NEUROPATHOLOGY SURVIVAL GUIDE

DR ESTHER QUICK

SA PATHOLOGY
AIM

- SMALL BIOPSY EXAM
- FROZEN SECTION FOCUS PLUS THE BASICS FOR SURVIVING A BRAIN LANDING ON YOUR DESK
  - GBM AND DDX
  - LOW GRADE LESIONS
  - NICE CASES
THE NEURO FROZEN SECTION

• PURPOSE OF NEURO FROZEN SECTION?
  • TO PROVIDE A DEFINITIVE AND COMPREHENSIVE HISTOLOGICAL DIAGNOSIS?
  • TO ASSESS MARGINS?
  • FOR INTEREST?
  • TO TERRIFY THE JUNIOR PATHOLOGIST?
PURPOSE

• DETERMINE IF LESIONAL TISSUE HAS BEEN SAMPLED
• DETERMINE IF REPRESENTATIVE TISSUE HAS BEEN SAMPLED (PATHOLOGICAL-RADIOLOGICAL CORRELATION)
• DETERMINE NATURE OF LESION
  • NEOPLASTIC
    • PRIMARY GLIAL
    • LYMPHOMA
    • MET
  • NON NEOPLASTIC
• TRIAGE TISSUE FOR FURTHER WORK UP
HOW TO APPROACH THE NEURO FROZEN

• WHAT DOES THE SURGEON REALLY NEED TO KNOW?

• IS ADEQUATE, REPRESENTATIVE LESIONAL TISSUE PRESENT?
  • DO THE FEATURES ACCOUNT FOR THE IMAGING FINDINGS?
  • SUFFICIENT MATERIAL FOR ANCILLARY TESTS?
  • ADDITIONAL SAMPLES FOR MICRO OR FLOW?

• IDENTIFICATION OF TUMOURS TREATED BY GROSS TOTAL RESECTION
LIMITATIONS OF FROZEN SECTION

- SAMPLING ERROR!!
- LIMITED TISSUE
- VARIABLE QUALITY
- LIMITED MORPHOLOGICAL ASSESSMENT AND LOSS OF CHARACTERISTIC FEATURES
- ABSENCE OF ADEQUATE CLINICAL/RADIOLOGICAL INFORMATION
- AVAILABILITY OF EXPERTISE
COMMON PROBLEMS: ARTIFACTS

• ICE CRYSTAL ARTIFACT (OEDEMATOUS TISSUE)
• CHATTERING
• CAUTERY
• FREEZE ARTIFACT
• EMBEDDING ARTIFACTS
• INCREASED HYPERCHROMASIA AND ATYPIA
• ABSENCE OF PERINUCLEAR HALOS
COMMON PROBLEMS

- TINY SPECIMEN
- ARTIFACT RENDERING INTERPRETATION IMPOSSIBLE
- NORMAL TISSUE/MINIMAL ABNORMALITY
- ENHANCING LESION WITH ONLY FEATURES OF LOW GRADE GLIOMA/NO TUMOUR
- NECROSIS ONLY
- MULTIPLE SAMPLES WITH NO SPECIFIC DIAGNOSIS
- UNFAMILIAR TUMOUR!
HOW TO DEAL WITH COMMON PROBLEMS

• REVIEW RADIOLOGY
• COMMUNICATE WITH SURGEON
• PHONE A FRIEND
• DEFER TO PARAFFINS
INTRAOPERATIVE ASSESSMENT MY APPROACH

• FROZEN SECTION
• SMEAR (TOUCH OR CRUSH PREPARATION)
• ***FREEZE ALL***

• *IF NO MORE TISSUE COMING CUT SPARES BEFORE RE-EMBEDDING
CJD AND THE FROZEN SECTION

• DON’T DO IT!!!!!!!!!!!!!!!!!!

• INFECTION RISK
  • CAN’T DECONTAMINATE CRYOSTAT AND OTHER INSTRUMENTS

• HISTOLOGICAL FEATURES OF SPONGIOFORM ENCHEPALOPATHY NOT RELIABLY SEEN ON FS
BUT FIRST...
CASE 1.

- M 68. MULTIFOCAL ENHANCING CEREBRAL LESIONS
- ?GLIOMA ?METS
- FROZEN SECTION
DIAGNOSIS

• GLIOBLASTOMA, IDH-WILDETYPE, WHO GRADE IV
GLIOBLASTOMA

- HIGH GRADE GLIOMA
- NUCLEAR ATYPIA
- MITOTIC ACTIVITY
- MICROVASCULAR PROLIFERATION
- NECROSIS

- MOSTLY IDH-WILDETYPE
- 10% IDH-MUTANT, OFTEN SECONDARY, YOUNGER PATIENTS, BETTER PROGNOSIS
DDX OF RING ENHANCING Lesion

- GLIOBLASTOMA (IRREGULAR, SHAGGY)
- LYMPHOMA
- METS
- ABSCESS (THIN, UNIFORM)
- CYST WALL OF SOME TUMOURS (PILOCYTIC ASTROCYTOMA)
- INFARCT
- DEMYELOGATING LESIONS (“OPEN RING”)
- BEWARE MACROPHAGES!
CASE 2

- M 60 PRESENTED WITH ACUTE VISUAL LOSS
- RIGHT CAVERNOUS SINUS/ORBIT MASS
- FOR FROZEN SECTION
- ?MENINGIOMA
DIAGNOSIS

- FROZEN DX: LESIONAL TISSUE PRESENT, FAVOUR LYMPHOMA.
- PARAFFIN DX: DLBCL
PRIMARY CNS LYMPHOMA

- DIFFUSE LARGE B-CELL LYMPHOMA OF THE CNS
- IMMUNODEFICIENCY-ASSOCIATED CNS LYMPHOMA
- INTRAVASCULAR LARGE B-CELL LYMPHOMA
- LOW GRADE B-CELL LYMPHOMAS
- T-CELL AND NK/T-CELL LYMPHOMAS
- ANAPLASTIC LARGE CELL LYMPHOMA
- MALT LYMPHOMA OF THE DURA
PRIMARY CNS LYMPHOMA

• 2-3% OF ALL BRAIN TUMOURS
• ADULTS >60YRS
• OCCULAR MANIFESTATIONS IN 20%
• SINGLE OR MULTIPLE MASSES
• ENHANCE HOMOGENEOUSLY
PRIMARY CNS LYMPHOMA

• SMEAR:
  • DISPERSED POPULATION
  • SCANT CYTOPLASM
  • ROUND NUCLEI
  • COARSE CHROMATIN
  • PROMINENT NUCLEOLI
  • MITOSES AND APOPTOSIS
PRIMARY CNS LYMPHOMA

- FROZEN:
  - INFILTRATIVE GROWTH
  - PATCHY DISTRIBUTION
  - ANGIOCENTRICITY AND ANGIOINVASIVE
  - ROUND NUCLEI WITH PROMINENT NUCLEOLI
  - APOPTOSIS AND MITOSES
  - VARIABLE REACTIVE LYMPHOCYTES
  - +/-NECROSIS
  - STEROID RX: ONLY SMALL LYMPHOCYTES AND MACROPHAGES
PRIMARY CNS LYMPHOMA

- DDX:
  - OLIGODENDROGLIOMA: UNIFORM NUCLEI, NO ANGIOINVASION, CALCS, PERINEURONAL SATELITOSIS
  - GBM: TISSUE FRAGMENTS, FIBRILLARY PROCESSES, ELONGATED NUCLEI, VASCULAR PROLIFERATION
  - METS: TISSUE FRAGMENTS, CYTOPLASM, LESS INFILTRATIVE, DIFFERENTIATION
CASE 11

• F 73. RIGHT FRONTAL RING ENHANCING MASS
• FROZEN SECTION
• ? GBM
DIAGNOSIS

• METASTATIC SMALL CELL CARCINOMA.
METASTATIC TUMOURS

• METASTASES MORE COMMON THAN PRIMARY NEOPLASMS!
• BLOOD BRAIN BARRIER PROTECTS FROM SOME CHEMOTHERAPIES
• HAEMATOGENOUS ROUTE
• RARELY RETROGRADE PERINEURAL SPREAD VIA CRANIAL NERVES OF HEAD AND NECK TUMOURS
• DIRECT SPREAD FROM ADJACENT BONES
• LUNG>MELANOMA>KIDNEY>GIT
• NON-PULMONARY TUMOURS USUALLY METASTASISE TO LUNG FIRST
• SOLITARY OR MULTIPLE
• MENINGEAL CARCINOMATOSIS: LUNG AND BREAST
METASTATIC TUMOURS

• RADIOLOGY:
  • COMMONLY MCA TERRITORY
  • SOLITARY OR MULTIPLE
  • SHARPLY DEMARCATED, CONTRAST ENHANCING,
  • +/- CENTRAL NECROSIS
  • HAEMORRHAGIC: RCC, MELANOMA, CHORIOCARCINOMA, LUNG
  • DURAL/LEPTOMENINGEAL: BREAST
  • LEPTOMENINGEAL CARCINOMATOSIS: BREAST & LUNG (CSF CYTOLOGY +)
METASTATIC TUMOURS

• CYTOLOGY:
  • TISSUE FRAGMENTS
  • SHEETS/FRAGMENTS WITH SHARP BORDERS
  • DIRTY BACKGROUND
  • PROMINENT CYTOPLASM
  • DISCRETE CELL BORDERS
  • NO CELL PROCESSES (EXCEPT IN SOME MELANOMA)
  • LARGE NUCLEI (BIGGER THAN MOST GBM)
  • EVIDENCE OF DIFFERENTIATION
METASTATIC TUMOURS

• FROZEN SECTION:
  • COMPACT (NON-INFILTRATIVE) GROWTH
  • LARGER CELLS
  • NECROSIS OFTEN WITH SPARING OF VESSELS AND RESIDUAL “COLLAR” OF VIABLE TUMOUR CELLS
  • VASCULAR PROLIFERATION UNCOMMON EXCEPT IN RCC
  • VARIABLE DIFFERENTIATION
  • FIBROUS STROMA
  • PERITUMORAL CHRONIC INFLAMMATION
CASE 5

• F 70

• RING ENHANCING CEREBELLAR MASS
DIAGNOSIS

• CEREBELLAR ABSCESS.
ABSCESS

• CLINICAL:
  • MASS EFFECT
  • HX DENTAL WORK, ENDOCARDITIS, RECENT SURGERY

• RADIOLOGY:
  • USUALLY SOLITARY
  • CONTRAST UNIFORM CONTRAST ENHANCING (VS SHAGGY GBM)
HISTOLOGY

- MACROPHAGES AND NEUTROPHILS
- LYMPHOPLASMACYTIC INFILTRATE
- CEREBRITIS (IF EARLY)
- PURULENT MATERIAL (DEVELOPED)
- GRANULATION TISSUE/FIBROUS CAPSULE
- OEDEMA
- SCATTERED MITOSES!
- ORGANISMS (IF YOU’RE VERY LUCKY)
CASE 7

- M 74
- 2 YEARS POST RESECTION OF BRAIN TUMOUR
- NEW CONTRAST RING ENHANCING LESION
- ? RECURRENCE
- FROZEN SECTION
DIAGNOSIS

- FROZEN DX: GLIOSIS, NO TUMOUR IDENTIFIED.
- RADIONECROSIS ON PARAFFINS
TREATMENT EFFECTS

- RADIONECROSIS: DELAYED REACTION MONTHS-YEARS AFTER TREATMENT
- PSEUDOPROGRESSION
- RADIATION VASCULOPATHY
- RADIATION ENCEPHALOPATHY
- RADIONECROSIS VS RECURRENCE COMMON CAUSE FOR RE-BIOPSY +/-FS
- TREATMENT FOR RECURRENCE VS RADIONECROSIS DIFFERENT
RADIONECROSIS

• RADIOLOGY:
  • SOAP BUBBLE OR SWISSE CHEESE INTERIOR ON MRI
  • RING ENHANCING LesION INDISTINGUISHABLE FROM GBM!

• HISTOLOGY:
  • PROMINENT VASCULAR CHANGES (TELANGIECTATIC, HYALINIZED, ANGIONECROTIC)
  • COAGULATIVE NECROSIS WITH HYPOCELLULAR EDGES
  • DYSTROPHIC CALCIFICATIONS
  • ADJACENT BRAIN: VACUOLATED, GLIOTIC, PALE, HISTIOCYTIC INFILTRATE
  • BIZARE NUCLEAR CYTOLOGICAL ATYPIA, ABUNDANT CYTOPLASM
  • RARE MITOSES
  • IHC: LOW MIB-1, IDH1 NEGATIVE OR RARE CELLS
TUMOUR PROGRESSION

- INCREASED PLEOMORPHISM, NECROSIS AND TELANGIECTATIC VESSELS CAN RESEMBLE MICROVASCULAR PROLIFERATION, STRICT CRITERIA NEEDED BEFORE UPGRADING AN IRRADIATED GliOMA
- MICROVASCULAR PROLIFERATION (MULTILAYERING OF HYPERTROPHIC ENDOTHELIAL CELLS) AND PALISADING/SPONTANEOUS TUMOUR NECROSIS REQUIRED FOR DIAGNOSIS OF GLIOBLASTOMA IN SETTING OF RT
- INCREASED MITOTIC COUNT AND PROLIFERATIVE INDEX NOT TYPICAL OF RADIATION AND ARE MORE RELIABLE FEATURE OF TUMOUR PROGRESSION
- SCATTERED IDH1 + CELLS ON IHC (OFTEN RESEMBLING REACTIVE ASTROCYTES) OF UNCERTAIN PROGNOSTIC SIGNIFICANCE
- ***RT EFFECTS MAKE OLIGODENDROGLIOMAS APPEAR MORE ASTROCYTIC!!
CASE 3

• M 53 REDO DEBULKING RIGHT FRONTAL GLIOMA
DIAGNOSIS

RADIONECROSIS
CASE 4

• M 53
• RIGHT FRONTAL LESION
• FROZEN SECTION
• ? GLIOMA
DIAGNOSIS

- FROZEN SECTION DX: LESIONAL TISSUE PRESENT, CONSISTENT WITH INFILTRATING GLIOMA, NO HIGH GRADE FEATURES PRESENT
- PARAFFIN SECTIONS: ANAPLASTIC OLIGODENDROGLIOMA, IDH-MUTANT, 1P/19Q-CODELETED, WHO GRADE III
LOW GRADE GLIOMA ON FROZEN SECTION

- RADIOLOGY: GRADE II LESIONS NON-ENHANCING, GRADE III +/- FOCALLY ENHANCING
- INFILTRATIVE GROWTH
- OEDEMA (ICE CRYSTAL ARTIFACT)
- MICROCYSTS
- INCREASED CELLULARITY (BEWARE NORMAL WHITE MATTER!!)
- UNEVEN CELL DISTRIBUTION
- PERINEURONAL SATELLITOSIS AND SUBPIAL CONDENSATION (ESP OLIGO)
- HYPERCHROMASIA
- MITOSES
OLIGODENDROGLIOMA

• CYTOLOGY:
  • TISSUE FRAGMENTS
  • MINIMAL FIBRILLARY BACKGROUND, PAUCITY OF PROCESSES
  • ROUND NUCLEI
  • NAKED NUCLEI
  • SMALL NUCLEOLI
  • CHICKENWIRE VASCULTURE
OLIGODENDROGLIOMA

- FROZEN SECTION:
  - INFLTRATIVE GROWTH, ENTRAPPED NEURONS
  - MICROCYSTS
  - CORTICAL CALCIFICATIONS
  - EVEN CELL DISTRIBUTION
  - ROUND, REGULAR, MONOMORPHIC NUCLEI WITH DISTINCT NUCLEOLI
  - ASTROCYTE-LIKE CELLS AND MINI GEMISTIOCYTES
  - PERINUCLEAR HALOS/FRIED EGG A FORMALIN FIXATION ARTIFACT NOT SEEN AT FS
ANAPLASTIC OLIGODENDROGLIOMA

• INCREASED CELULARITY
• INCREASED CYTOLOGICAL ATYPIA (OFTEN MORE EPITHELIOD MORPHOLOGY)
• HIGH MITOTIC ACTIVITY \( \geq 6 \) PER \( 10 \) HPF
• MICROVASCULAR PROLIFERATION
• NECROSIS
• WHO GRADE III

• WHO RECOMMENDS “AT LEAST THE PRESENCE OF CONSPICUOUS MICROVASCULAR PROLIFERATION OR BRISK MITOTIC ACTIVITY”.
• PRESENCE OF A SINGLE MITOSIS IN RESECTION SPECIMEN IS INSUFFICIENT
OLIGODENDROGLIOMAS

• NOW DEFINED BY MOLECULAR SIGNATURE
• IDH-MUTANT AND 1P/19Q-CODELETION

• OLIGOASTROCYTOMA NOW DISCOURAGED
• MOLECULAR RESULTS NOW DETERMINE THE DIAGNOSIS OF TUMOURS SHOWING A MIXED OR AMBIGUOUS MORPHOLOGY
WHO 2016

- RECLASSIFICATION OF GLIOMAS WITH 2016 WHO UPDATE
- INTEGRATED DIAGNOSIS REQUIRING MORPHOLOGY AND MOLECULAR FINDINGS FOR FINAL DIAGNOSIS
# WHO classification of tumours of the central nervous system

## Diffuse astrocytic and oligodendrogial tumours

<table>
<thead>
<tr>
<th>Tumour Type</th>
<th>Code</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diffuse astrocytoma, IDH-mutant</td>
<td>9400/3</td>
</tr>
<tr>
<td>Gemistocytic astrocytoma, IDH-mutant</td>
<td>9411/3</td>
</tr>
<tr>
<td>Diffuse astrocytoma, IDH-wildtype</td>
<td>9400/3</td>
</tr>
<tr>
<td>Diffuse astrocytoma, NOS</td>
<td>9400/3</td>
</tr>
<tr>
<td>Anaplastic astrocytoma, IDH-mutant</td>
<td>9401/3</td>
</tr>
<tr>
<td>Anaplastic astrocytoma, IDH-wildtype</td>
<td>9401/3</td>
</tr>
<tr>
<td>Anaplastic astrocytoma, NOS</td>
<td>9401/3</td>
</tr>
<tr>
<td>Glioblastoma, IDH-wildtype</td>
<td>9440/3</td>
</tr>
<tr>
<td>Giant cell glioblastoma</td>
<td>9441/3</td>
</tr>
<tr>
<td>Gliosarcoma</td>
<td>9442/3</td>
</tr>
<tr>
<td>Epithelioid glioblastoma</td>
<td>9440/3</td>
</tr>
<tr>
<td>Glioblastoma, IDH-mutant</td>
<td>9445/3*</td>
</tr>
<tr>
<td>Glioblastoma, NOS</td>
<td>9440/3</td>
</tr>
<tr>
<td>Diffuse midline glioma, H3 K27M-mutant</td>
<td>9385/3*</td>
</tr>
<tr>
<td>Oligodendroglioma, IDH-mutant and 1p/19q-codeleted</td>
<td>9450/3</td>
</tr>
<tr>
<td>Oligodendroglioma, NOS</td>
<td>9450/3</td>
</tr>
<tr>
<td>Anaplastic oligodendroglioma, IDH-mutant and 1p/19q-codeleted</td>
<td>9451/3</td>
</tr>
<tr>
<td>Anaplastic oligodendroglioma, NOS</td>
<td>9451/3</td>
</tr>
<tr>
<td>Oligoastrocytoma, NOS</td>
<td>9382/3</td>
</tr>
<tr>
<td>Anaplastic oligoastrocytoma, NOS</td>
<td>9382/3</td>
</tr>
</tbody>
</table>

## Neuronal and mixed neuronal-glial tumours

<table>
<thead>
<tr>
<th>Tumour Type</th>
<th>Code</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dysembryoplastic neuroepithelial tumour</td>
<td>9413/0</td>
</tr>
<tr>
<td>Gangliocytoma</td>
<td>9492/0</td>
</tr>
<tr>
<td>Ganglioglioma</td>
<td>9505/1</td>
</tr>
<tr>
<td>Anaplastic ganglioglioma</td>
<td>9505/3</td>
</tr>
<tr>
<td>Dysplastic cerebellar gangliocytoma (Lhermitte–Duclos disease)</td>
<td>9493/0</td>
</tr>
<tr>
<td>Desmoplastic infantile astrocytoma and ganglioglioma</td>
<td>9412/1</td>
</tr>
<tr>
<td>Papillary glioneuronal tumour</td>
<td>9509/1</td>
</tr>
<tr>
<td>Rosette-forming glioneuronal tumour</td>
<td>9509/1</td>
</tr>
<tr>
<td>Diffuse leptomeningeal glioneuronal tumour</td>
<td></td>
</tr>
<tr>
<td>Central neurocytoma</td>
<td>9506/1</td>
</tr>
<tr>
<td>Extraventricular neurocytoma</td>
<td>9506/1</td>
</tr>
<tr>
<td>Cerebellar liponeurocytoma</td>
<td>9506/1</td>
</tr>
<tr>
<td>Paraganglioma</td>
<td>8693/1</td>
</tr>
</tbody>
</table>

## Tumours of the pineal region

<table>
<thead>
<tr>
<th>Tumour Type</th>
<th>Code</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pineocytoma</td>
<td>9361/1</td>
</tr>
<tr>
<td>Pineal parenchymal tumour of intermediate differentiation</td>
<td>9362/3</td>
</tr>
<tr>
<td>Pineoblastoma</td>
<td>9362/3</td>
</tr>
<tr>
<td>Papillary tumour of the pineal region</td>
<td>9395/3</td>
</tr>
</tbody>
</table>

## Embryonal tumours

<table>
<thead>
<tr>
<th>Tumour Type</th>
<th>Code</th>
</tr>
</thead>
<tbody>
<tr>
<td>Medulloblastomas, genetically defined</td>
<td></td>
</tr>
<tr>
<td>Medulloblastoma, WNT-activated</td>
<td>9475/3*</td>
</tr>
<tr>
<td>Medulloblastoma, SHH-activated and TP53-mutant</td>
<td>9476/3*</td>
</tr>
<tr>
<td>Medulloblastoma, SHH-activated and TP53-wildtype</td>
<td>9471/3</td>
</tr>
<tr>
<td>Medulloblastoma, non-WNT/non-SHH</td>
<td>9477/3*</td>
</tr>
<tr>
<td>Medulloblastoma, group 3</td>
<td></td>
</tr>
<tr>
<td>Medulloblastoma, group 4</td>
<td></td>
</tr>
<tr>
<td>Medulloblastomas, histologically defined</td>
<td></td>
</tr>
<tr>
<td>Medulloblastoma, classic</td>
<td>9470/3</td>
</tr>
<tr>
<td>Medulloblastoma, desmoplastic/nodular</td>
<td>9471/3</td>
</tr>
</tbody>
</table>
ANCILLARY TESTING

• IDH1 R132H ICH
• IDH1/2 SEQUENCING
• ATRX IHC (LOSS OF STAINING IN IDH-MUTANT ASTROCYTOMAS)
• P53 IHC (>10% STAINING IN TUMOUR CELLS INDICATOR OF ASTROCYTIC DIFFERENTIATION IN IDH-MUTANT TUMOURS)
• MGMT METHYLATION STUDIES
• IP/19Q CO-DELETION
  • LOH STUDIES
  • FISH
**Histology**

- Astrocytoma
- Oligoastrocytoma
- Oligodendroglioma
- Glioblastoma

**IDH status**

- IDH mutant
- IDH wild-type

**1p/19q and other genetic parameters**

- ATRX loss
- TP53 mutation
- 1p/19q codeletion

- **Diffuse astrocytoma, IDH mutant**
- **Oligodendroglioma, IDH mutant and 1p/19q codeleted**

- **Glioblastoma, IDH mutant**
- **Glioblastoma, IDH wild-type**

- Genetic testing not done or inconclusive

**After exclusion of other entities:**

- Diffuse astrocytoma, IDH wild-type
- Oligodendroglioma, NOS

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* = characteristic but not required for diagnosis
CASE 8

• F 62
• DIFFUSE CEREBRAL LESION
• ? GLIOMA
• FS FOR CONFIRMATION OF LESIONAL TISSUE
MOLECULAR

- IDH1 MUTANT
- 1P/19Q LOH NOT DETECTED
DIAGNOSIS

• FROZEN SECTION: HIGH GRADE GLIOMA (ON BASIS OF MITOSIS)
• PARAFFINS: GEMISTIOCYTIC ASTROCYTOMA, IDH-MUTANT, WHO GRADE II
GEMISTIOCYTIC GLIOMA

• CONSPICIOUS BUT VARIABLE (≥ 20%) PROPORTION OF GEMISTIOCYTIC NEOPLASTIC ASTROCYTES

• LARGE CELLS WITH ECCENTRIC NUCLEI WITH GLASSY EOSINOPHILIC CYTOPLASM

• PERIVASCULAR LYMPHOCYTES

• IDH-MUTANT GEMISTIOCYTIC ASTROCYTOMA CORRESPONDS TO WHO GRADE II UNDER CURRENT WHO CLASSIFICATION

• LIKELY PROGRESS MORE RAPIDLY THAN OTHER IDH-MUTANT ASTROCYTOMAS
CASE 6

- M 23
- INTRAMEDULLARY UPPER CERVICAL CORD TUMOUR
- FROZEN SECTION
- ? EPENDYMOMA ? GLIOMA
DIAGNOSIS

• FROZEN: PILOID LESION

• DEFINITIVE DX: LOW GRADE GLIAL LESION WITH PILOID FEATURES, FAVOURING PILOCYTIC ASTROCYTOMA PROVIDED THE TISSUE IS REPRESENTATIVE, CLINICORADIOLOGICAL CORRELATION REQUIRED.
PILOCYTIC ASTROCYTOMA

- CHILDREN AND YOUNG ADULTS
- WELL CIRCUMSCRIBED, SLOW GROWING
- TYPICALLY CEREBELLUM
- CYST WITH ENHANCING MURAL NODULE
- OFTEN “SHELLS OUT” AT SURGERY
PILOCYTIC ASTROCYTOMA

- FIBRILLARY TUMOUR CELLS
- SOLID, MICROCYSTIC, BIPHASIC PATTERN
- TYPICALLY ALTERNATING DENSELY FIBRILLARY AND MICROCYSTIC COMPONENT
- ASSOC ROSENTHAL FIBERS & EOSINOPHILIC GRANULAR BODIES
- LONG HAIR-LIKE PROCESSES (BEST ON SMEARS)
- CAN HAVE ROUND OLIGODENDROGLIOMA-LIKE AREAS
- IDH NEGATIVE
- KIAA1549 BRAF MUTATION
DDX: PILOID GLIOSIS

- ROSENTHAL FIBERS DO NOT = PA
- ROSENTHAL FIBERS INDICATE PRESENCE OF SLOW GROWING LESION
- CAN BE SEEN NEXT TO MANY SLOW GROWING TUMOURS
- EPENDYMOMAS, ADAMANTINOMAS
- ALWAYS ESTABLISH IF SURGEON IS IN THE LESION (THEY MAY GET CRANKY)!
CASE 9

• M 18 PINEAL LESION
• OBSTRUCTIVE HYDROCEPHALUS
• ?EPIDERMOID CYST
DIAGNOSIS

• EPIDERMOID CYST
EPIDERMOID CYST

- USUALLY BASILAR
  - CEREBELLOPONTINE ANGLE, SUPRASELLAR, FLOOR OF 4TH VENTRICLE, SPINAL CORD
- OFTEN LARGE AT TIME OF PRESENTATION AND INCORPORATING IMPORTANT STRUCTURES, HENCE INCOMPLETE EXCISION
- ANUCLEAR SQUAMES
- THIN KERATINIZING SQUAMOUS EPITHELIUM
CASE 10

- M 18 RESIDUAL THIRD VENTRICLE TUMOUR PREVIOUS BIOPSY = EPIDERMOID CYST
- FOR FROZEN SECTION
DIAGNOSIS

• INTRAOPERATIVE: LESIONAL TISSUE PRESENT, DEFER TO PARAFFINS

• FINAL DIAGNOSIS: MIXED MALIGNANT GERM CELL TUMOUR (GERMINOMA AND TERATOMA)
GERM CELL TUMOURS

- CHILDREN AND YOUNG ADULTS
- PINEAL/THIRD VENTRICLE/SUPRASELLAR REGION > BASAL GANGLIA, THALAMUS
- HOMOGENOUS ENHANCING MASS
GERMINOMA

- LARGE ROUND CELLS WITH PROMINENT NUCLEI
- LYMPHOCTYES
- GRANULOMAS
- CALCIFICATION ("BRAIN SAND" IN PINEAL LESIONS)
- SEVERE CRUSH ARTIFACT AT FS
TERATOMA

- TERATOMA IN CNS THOUGHT TO BEHAVE SIMILAR TO OVARIAN COUNTERPART, IE. PURE MATURE TERATOMA PROBABLY BENIGN
- TERATOMA AS PART OF MIXED GERM CELL TUMOUR MALIGNANT
OTHER GERM CELL TUMOURS

- EMBRYONAL CARCINOMA
- YOLK SAC TUMOUR
- RARELY PURE IN THE CNS, USUALLY SEEN AS PART OF MIXED MALIGNANT GERM CELL TUMOUR
- CHORIOCARCINOMA: RARE
CASE 12

- F 13 INTERVENTRICULAR LESION
- FROZEN SECTION
DIAGNOSIS

• SUBEPENDYMAL GIANT CELL TUMOUR IN A PATIENT WITH TUBEROUS SCLEROSIS
SEGA

- BENIGN (WHO GRADE I), SLOW GROWING DISCRETE TUMOUR
- WALL OF LATERAL VENTRICLE IN VICINITY OF FORAMEN OF MONRO
- CHILDREN AND YOUNG ADULTS
- CLOSELY ASSOCIATED WITH TUBEROUS SCLEROSIS COMPLEX
HISTOLOGY

• DISCRETE
• SWEEPING FASCICLES AND NESTS WITH FIBROUS SEPTA
• SPINDLED, EPITHELIOID, GEMISTIOCYTIC CELLS
• ABUNDANT GLASSY CYTOPLASM
• PROMINENT NUCLEOLI
• SCATTERED BIZARRE NUCLEI
• CALCIFICATION COMMON
• IHC: GFAP + S100 + TFF1+ IDH- +/-NEURONAL MARKERS
LEARNING POINT

• BE CAREFUL GRADING GLIOMAS ON FROZEN SECTION
• BEWARE THE SINGLE MITOSIS ON FROZEN
• BEWARE DIAGNOSIS OF “LOW GRADE GLIOMA” ON FROZEN
• “INfiltrATING GLIOMA” SUFFICIENT UNLESS MULTIPLE MITOSES, SUBSTANTIAL HYPERCELLULARITY, CONVINCING NECROSIS OR MICROVASCULAR PROLIFERATION
• BEWARE PILOID GLIOSIS
• NEVER DECLARE YOUR HAND BEFORE THE SURGEON HAS GIVEN YOU ALL THE INFORMATION
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