Central Nervous System Case Scenarios

Case Scenario 1: Pediatric

Patient History:	16-year-old white male presented to reporting hospital for interval imaging. He has a personal medical history of NF1 and was treated in 2017 for an anaplastic ependymoma. Has had a confirmation of NF1 since two years of age. His mom also has NF1. He has some behavioral issues as well as some cognitive delays.
Physical Exam:	The patient showed no new neurological deficits. During his most recent imaging studies, the newest mass in the brain was noted to have increased in size. It was decided that a resection should be done due to his PHX of NF1 and anaplastic ependymoma of the left temporal lobe in 2017.
Pre-Op Imaging:	MRI BRAIN 4/17/2021 IMPRESSION: HYPERINTENSE MASS CENTERED WITHIN ATRIUM OF RIGHT LATERAL VENTRICLE, 2.8CM SIZE, INCREASE SINCE LAST EXAM IN 2020 MRI BRAIN 4/9/2020 IMPRESSION: NEW 2CM MASS WITHIN RIGHT LATERAL VENTRICLE, STABLE POST-OP CHANGES FROM PREVIOUS RESECTION IN LEFT TEMPORAL LOBE NOTED
Surgery:	Surgery completed at reporting institution: 4/18/21 Gross Total Resection of Brain Tumor
Operative Report:	4/18/21 Operative Report: the operating room microscope was draped in sterile fashion and brought into the operative field. With its assistance, we were able to identify some of the landmarks of the intraventricular space. The tumor was seen to be filling the space, and we gently used tumor forceps to dissect around the periphery of the tumor, marking this border with cottonoid micropatties. The stereotactic guidance system was used to confirm our location around the tumor in the trigone of the ventricle. We were able to successfully identify the superior aspect as well as the deep/medial aspect of the tumor in this way. Several small biopsies of the tumor were obtained with tumor biopsy forceps and sent to pathology for frozen analysis. Taking the small biopsies of the firm, gray tumor resulted in significant bleeding, indicating to us that the tumor was indeed very vascular. I discussed with the neuropathologist the results of the frozen section which were consistent with a low grade glioma, most likely a pilocytic astrocytoma. Meticulous hemostasis was obtained with bipolar cautery. Given the relatively large size of the tumor within the ventricle, we began at this time to debulk the tumor in order to afford us more room to dissect around its borders within the trigone. Bipolar cautery as well as suction was used to debulk the tumor. Several pieces of the tumor were collected with biopsy forceps and saved for permanent analysis. As we proceeded to resect the tumor, we encountered innumerable feeders which arose from the hypertrophied choroid plexus within the trigone itself. At various times during the resection, we simply had to pack the trigone with thrombin-soaked Gelfoam and patties in order to obtain hemostasis. As we began to define the plane along the rostral aspect of the tumor, we identified many arterial feeders arising off of the hypertrophied choroid plexus glomus. All these were coagulated with bipolar cautery and sectioned sharply with microscissors. The entire rostral aspect of the tumor was resected and we continued to dissect anteriorly towards the pulvinar of the thalamus. We ensured meticulous hemostasis intradurally within the ventricular system. The dura was then closed with interrupted and running 4-0 Nurolon sutures. Dural and epidural hemostasis was

	obtained with bipolar cautery as well as thrombin-soaked Gelfoam and FloSeal. The bone flap was then secured back into its native position utilizing the low profile cranial plating system. The external ventricular drain was allowed to exit through the superior bur hole at the level of the craniotomy. It then was tunneled in the subgaleal plane a few cm rostral and anterior to the incision site. It was secured to the scalp at its exit site with 3-0 nylon suture. The wound was irrigated with copious amounts of antibiotic laden solution. Meticulous hemostasis was obtained with bipolar cautery. The scalp was closed with interrupted, inverted 3-0 Vicryl sutures. The skin was closed with a running 3-0 nylon suture. A sterile dressing of Telfa and Tegaderm was then applied.
Pathology:	Final Diagnosis: PILOCYTIC ASTROCYTOMA OF RIGHT LATERAL VENTRICLE, UNIFOCAL, WHO GRADE 1, SIZE CANNOT BE DETERMINED Biomarker Studies: ATRX ATRX expression (immunohistochemistry) Intact nuclear expression BRAF alterations KIAA:BRAF rearrangement/duplication Absent BRAF V600E expression (immunohistochemistry) Negative Histone H3 K27M expression (immunohistochemistry) Negative Ki-67 expression (immunohistochemistry) Hotspot percentage of positive tumor cell nuclei: 1 % Other biomarker(s) Deletions (specify): CDKN2A-negative
Post-Op Imaging:	5/24/21 MRI BRAIN IMPRESSION: 1. SIGNIFICANT DECREASE IN ENHANCEMENT AT THE PERIPHERY OF THE RESECTION CAVITY STATUS POST RIGHT INTRAVENTRICULAR TUMOR RESECTION. SURROUNDING VASOGENIC EDEMA IS DECREASED. HETEROGENEOUS ENHANCEMENT WITHIN THE OPERATIVE CAVITY AT LEAST IN PART REPRESENTS RESIDUAL CHOROID PLEXUS, RESIDUAL TUMOR IS NOT ENTIRELY EXCLUDED. ON REVIEW OF PRIOR STUDIES, THE PRIMARY TUMOR DID NOT SIGNIFICANTLY ENHANCE THEREFORE THIS IS MOST LIKELY RELATED TO POSTOP GRANULATION TISSUE RATHER THAN TUMOR. 2. STABLE, NONENHANCING MULTIFOCAL T2 HYPERINTENSE LESIONS, CONSISTENT WITH NEUROFIBROMATOSIS TYPE 1
Radiation:	No radiation delivered
Chemotherapy	No Chemotherapy Delivered

Central Nervous System Case Scenarios

Case Scenario 1 Worksheet: Pediatric

- **What is the primary site?**
  LATERAL VENTRICLE [C71.5]
- **What is the laterality?**
  Right [01]
- **What is the histology?**
  PILOCYTIC ASTROCYTOMA [9421/3]
- **What is the grade/differentiation?**
  CLINICAL 9, PATHOLOGICAL 1
- **What is the sequence number?**
  02
- **What is the diagnosis date?**
  4/18/2021

Stage/ Prognostic Factors

Tumor Size Summary	028	Brain Molecular Markers	85
Tumor Size Clinical	028	Chromosome 1p Status	9
Tumor Size Pathological	999	Chromosome 19q Status	9
Regional Nodes Positive	99	MGMT	9
Regional Nodes Examined	99	SEER Sum Stage	1

Treatment

Diagnostic Staging Procedure	00		Phase		
Surgery Codes		**Radiation Codes**	1	2	3
Surgical Procedure of Primary Site	30	Radiation Treatment Volume	00		
Scope of Regional LN Surgery	9	Radiation to Draining Lymph Nodes	00		
Surgical Procedure/ Other Site	0	Regional Treatment Modality	00		
Systemic Therapy Codes		External Beam Radiation Planning Technique	00		
Chemotherapy	00	Dose Per Fraction	00000		
Hormone Therapy	00	Number of Fractions	00		
Immunotherapy	00	Total Dose	00000		
Hematologic Transplant/Endocrine Procedure	00	Number of Phases	00		
Systemic/Surgery Sequence	0	Number of Treatments to Volume	00		
		Radiation Discontinued Early	00		
		Radiation Course Total Dose	000000		
		Radiation/Surgery Sequence	0		
		Reason No Radiation	1		

Case Scenario 2: Adult

68 YR W/F presents w/worsening vision in left eye and difficulty speaking

8/13/21 MRI Brain:

FINDINGS:
There is 5.7 x 2.6 x 2.6 cm (AP, TR, CC) intra-axial mass in the left temporal lobe which is predominantly T1 hypointense and T2 heterogeneously hyperintense, increased diffusivity and has heterogeneous postcontrast enhancement. There is mild surrounding vasogenic edema and mass effect on the left lateral ventricle trigone with entrapment and dilatation of left lateral ventricular temporal horn and early entrapment of the occipital horn. Minimally early changes of left uncal herniation and up to 2-3 mm rightward midline shift are noted.

There is T2 hyperintense and T1 mixed signal intensity lesion within the clivus in the midline and extending to left with the small T1 hypointense component and large and T1 hyperintense component without postcontrast enhancement. This may be related to sinusitis versus metastasis.

Impression

1. Large intra-axial mass in left temporal lobe with surrounding vasogenic edema. Differential considerations include lymphoma, high-grade glial tumor like glioblastoma or less likely metastasis.
2. Endymal enhancement along the occipital horn left lateral ventricle may suggest transependymal spread.
3. Mild mass effect and entrapment of the left temporal horn.
4. Mixed signal intensity nonenhancing clival lesion. This may be related to sinusitis or metastasis. Correlation with CT and/or bone scan would be helpful.
5. Left mastoid effusion, likely serous. Question mastoiditis, correlate clinically.

8/17/21

Procedure:
1. Left temporal craniotomy and resection of tumor
2. Medtronic Stealth frameless stereotactic guidance
3. Use of operating microscope

Detailed Procedure: Informed consent was obtained prior to the procedure. She was placed in the supine position. The extremities were well-padded to avoid undue pressure points. The head was placed in Mayfield pins. An MRI had been obtained preoperatively for use with the Medtronic Stealth frameless stereotactic guidance system. The fiducials were carefully registered in the approximate location of the lesion in the left temporal area as well as a trajectory to the lesion were planned. The left occipito-temporal area was then shaved prepped and draped in a sterile fashion. A linear incision was planned and infiltrated with local anesthetic. The skin was incised sharply and subcutaneous tissues were dissected using electrocautery until the underlying bone was encountered. Periosteal elevator was used

to elevate the periosteum and a self-retaining retractor was placed. The Medtronic Stealth frameless stereotactic guidance system was used to identify the location of the midline in the transverse sinus. The Medtronic drill was then used to place a series of bur holes and the craniotome was used to turn a left occipital temporal bone flap. Wound was thoroughly irrigated and hemostasis was achieved. The Medtronic Stealth frameless stereotactic guidance system was used to plan an entry point in a trajectory to the lesion. Dura was then opened in a curvilinear fashion and retracted inferiorly using a 4-0 Nurolon suture. The pia was cauterized and a corticectomy was made. Using microdissection techniques and the Medtronic Stealth frameless stereotactic guidance system, dissection proceeded until abnormal tissue was encountered. Several tissue samples were collected and sent to pathology for analysis. Intraoperative pathology was consistent with a high-grade neoplasm. The operating microscope was brought into the operative field. Using a combination of suction and microdissection, the tumor was gradually debulked and then resected. Care was taken to preserve the lateral cortex overlying this lesion. Care was also taken to avoid entry into the temporal horn of the lateral ventricle. Resection proceeded until a gross total resection of the lesion was achieved. Hemostasis was achieved using a combination of Gelfoam and Surgi-Flo. After the tumor had been resected the dura was reapproximated using 4-0 Nurolon interrupted sutures. The bone flap was replaced and fixed in place using titanium plates and screws. The scalp was closed in layers. The subcutaneous tissues were reapproximated using 2-0 Vicryl interrupted sutures. The skin was closed using 3-0 nylon simple running suture. Sterile dressings were applied to the wounds. The procedure was uncomplicated. The patient was extubated in the operating room and taken to the recovery room in stable condition.

8/18/21 Post Op MRI:

FINDINGS:
Postsurgical changes are seen from left parietal craniotomy with resection cavity seen in the left temporal lobe with blood degradation products and surrounding vasogenic edema. Residual ring enhancement is seen in the superior portion of the tumor likely representing residual tumor. There is persistent mass effect on the occipital horn of left lateral ventricle with ependymal enhancement. Pneumocephalus is seen along the frontal lobe. The appearance of the clival lesion is similar to the prior study. No acute infarct. Basilar cisterns are patent. The cervicomedullary junction is unremarkable. Major intracranial vessels are unremarkable. Orbital and sellar/parasellar structures are unremarkable. Retention cyst/polyp seen in the right maxillary sinus with mucosal thickening seen in the ethmoid and frontal sinuses. Left mastoid effusion is seen.

Impression

1. Postsurgical changes are seen from partial resection of left temporal mass with residual tumor seen along its superior part with persistent mass effect on the left lateral ventricle with pneumocephalus and blood degradation products. Follow-up MRI of the brain is recommended once the postsurgical changes resolve.
2. Unchanged clival region and epididymal enhancement along the occipital horn of left lateral ventricle.

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Summary of Radiation Therapy:

Treatment Intent: Palliative w/chemo

- **Site:** L_Temporal
- **Plan(s):** A1_L_Temporal
- **Modality/Energy:** 6MV
- **Technique:** IMRT
- **Number of Fields:** 3
- **Fractional Dose:** 200 cGy
- **Frequency:** Once Daily
- **Number of Fractions:** Planned 30 Delivered 30
- **Delivered Dose:** 6000 cGy
- **Planned Dose:** 6000 cGy
- **Date(s) of Treatment:** Sep 21, 2021 to Nov 2, 2021
- **Elapsed Days:** 43

Systemic Therapy

9/21/2021 Supportive; TEMOZOLOMIDE 75MG/M2/DAY

Pathology report:

BRAIN, LEFT TEMPORAL LESION, BIOPSY, (08/17/2021):

GLIOBLASTOMA
  W.H.O. grade IV
  IDH1 R132H status: negative (by IHC)
  MGMT Promoter: Unknown
  NEWLY DIAGNOSED
  Comment: Surgery #1
NOTE:
  The overall size of the specimen is large

W.H.O. Histologic Grading Criteria
  Cellularity: Dense
  Atypia: Moderate
  Mitoses: Present
  Vascular Proliferation: Present
  Necrosis: Present
  Immunohistochemistry performed shows the following staining profile in tumor cells: Block: 1C
  IDH1 R132H: negative
  ATRX: positive (retained, not suggestive of mutation)
  P53: low (non-mutant pattern): 5%
GFAP: positive
OLIG2: positive
  MIB-1: 10% (not formally quantified)

Cytogenetics:

RESULTS: ABNORMAL MICROARRAY (See Tables below)

INTERPRETATION:
Microarray analysis was performed on this formalin-fixed, paraffin-embedded (FFPE) primary brain tumor specimen. The following genomic imbalances were noted:
(1) 63.7 kb homozygous loss of 9p, including CDKN2A and CDKN2B,
(2) 514.8 kb single copy loss of 17p, including TP53,
(3) polysomy 19,
(4) polysomy 20, and
(5) monosomy 22, including loss of NF2

NOTE: Together these genomic changes are consistent with a histologic diagnosis of GLIOBLASTOMA, WHO GRADE 4.

Molecular diagnostics:

DNA was isolated from a paraffin block of the brain tumor biopsy. DNA methylation patterns in the CpG island of the MGMT gene was determined by chemical(bisulfite) modification of unmethylated, but not methylated, cytosines to uracil and subsequent PCR using primers specific for either methylated or the modified unmethylated DNA (Esteller et al. Cancer Res. 1999;59:793-797.) The PCR products were analyzed in duplicate parallel runs by capillary gel electrophoresis. The sensitivity of the assay based on DNA dilutions studies is at least 1:1000.

RESULT:
The analyzed region of the MGMT promoter is METHYLATED.

INTERPRETATION:
MGMT (O6-methylguanine DNA methyltransferase) is a DNA repair gene. Methylation of the promotor leads to gene silencing and loss of MGMT expression. A recent study that tested the methylation status of the same region of the MGMT promoter in glioblastomas found that MGMT promoter methylation was an independent favorable prognostic factor and was associated with a survival benefit in patients treated with temozolamide and radiotherapy. (Hegi M, Diserans A, Gorlia T et al. MGMT Gene Silencing and Benefit from Temozolomide in Glioblastoma. N Engl J Med 2005;352:997-1003.)

INTEGRATED DIAGNOSIS:

GLIOBLASTOMA, IDH-WILDTYPE
W.H.O. GRADE IV
MGMT promoter: METHYLATED
NEWLY DIAGNOSED

TERT C250T
CDKN2A and CDKN2B 2 copy loss
MLH1 c.790+1G>A
MSH6 p.F1088Sfs*2
MAP2K1 K57N
Biallelic inactivation of TP53 (deletion + mutation)

Negative for IDH1/IDH2 mutations
Negative for 1p/19q co-deletion

Central Nervous System Case Scenarios

Case Scenario 2 Worksheet: Adult

Single tumor per rule M2. Single Histology H3

- **What is the primary site?** Temporal Lobe C71.2
- **What is the laterality?** Left 02
- **What is the histology?** Glioblastoma, IDH Wildtype 9440/3
- **What is the grade/differentiation?** Grade Clinical-9 Grade Path-4
- **What is the sequence number?** 00
- **What is the diagnosis date?** 8/13/21

Stage/ Prognostic Factors			
Tumor Size Summary	057	Brain Molecular Markers	05- Glioblastoma, IDH-wildtype (9440/3)
Tumor Size Clinical	057	Chromosome 1p Status	0-not present
Tumor Size Pathological	999	Chromosome 19q Status	0-not present
Regional Nodes Positive	99	MGMT	3- MGMT methylation present, level unspecified
Regional Nodes Examined	99	SEER Sum Stage	1-Localized

Treatment					
Diagnostic Staging Procedure	00		Phase		
Surgery Codes		**Radiation Codes**	1	2	3
Surgical Procedure of Primary Site	30	Radiation Treatment Volume	13		
Scope of Regional LN Surgery	9	Radiation to Draining Lymph Nodes	00		
Surgical Procedure/ Other Site	0	Regional Treatment Modality	02		
Systemic Therapy Codes		External Beam Radiation Planning Technique	05		
Chemotherapy	02	Dose Per Fraction	00200		
Hormone Therapy	00	Number of Fractions	30		
Immunotherapy	00	Total Dose	006000		
Hematologic Transplant/Endocrine Procedure	0	Number of Phases	01		
Systemic/Surgery Sequence	3	Number of Treatments to Volume	30		
		Radiation Discontinued Early	01		
		Radiation Course Total Dose	006000		
		Radiation/Surgery Sequence	3		

Commented [JH2]: First tissue was from excision of primary tumor.

Commented [JH1]: Include wildtype in histology description

Commented [JH3]: No size given of tumor on pathology report.

Commented [JH4]: Methylation present. MGMT is a gene that repairs genes. Methylation means those repair genes are suppressed. This is good. We don't want the MGMT gene repairing cells the chemo is trying to kill.

Commented [JH5]: Tumor is confined to the left temporal region. We are looking for extension across the midline or extension from the supratentorial portion of the brain to the infratentorial. The temporal lobe is suparentorial and the tumor is confined to the temporal regional. Even if it invaded into the ventricals, it would still be localized. This would be SEER EOD code 100.

Commented [JH6]: Partial brain

Commented [JH7]: Photons

Commented [JH8]: IMRT

Commented [JH9]: 2Gy

Commented [JH10]: 30 fractions

Commented [JH11]: Total 60Gy

Commented [JH12]: Single phase

Commented [JH13R12]: Total fractions is 30

Central Nervous System Case Scenarios

		Reason No Radiation	0