AMSER Case of the Month

Recurrent Glioblastoma

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Patient Presentation

HPI: A 67-year-old male with known history of glioblastoma, IDH wild type, MGMT unmethylated status-post gross total resection of a 4.5 x 7 cm right-sided parietal mass on 9/24/2018 presented with lightheadedness, persistent left-sided weakness, and gait dysfunction. He continues to walk with a cane.

He previously received hypofractionated adjuvant radiation (40 Gy/16 Fx) utilizing IMRT technique ending 11/2018 and maintenance Temodar pharmacotherapy (5 days every 4 weeks for 6 cycles). He presented to clinic for a follow-up MRI.

Patient Presentation

Pertinent Social History: The patient has a 20-pack-year smoking history and quit 34 years ago.

Pertinent Medical History: Glioblastoma, CAD, DM2, Diabetic Neuropathy, HTN, HLD, Psoriasis, Sleep Apnea, Obesity.

Pertinent Surgical History: Right parietal craniotomy for tumor excision.

Pertinent Family History: Aneurysm in maternal grandmother; cancer in maternal grandmother, mother, and sister. Prostate cancer in brother. Stroke in father and sister. CAD in mother. DM in father, mother, brother, and sister. MI in father and mother, heart disease in father, mother, brother, and sister. HTN in sister.

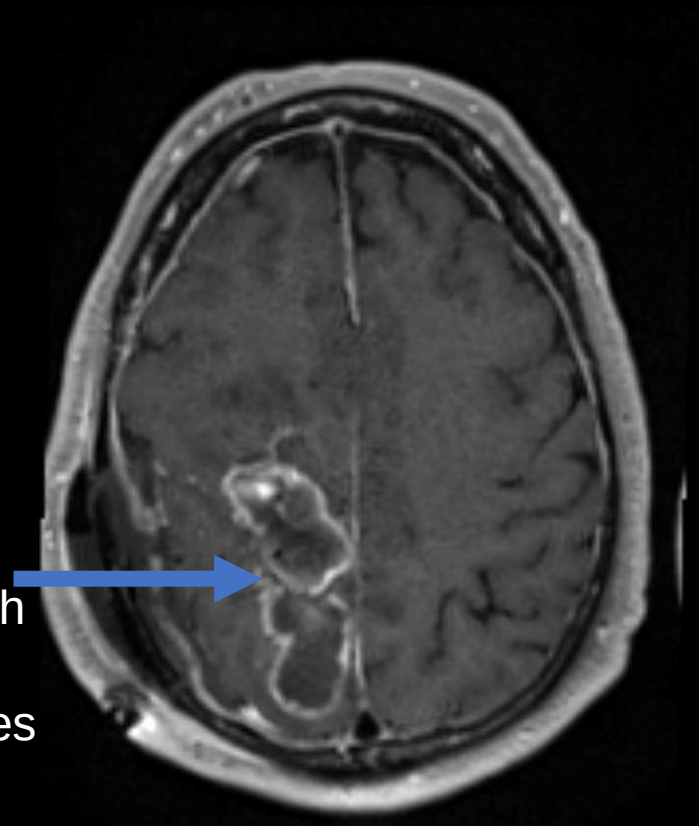
Patient Presentation

Pertinent physical exam findings:

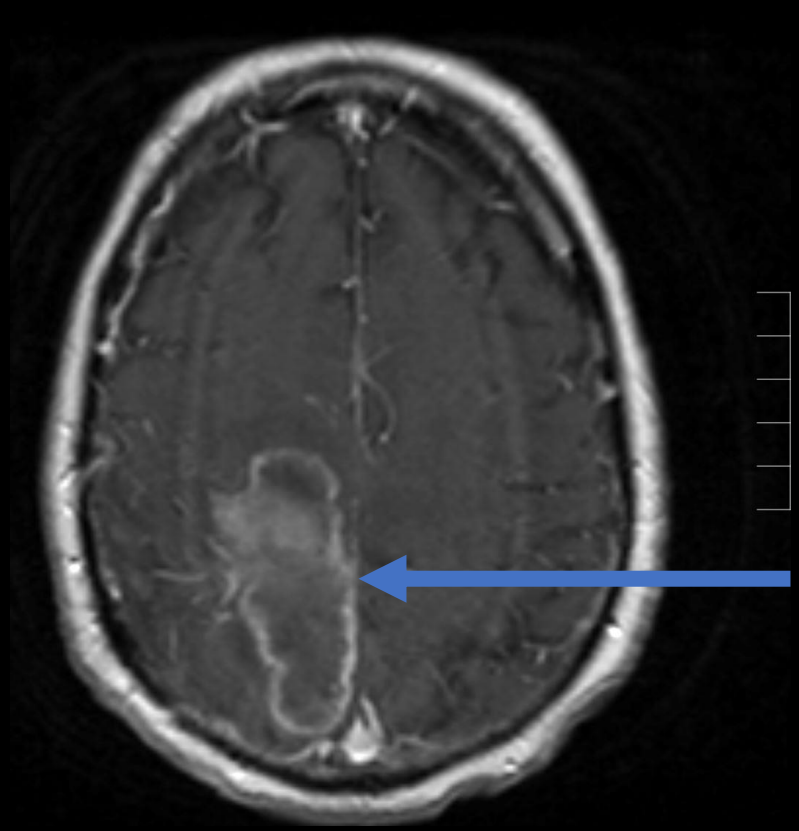
- Mental status, cranial nerves, sensory, coordination, and reflexes were intact.
- On motor exam, the patient was 5/5 in all major muscle groups on the right. However, his left upper extremity major muscle groups were 4 to 4+ out of 5 while the patient was 4 out of 5 in bilateral hip flexors and 3/5 in left quadriceps, hamstrings, gastrocnemius, and anterior tibialis.

Previous Imaging

Ring enhancement with hypointense (necrotic) center with interspersed hyperintense nodules



T1 + GC Pre-Operative Scan
9/25/18



Resection cavity

T1 + GC Post-Operative Scan
12/28/18

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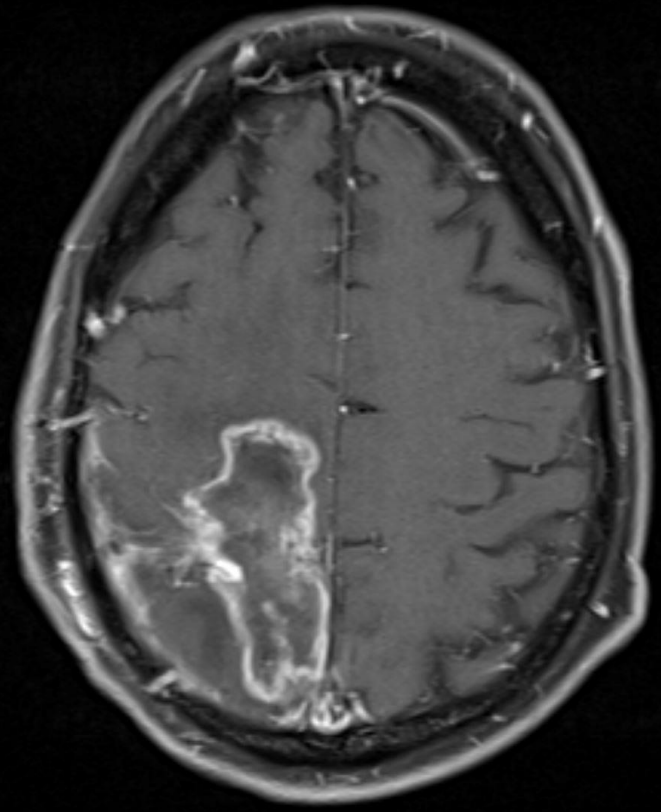
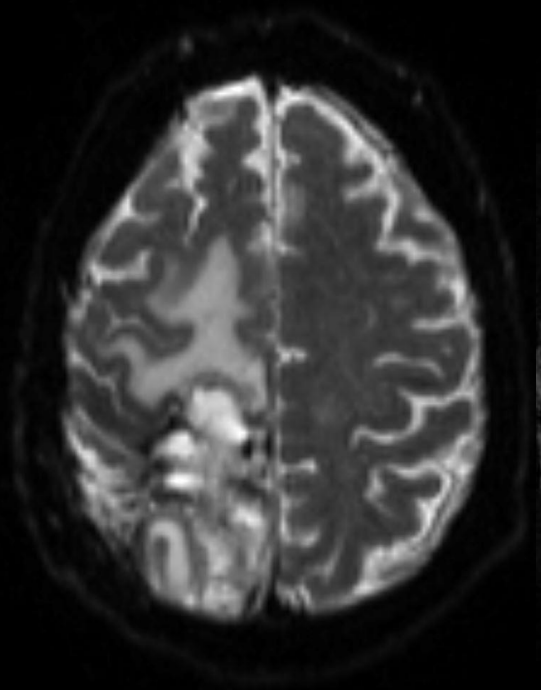
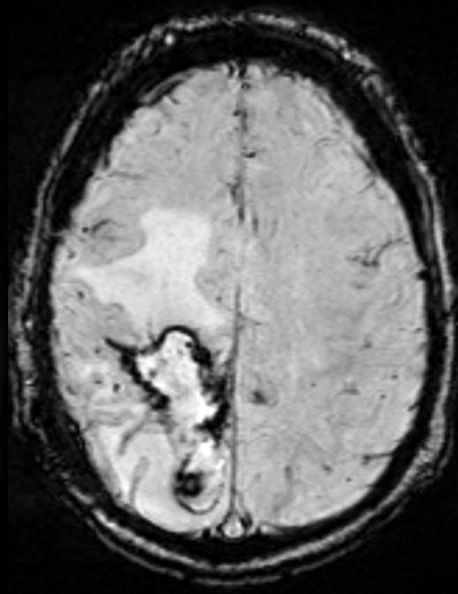
Current Imaging



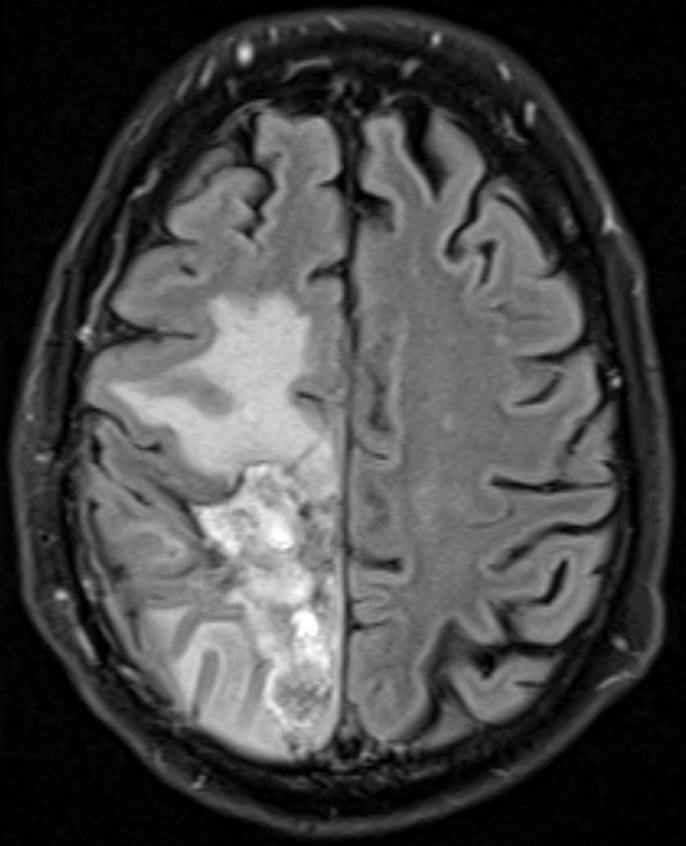
T1 + GC



DWI



SWI



FLAIR

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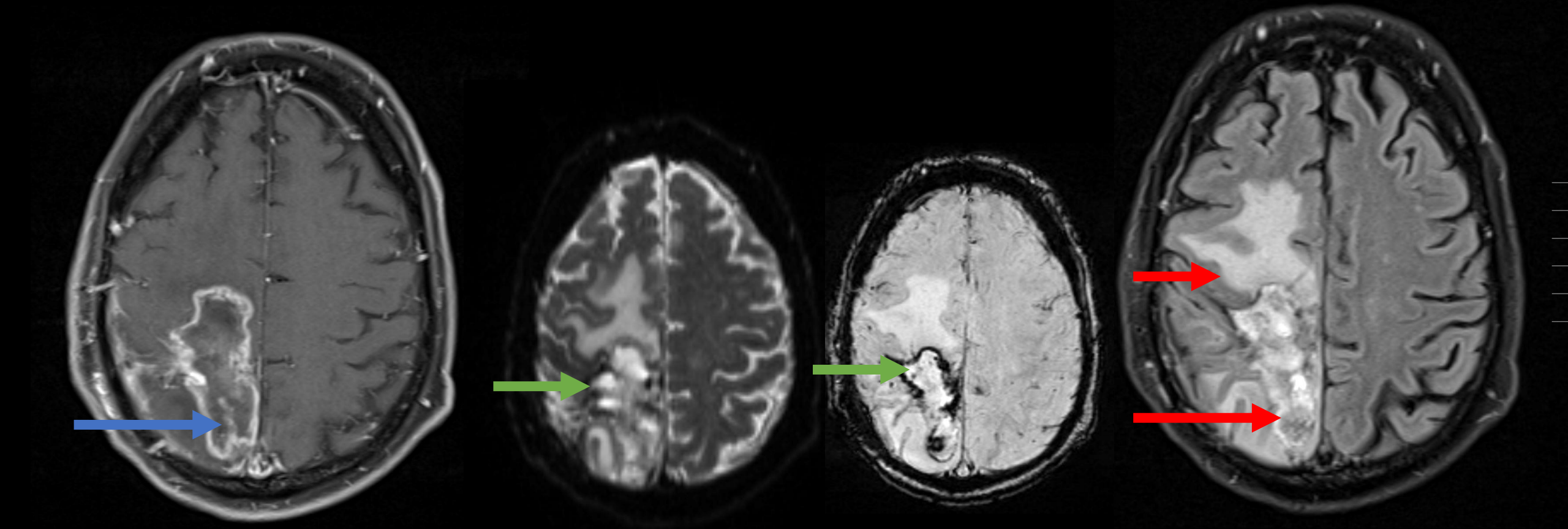
Current Imaging



T1 + GC | DWI | SWI | FLAIR

Enhancement surrounding the resection cavity has progressed from previous scans and is more nodular throughout, especially as the posterior and inferior aspect of the cavity (blue arrow). There is diffusion restriction and susceptibility artifact within the resection cavity likely secondary to blood Products (green arrow). FLAIR hyperintensity surrounding the resection cavity is also present (red arrows).

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Differential Diagnosis

Recurrent Glioblastoma

Radiation Necrosis

Abscess

Metastasis

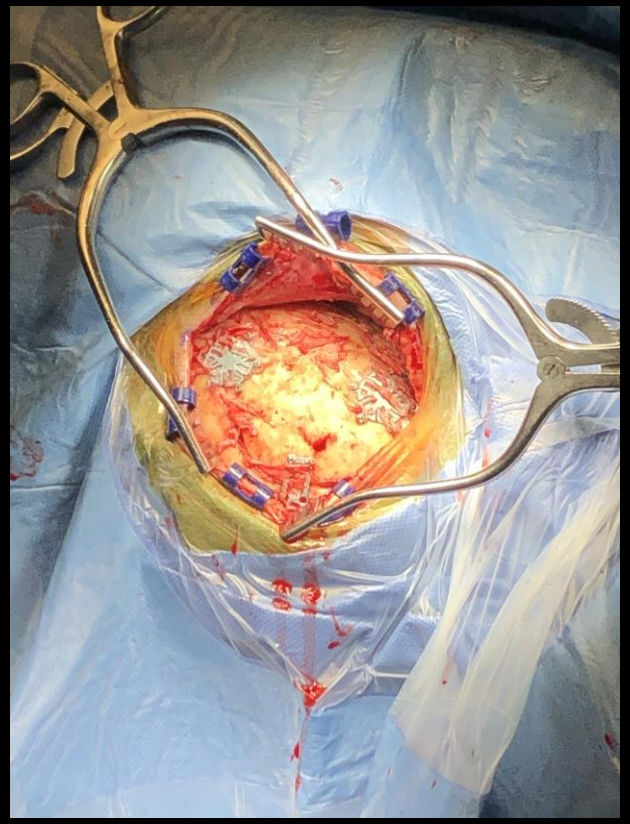
Secondary CNS Lymphoma

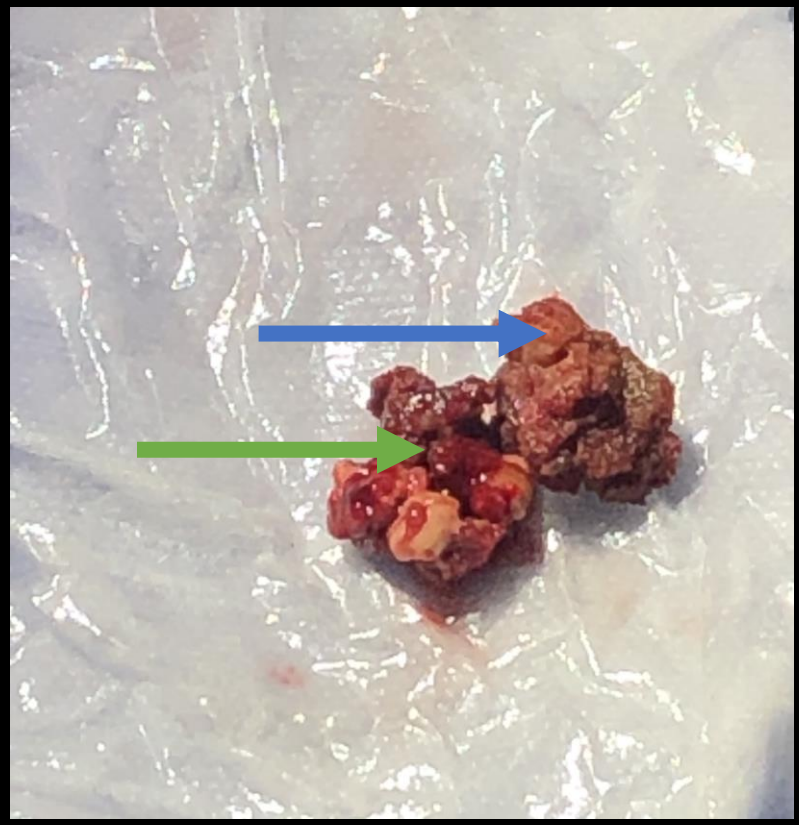
Primary CNS Lymphoma

Gross Pathology

Left Image: Right-sided parietal craniotomy with dura reflected to reveal underlying recurring tumor

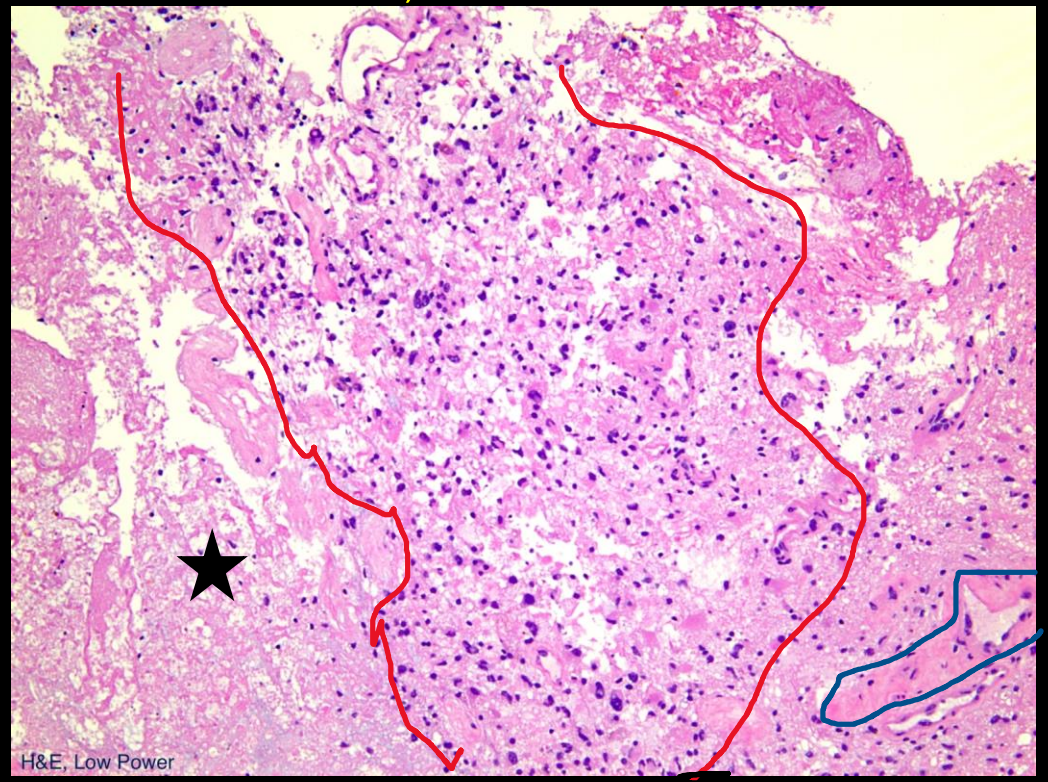
Right Image: Multiple pieces of tan-pink (blue arrow), focally hemorrhagic tissue (green arrow) measuring 1.6 x 1.0 x 0.4 cm in aggregate.





Pathology/Histology

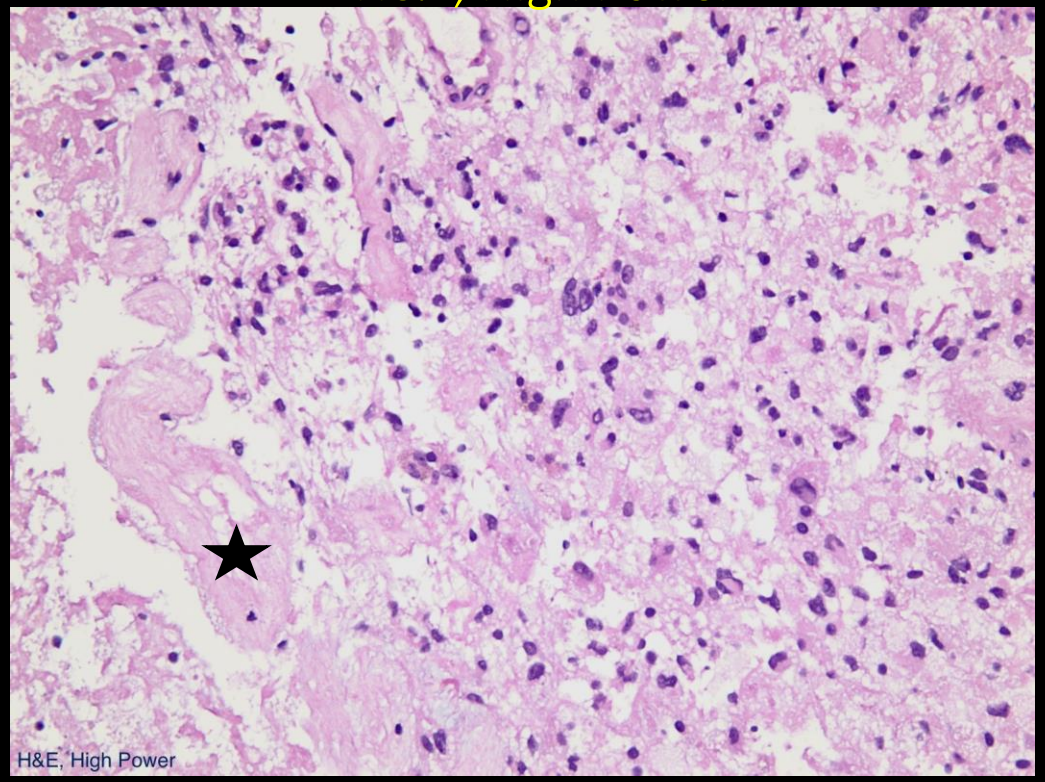
H&E, Low Power



High grade astrocytoma with anaplastic glial cells and hypercellularity. Vascular proliferation and necrotic tissue are also present.

- Black star: necrotic tissue
- Blue outline: vascular proliferation
- Red outline: area of increased cellularity and anaplastic glial cells

H&E, High Power



Multinucleated glial cells with nuclear atypia present. Glial cells are pleomorphic and demonstrate anaplasia. Necrotic tissue is also present (black star).

Final Diagnosis:

Recurrent/Residual Glioblastoma with possible Radiation Therapy Effect

Case Discussion

- Glioblastoma is a malignant, primary brain tumor with predominant astrocytic differentiation (WHO grade IV).
  - ‘Multiforme’ secondary to variegated gross appearance as well as diverse histological features.
  - Incidence: 12-15% of adult intracranial tumors (50-60% of astrocytic neoplasms).
    - Males > Females (1.6:1).
    - Median age of presentation: 64 years.
- Originally thought to be derived from glial cells, although current evidence suggests that multiple cell types with neuronal stem cell-like properties are the originating cells.

Case Discussion

- 61% of all primary gliomas occur in the four lobes of the brain.
  - Frontal (25%) > Temporal (20%) > Parietal (13%) > Occipital (3%).
  - Less commonly, they may arise from the brain stem (pediatric populations), cerebellum, and spinal cord.
  - In adult populations, they are typically supratentorial lesions.
- Ionizing radiation is the only known risk factor to definitively show an increased risk of glioma development (occurring years secondary to another tumor or condition).
  - Clinical conditions associated with tumor development include NF1 and NF2, tuberous sclerosis, Li-Fraumeni syndrome, retinoblastoma, and Turcot syndrome.
  - <1% of the glioma population have an associated genetic condition.

Case Discussion

- Clinical presentation varies depending on the size and location of the tumor as well as the anatomic structures involved within the brain.
  - May often present with symptoms of increased ICP (headache, progressive neurologic deficits) or seizures (25% initially and as many as 50% at a later stage of disease).
  - These symptoms are managed by the use of AEDs (only used in cases with seizures present) and/or corticosteroids (to control vasogenic edema and alleviate accompanying signs and symptoms).
- Initial diagnostic imaging may be accomplished with CT or MRI, however, MRI with contrast will show a classic ring-enhancing mass with a hypointense center of necrosis.
  - Central necrosis is needed for the diagnosis of a WHO grade IV brain tumor or GBM.

Case Discussion

- The treatment of GBM is multidisciplinary:
  - Maximal safe surgical resection +
  - Radiotherapy and concomitant temozolomide (Stupp Protocol)
- Disease recurs in 70% of patients within one year of diagnosis.
  - Less than 5% survive after 5 years.
  - For treatment purposes, reoperation and resection may alleviate mass effect and symptoms, however, there is conflicting evidence whether overall survival is marginally improved or not at all.
  - Other chemotherapeutic options for recurrence of disease that have been FDA approved include bevacizumab or Optune.
    - Anti-VEGF agents such as bevacizumab given for recurrent GBM often result in rapid reduction of contrast enhancement of the tumor.
    - If there is enlargement of the non-enhancing portion of the tumor or increased perfusion, findings likely the result of “Pseudoresponse.”

Case Discussion

- Is there tumor progression or pseudoprogression?
  - MRI enhancement following treatment can be observed as a result of inflammation, ischemia, radiation effects, or radiation necrosis.
  - Pseudoprogression: Imaging shows increased size of a contrast enhancing lesion followed by subsequent improvement or stabilization without further treatment (thus mimicking true progression via inflammation, edema, and vessel permeability).
    - Observed only in the first 3 months following treatment and diagnosed via serial MRI.
      - Pseudoprogession: Moderate decrease in rCBV (relative cerebral blood volume) following treatment in MRI perfusion scan.
      - True progression: Mild increase in rCBV relative to imaging before treatment.
      - Radiation necrosis: Decreased rCBV; ring enhancement that typically occurs after 18-24 months, but no earlier than 6 months.
    - Most frequently observed following TMZ + RT (Stupp Protocol).
    - Associated with increased survival.
  - Methylated MGMT tumors show more propensity to demonstrate pseudoprogression vesrus unmethylated MGMT tumors.
    - Bottom Line: Methylated tumors with increased enhancement likely represent pseudoprogession (~90%) whereas unmethylated tumors less likely to demonstrate pseudoprogression.

References:

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