenase 1 R132H mutation (immunohistochemistry);
KPS, Karnofsky Performance Status;
mGBM, multifocal/multicentric glioblastoma;
MRI, magnetic resonance imaging;
MSR, maximal safe resection;
MRS, magnetic resonance spectroscopy;
MVP, microvascular proliferation;
NAA, N-acetylaspartate;
NICU, neurointensive care unit;
OS, overall survival;
PFS, progression-free survival;
PR, partial resection;
RT, radiotherapy;

STR, subtotal resection;
TMZ, temozolomide;

MGMT, O6-methylguanine-DNA methyltransferase;
WHO, World Health Organization.

Declarations

Ethics approval and consent to participate

Ethical approval was obtained from the Clinical Research Ethics Committee of Shenzhen Second People's Hospital (Approval No. 2025-723-01PJ). The requirement for informed consent to participate was waived by the ethics committee due to the retrospective nature of this report.

Consent for publication

The patient is deceased. Written informed consent for publication of this case report and any accompanying images was obtained from the patient's next of kin/legal representative. Publication of this case report was approved by the Clinical Research Ethics Committee of Shenzhen Second People's Hospital (Approval No. 2025-723-01PJ). All data and images have been anonymized and contain no identifiable personal information.

Availability of data and materials

All data supporting the findings of this case report are included in this published article. Original imaging data are not publicly available due to privacy considerations but may be available from the corresponding author on reasonable request and with appropriate ethical approval.

Competing interests

The authors declare that they have no competing interests.

Funding

None.

Authors' contributions

Xiemulin Xie conceived the report and supervised the study. Guiliang Liu interpreted neuroimaging and prepared the figures and critically revised the manuscript. Zhong Deng collected the clinical data and drafted the manuscript. Shuai Xiao contributed to clinical data collection and manuscript revision. Guodong Huang provided overall supervision and critically revised the manuscript. All authors read and approved the final manuscript.

Acknowledgements

Not applicable.

References

1. Yoshida D, Kogiku M, Noha M, Takahashi H, Teramoto A. A case of pleomorphic xanthoastrocytoma presenting with massive tumoral hemorrhage. J Neurooncol. 2005;71(2):169–71. 10.1007/s11060-004-0915-z.
2. Nozaki T, Sato H, Yamazoe T, Namba H. Diffuse astrocytoma initially presenting as a massive intracerebral hemorrhage: case report. Neurol Med Chir (Tokyo). 2015;55(1):86–8. 10.2176/nmc.cr.2013-0177.
3. Joseph DM, O'Neill AH, Chandra RV, Lai LT. Glioblastoma presenting as spontaneous intracranial haemorrhage: Case report and review of the literature. J Clin Neurosci. 2017;40:1–5. 10.1016/j.jocn.2016.12.046.
4. Baro V, Cerretti G, Todoverto M, et al. Newly Diagnosed Multifocal GBM: A Monocentric Experience and Literature Review. Curr Oncol. 2022;29(5):3472–88. 10.3390/curroncol29050280. Published 2022 May 11.
5. Showalter TN, Andrel J, Andrews DW, Curran WJ Jr, Daskalakis C, Werner-Wasik M. Multifocal glioblastoma multiforme: prognostic factors and patterns of progression. Int J Radiat Oncol Biol Phys. 2007;69(3):820–4. 10.1016/j.ijrobp.2007.03.045.
6. Hassaneen W, Levine NB, Suki D, et al. Multiple craniotomies in the management of multifocal and multicentric glioblastoma. Clinical article. J Neurosurg. 2011;114(3):576–84. 10.3171/2010.6.JNS091326.
7. Dimov D, Brainman D, Berger B, Coras R, Grote A, Simon M. The role of cytoreductive surgery in multifocal/multicentric glioblastomas. J Neurooncol. 2023;164(2):447–59. 10.1007/s11060-023-04410-7.
8. Krenzlin H, Jankovic D, Dauth A, et al. Multimodal treatment of glioblastoma with multiple lesions - a multi-center retrospective analysis. J Neurooncol. 2024;170(3):555–66. 10.1007/s11060-024-04810-3.
9. Di L, Heath RN, Shah AH, et al. Resection versus biopsy in the treatment of multifocal glioblastoma: a weighted survival analysis. J Neurooncol. 2020;148(1):155–64. 10.1007/s11060-020-03508-6.
10. Friso F, Rucci P, Rosetti V, et al. Is There a Role for Surgical Resection of Multifocal Glioblastoma? A Retrospective Analysis of 100 Patients. Neurosurgery. 2021;89(6):1042–51. 10.1093/neuros/nyab345.
11. Guerrini F, Mazzeo LA, Rossi G, et al. Is It Worth Considering Multicentric High-Grade Glioma a Surgical Disease? Analysis of Our Clinical Experience and Literature Review. Tomography. 2021;7(4):523–32. 10.3390/tomography7040045. Published 2021 Oct 5.
12. Hart MG, Grant GR, Solyom EF, Grant R. Biopsy versus resection for high-grade glioma. Cochrane Database Syst Rev. 2019;6(6):CD002034. 10.1002/14651858.CD002034.pub2. Published 2019 Jun

6.
13. Singh G, Mehrotra A, Sardhara J, et al. Multiple glioblastomas: Are they different from their solitary counterparts? Asian J Neurosurg. 2015;10(4):266–71. 10.4103/1793-5482.162685.
14. Patil CG, Yi A, Elramsisy A, et al. Prognosis of patients with multifocal glioblastoma: a case-control study. J Neurosurg. 2012;117(4):705–11. 10.3171/2012.7.JNS12147.
15. Meyfroidt G, Baguley IJ, Menon DK. Paroxysmal sympathetic hyperactivity: the storm after acute brain injury. Lancet Neurol. 2017;16(9):721–9. 10.1016/S1474-4422(17)30259-4.
16. Xu SY, Zhang Q, Li CX. Paroxysmal Sympathetic Hyperactivity After Acquired Brain Injury: An Integrative Review of Diagnostic and Management Challenges. Neurol Ther. 2024;13(1):11–20. 10.1007/s40120-023-00561-x.

Figures

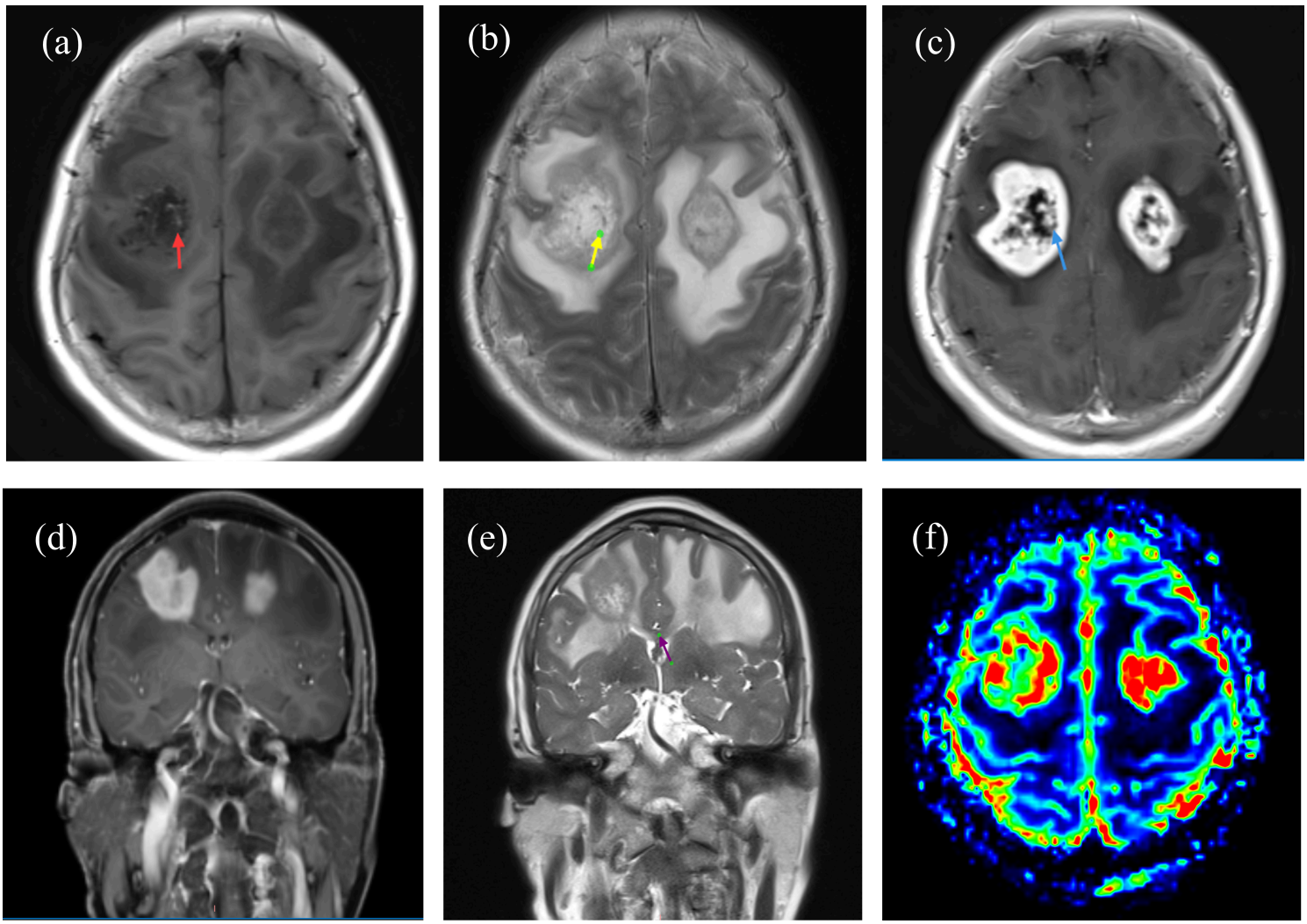


Figure 1

Preoperative imaging data.

(a) Axial T1-weighted image shows a right frontal ring-like lesion with mixed low signal and a focal intralesional T1 high signal compatible with hemorrhage (red arrow).

(b) Axial T2-weighted image shows mixed high signal in both lesions with intratumoral low-signal components (yellow arrow).

(c) Post-contrast axial T1 demonstrates thick ring enhancement surrounding non-enhancing necrotic cores; lesion sizes are ~43 × 35 × 39 mm (right) and ~33 × 28 × 31 mm (left).

(d) Post-contrast coronal T1 shows no enhancing continuity between the two frontal lesions.

(e) Coronal T2 reveals confluent perilesional edema across the midline connecting the edema of both hemispheres (purple arrow).

(f) DSC-PWI cerebral blood-flow (CBF) map shows marked hyperperfusion within the enhancing rims of both tumors with comparable CBF, whereas the surrounding edema is hypoperfused; perfusion maps match the enhancing regions.

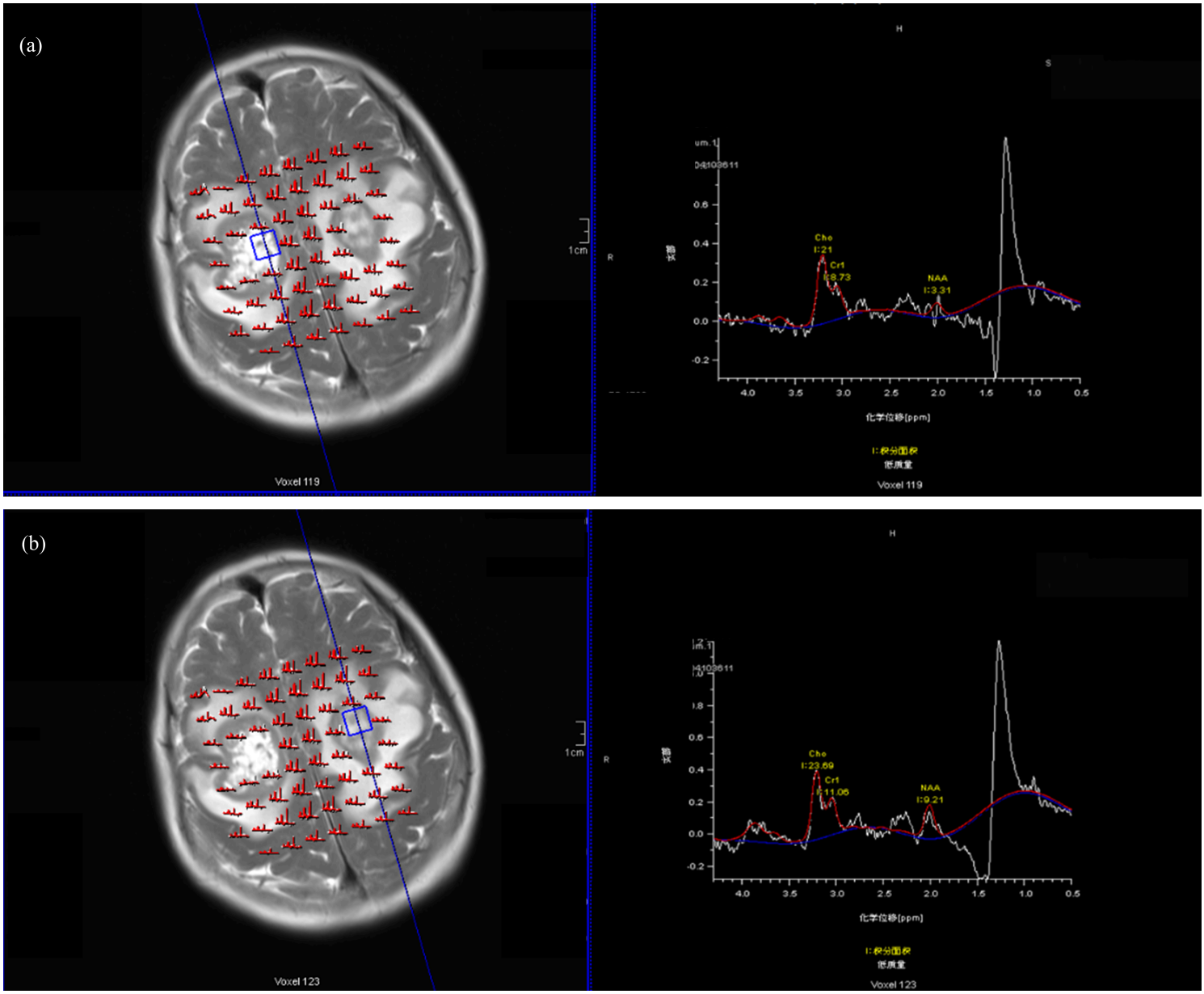


Figure 2

Preoperative imaging data(MRS)

(a) Voxel positioned over the right frontal lesion.

(b) Voxel positioned over the left frontal lesion. Contralateral normal-appearing brain was used as a reference. Tumor spectra show markedly elevated choline (Cho) with reduced N-acetylaspartate (NAA) and a prominent lipid/lactate peak. Quantitative metrics demonstrate Cho/Cr > 2, increased Cho/NAA, and decreased NAA/Cr relative to the contralateral reference—findings characteristic of a high-grade malignant glioma.

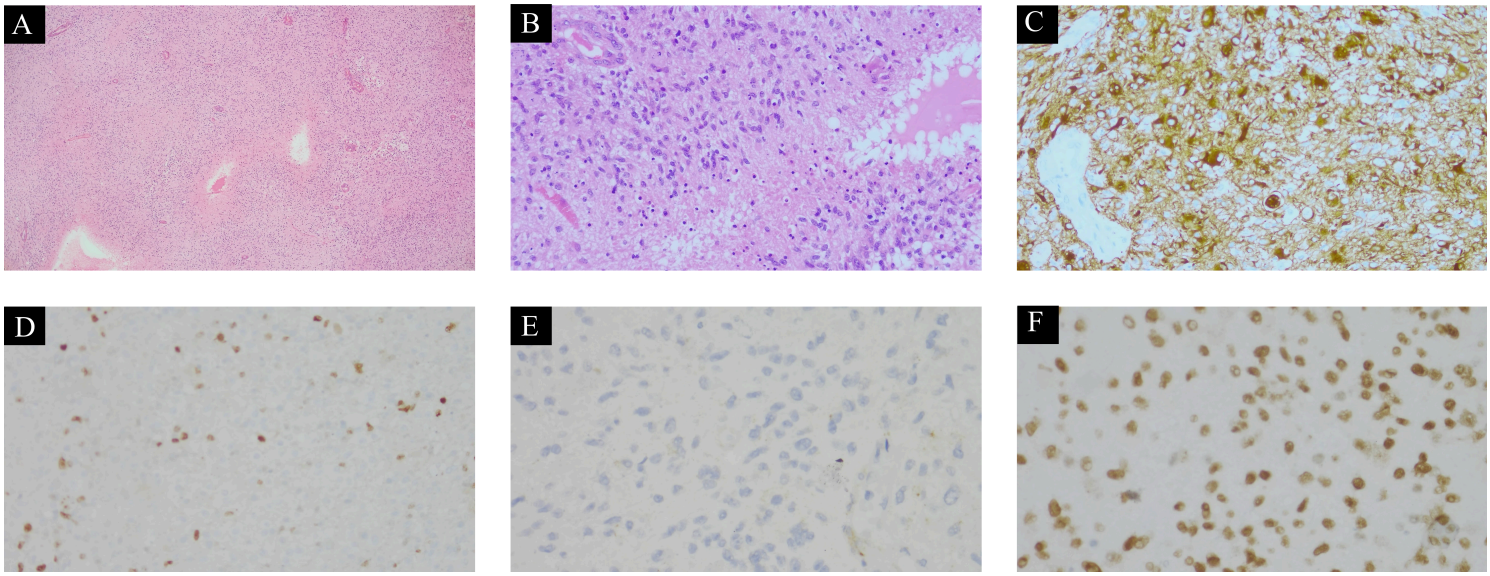


Figure 3

Histopathology and immunohistochemistry of the right frontal lobe mass.

(A) Low-power H&E shows a diffusely infiltrating astrocytic neoplasm with ill-defined borders, necrosis, and conspicuous microvascular proliferation.

(B) High-power H&E reveals markedly atypical astrocytic cells with nuclear pleomorphism, frequent mitoses, and pseudopalisading necrosis.

(C) Tumor cells are diffusely positive for GFAP.

(D) Ki-67 labeling index is ~30% in hotspots.

(E) IDH1 R132H immunostaining is negative, indicating an IDH-wildtype pattern.

(F) ATRX nuclear expression is retained (positive). Overall findings support glioblastoma, WHO grade 4, IDH-wildtype.

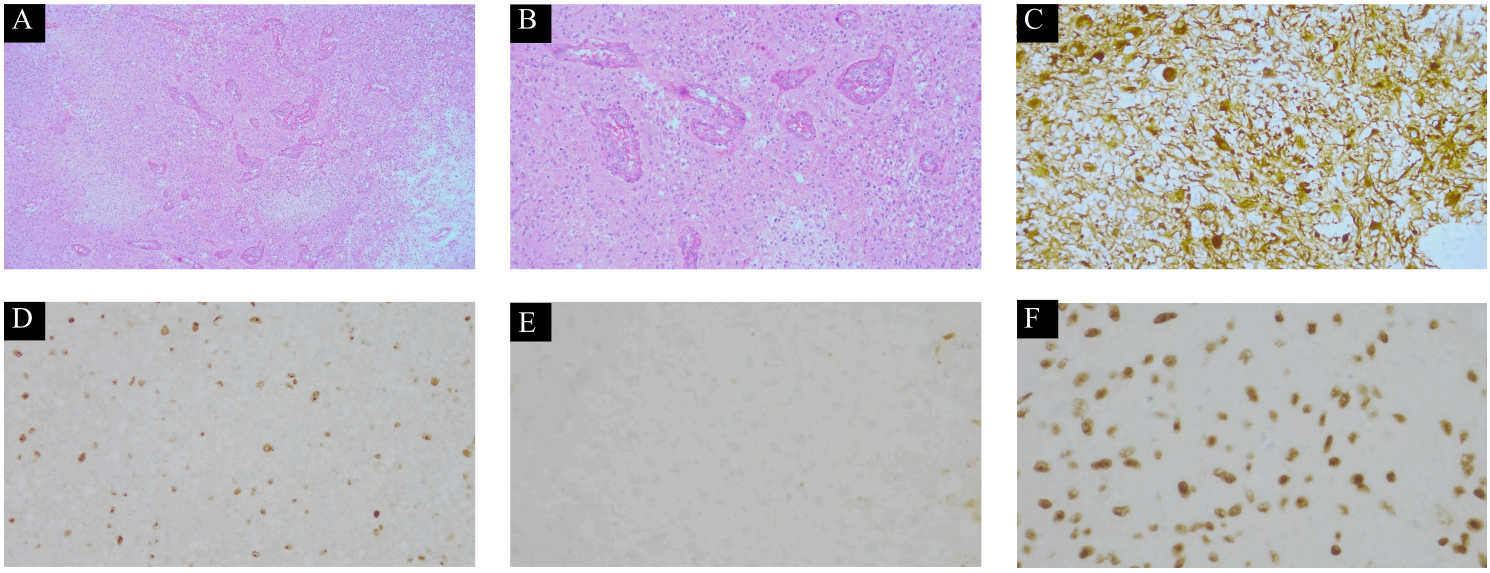


Figure 4

Histopathology and immunohistochemistry of the left frontal lobe mass.

(A) Low-power H&E shows a diffusely infiltrating astrocytic neoplasm with ill-defined borders, necrosis, and conspicuous microvascular proliferation.

(B) High-power H&E reveals markedly atypical astrocytic cells with nuclear pleomorphism, frequent mitoses, and pseudopalisading necrosis.

(C) Tumor cells are diffusely positive for GFAP.

(D) Ki-67 labeling index is ~30% in hotspots.

(E) IDH1 R132H immunostaining is negative, indicating an IDH-wildtype pattern.

(F) ATRX nuclear expression is retained (positive). Overall findings support glioblastoma, WHO grade 4, IDH-wildtype.

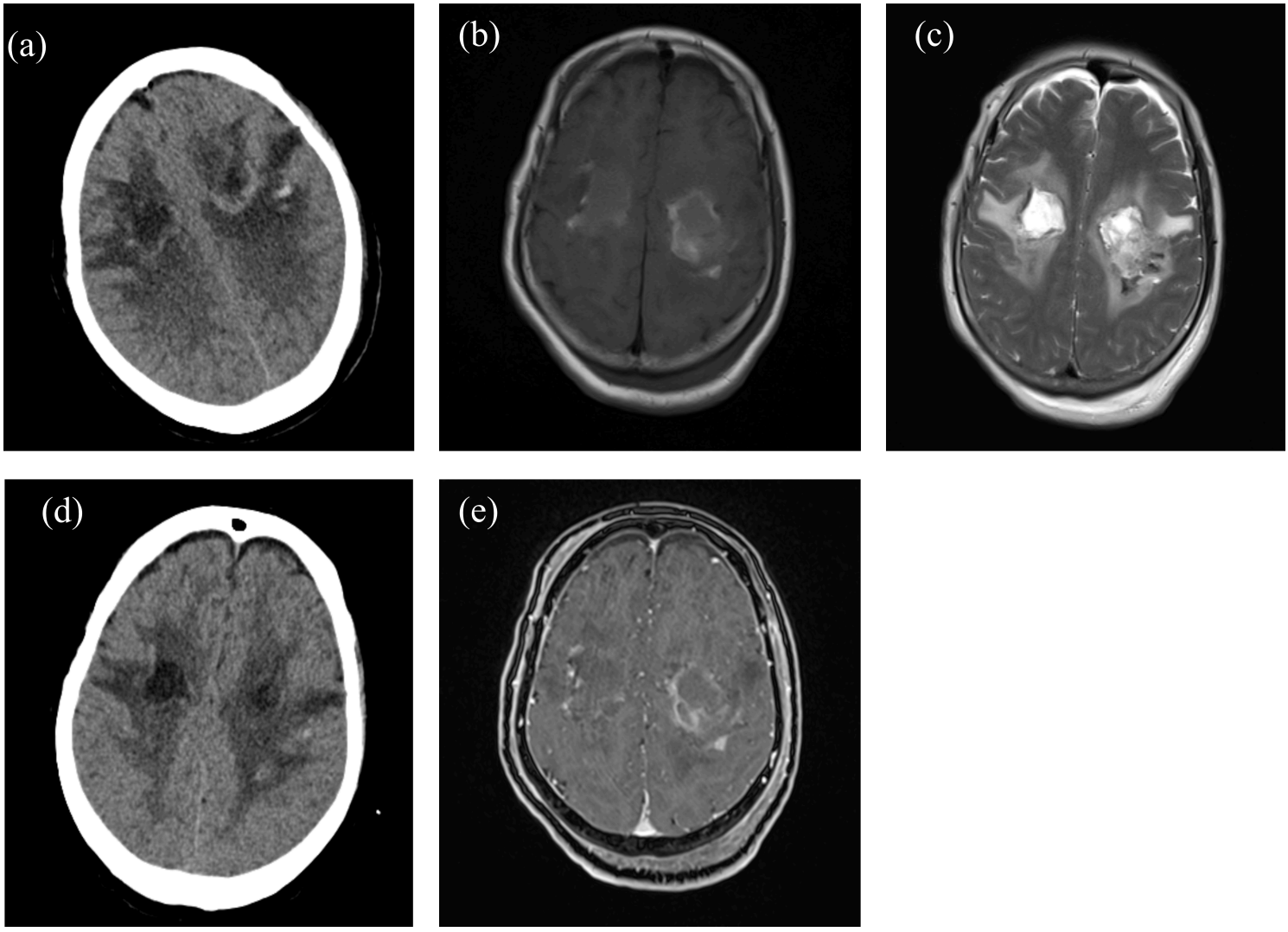


Figure 5

Postoperative imaging data.

(a) Immediate non-contrast CT shows extensive bilateral peritumoral hypodensity consistent with vasogenic edema.

(b) Immediate postoperative axial T1-weighted MRI shows bilateral postoperative cavities with surrounding hypointensity.

(c) Immediate postoperative axial T2-weighted MRI shows extensive hyperintense edema surrounding both cavities.

(d) Non-contrast CT on postoperative day 3 shows extensive pericavitary finger-like hypodensity, compatible with vasogenic edema.

(e) Contrast-enhanced axial T1-weighted MRI demonstrate gross-total resection of both frontal lesions, with postoperative cavities and no nodular enhancement or residual tumor. Midline structures remain preserved.

Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- CAREchecklistBMC.pdf