Glioblastoma Multiforme: Key Insights for Primary Care

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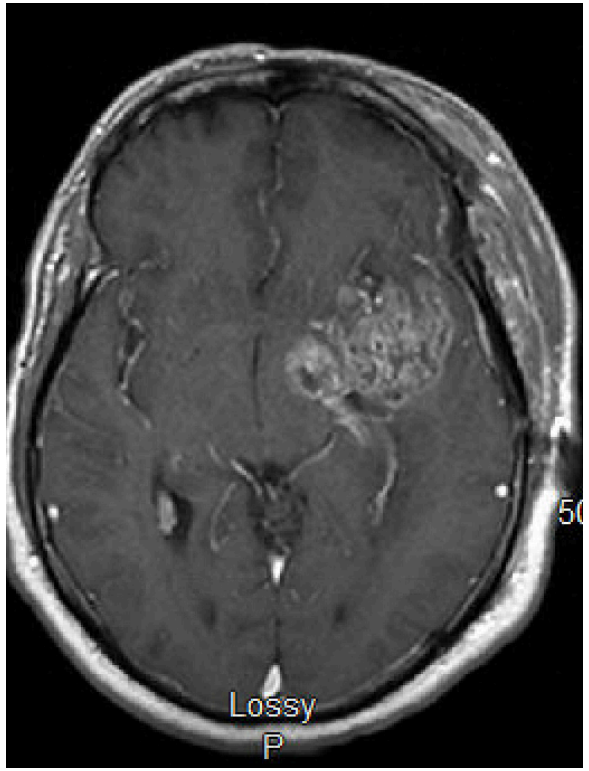
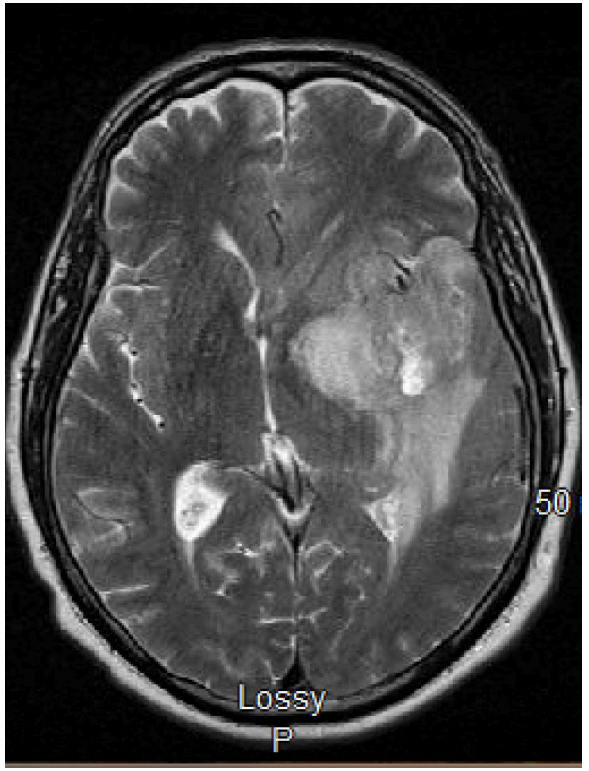
Objectives

- Define Glioblastoma Multiforme (GBM)
- Review epidemiology and risk factors
- Highlight clinical presentation
- Overview of diagnostic approach
- Discuss management principles and prognosis
- Identify supportive care needs

Case: man in his 50s with headaches

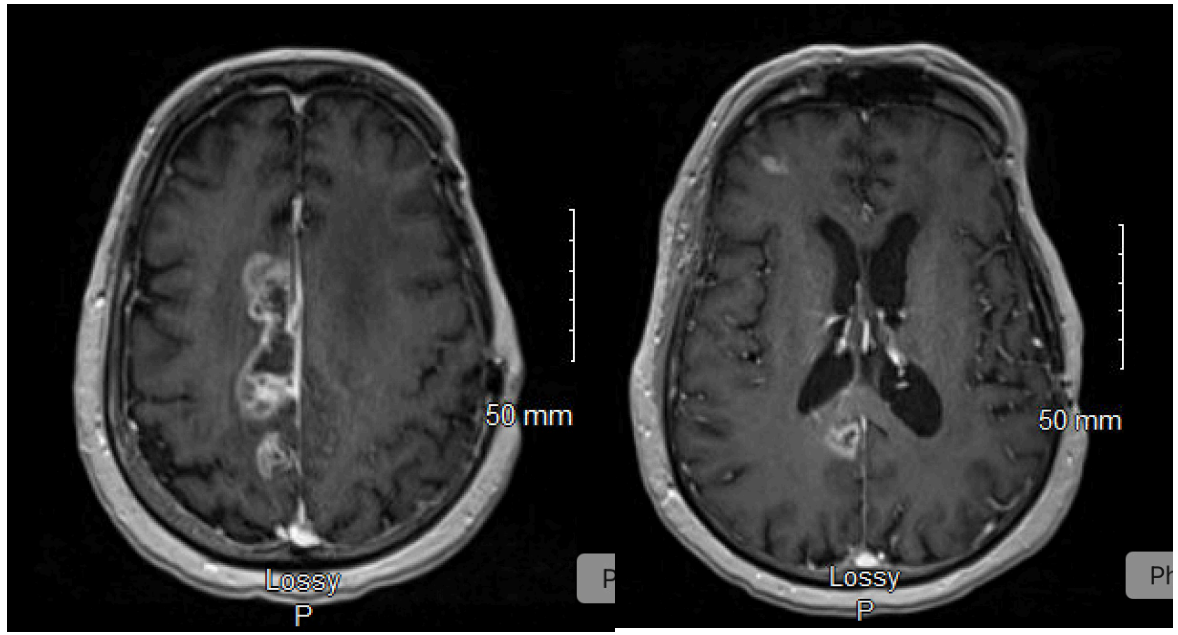
- **Day 1:** Presented with headache & balance difficulties; CT & MRI showed a left temporal lobe mass with mass effect.
- **Day 2:** CT CAP showed no metastases.
- **Day 7:** Underwent left temporal craniotomy with subtotal resection of tumor.
- **Day 19:** Seen by radiation oncology.
- **Day 27:** Radiation planning completed.
- **Day 41:** Seen by medical oncology.
- **Day 59:** Started concurrent chemoradiation.
- **Day 98:** Completed concurrent chemoradiation.





Case continued

- **Day 122:** Started maintenance TMZ.
- **Day 131:** MRI showed new small enhancing lesion in the left frontal lobe.
- **Day 157:** MRI showed recurrent disease in the left temporal & frontal lobes.
- **Day 166:** Underwent debulking surgery for basal tumor.
- **Day 185:** Restarted TMZ.
- **Day 450:** Completed maintenance TMZ.
- **Day 668:** MRI showed new 3.7 cm right frontoparietal mass consistent with progression.
- **Day 1053:** MRI showed progression with increased tumor size, new nodular enhancement, and worsening edema.
- **Day 1110:** patient passed away at hospice.



Introduction to GBM

- Most common and aggressive primary brain tumor in adults
- Grade IV per WHO classification
- Poor prognosis despite treatment advancements

Epidemiology

- Incidence: ~3-4 per 100,000 annually
- Median age at diagnosis: ~64 years
- Slight male predominance (M:F = 1.6:1)

Risk Factors

- Majority sporadic
- Radiation exposure (previous radiotherapy)
- Rare familial syndromes (Li-Fraumeni, NF1, Lynch syndrome)

Clinical Presentation

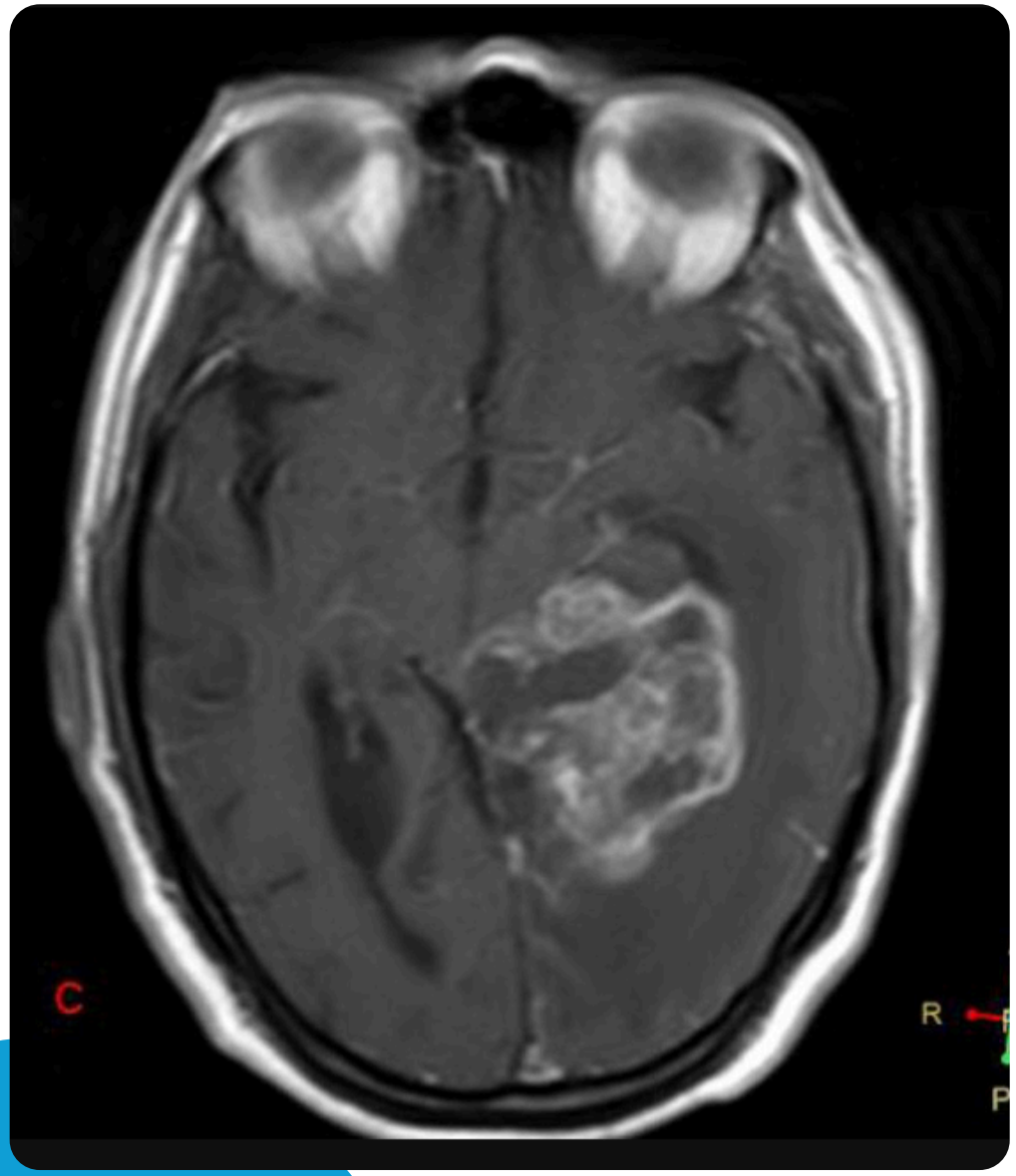
- Headache (often worse in the morning)
- Seizures (first-time adult seizures warrant imaging)
- Focal neurological deficits
- Cognitive and personality changes

Differential Diagnosis

- Metastatic brain tumors
- Abscess
- Stroke
- Lymphoma
- Other gliomas (low-grade)

Initial Workup

- Urgent brain MRI (preferred over CT)
- Referral to neurosurgery
- Steroids for symptomatic cerebral edema (e.g., dexamethasone)
- Antiepileptic drugs if seizures present



Imaging Findings in GBM

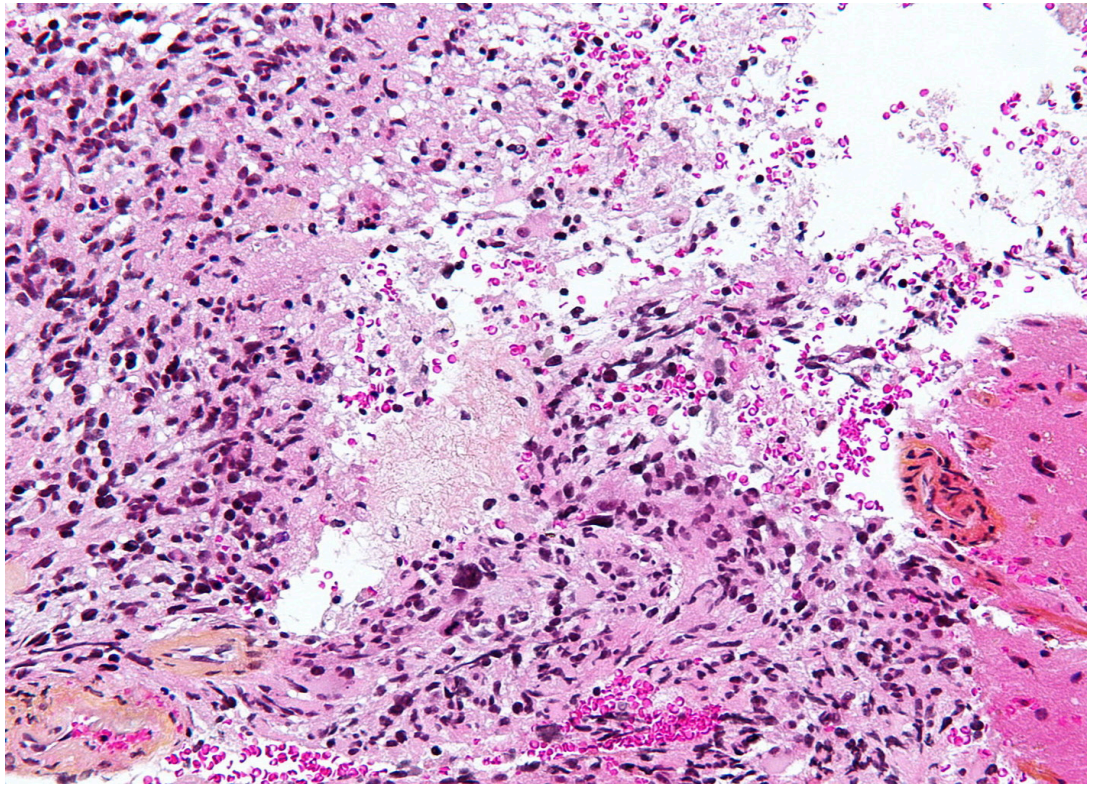
- MRI: irregularly enhancing mass, central necrosis, surrounding edema
- Often located in cerebral hemispheres (frontal, temporal lobes common)

Role of Biopsy and Surgery

- Essential for definitive diagnosis
- Maximal safe resection improves prognosis
- Balance between symptom relief and preserving neurological function

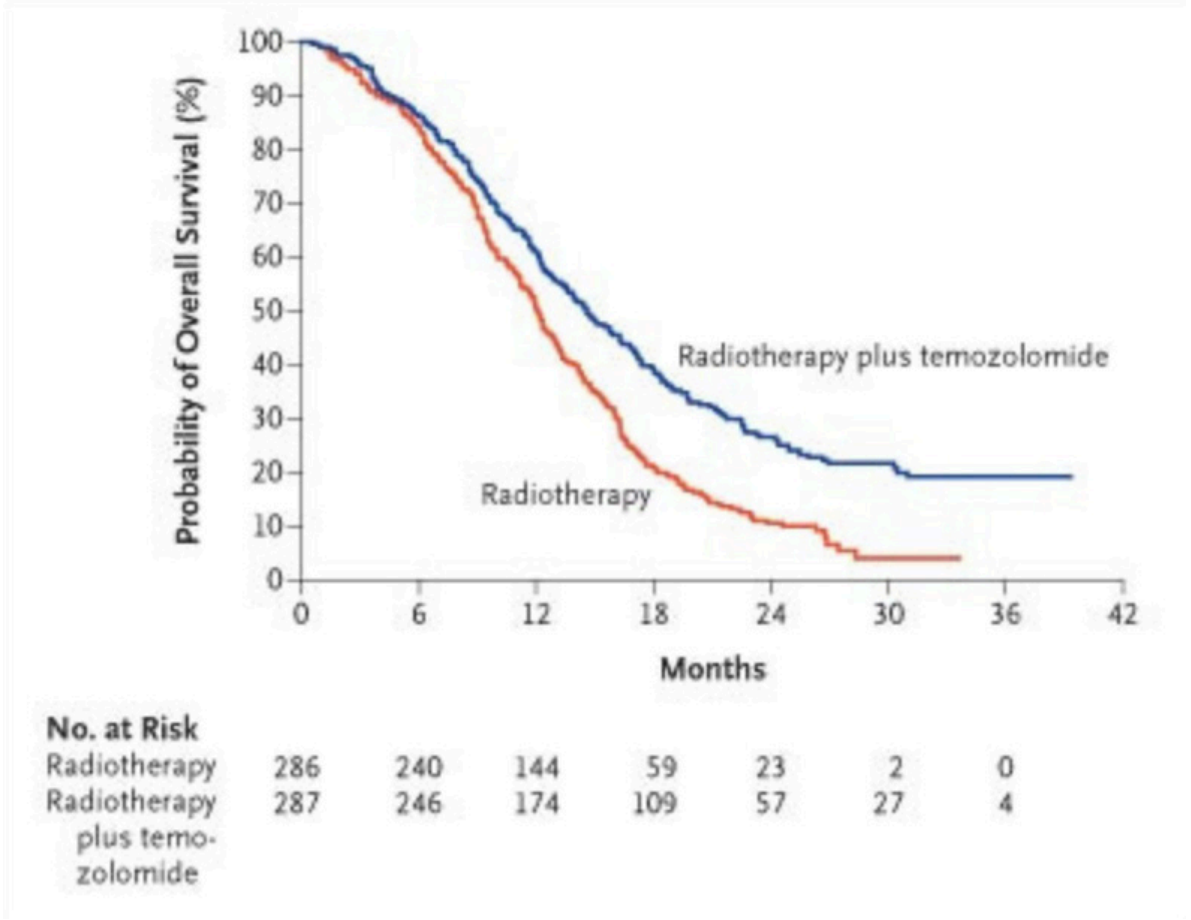
Pathology Overview

- High mitotic activity, necrosis, microvascular proliferation
- Glioblastoma is classified as a diffuse astrocytic glioma, IDH-wildtype, characterized by at least one of the following molecular features:
  - TERT promoter mutation
  - EGFR amplification
  - Combined chromosome 7 gain and chromosome 10 loss (+7/−10)
- Histological criteria alone (e.g., necrosis, vascular proliferation) without molecular confirmation are insufficient for definitive GBM classification according to the current WHO criteria.



Treatment Overview

- Standard of care: Surgery + Radiation + Chemotherapy (Temozolomide)
- Radiation: 60 Gy in 30 fractions
- Chemotherapy: concurrent and adjuvant temozolomide



Temozolomide: Key Points

- Oral alkylating chemotherapy, crosses blood-brain barrier
- Improves survival significantly (Stupp protocol)
- MGMT promoter methylation predicts better response
- Administration: concurrent daily during radiation, followed by adjuvant 5-day cycles every 28 days
- Standard duration: typically 6 cycles (may extend up to 12 in some cases)

Temozolomide: Side Effects

- Common: nausea, vomiting (use antiemetics), fatigue, constipation
- Hematologic toxicity: myelosuppression (leukopenia, thrombocytopenia, anemia)
- Rare but serious: opportunistic infections (e.g., Pneumocystis pneumonia—PCP prophylaxis may be considered)
- Monitoring: regular CBC required during treatment

Other options

- Alternating Electric Fields
- Low-intensity, intermediate-frequency (200 kHz) electrical fields.
- Disrupts cancer cell division by interfering with mitotic spindle formation.
- TTFields + temozolomide significantly increased median overall survival (20.9 vs. 16.0 months).

Prognosis and Survival

- Median overall survival ~15 months (with standard treatment)
- Five-year survival rate <10%
- Factors influencing prognosis: age, functional status, MGMT methylation

Management of Recurrence

- Typically inevitable
- Options: re-resection, chemotherapy (e.g., lomustine), clinical trials, supportive care
- Limited role for repeat radiotherapy

Supportive Care

- Steroids for cerebral edema (monitor for side effects)
- Antiepileptics for seizure control
- Rehabilitation (physiotherapy, occupational therapy, speech therapy)
- Psychosocial support

Common Treatment-Related Toxicities

- Myelosuppression (temozolomide)
- Fatigue
- Cognitive impairment
- Steroid-induced hyperglycemia, osteoporosis, myopathy

End-of-Life Care and Palliative Considerations

- Focus on symptom control, quality of life
- Advance care planning conversations early
- Hospice care and palliative support integration

Take-Home Messages

- GBM: aggressive tumor with poor prognosis
- Early recognition, referral crucial for outcomes
- Supportive care essential for quality of life
- Team-based multidisciplinary approach recommended