

# Tumors of the Nervous System

## GENERAL CHARACTERISTICS

### *Incidence*

- Primary tumors of the CNS – 9% of all 1<sup>o</sup> tumors
- CNS tumors – 1.2% of all deaths
- Glioma group tumors – 45% of all intracranial tumors in all age groups
- Children – CNS tumors 2<sup>nd</sup> most frequent form of malignancy (after hematological and lymphoreticular)
- 15,000 newly diagnosed brain tumors each year
- 5 year survival – 25%

### *Sites*

- Children – 70% **INFRA**tentorial
- Adults – 70% **SUPRA**tentorial
- Most common 1<sup>o</sup> malignant intracerebral tumor in **adults** – glioblastoma multiforme (**SUPRATENTORIAL**)
- Most common MALIGNANT tumor in **children** – medulloblastoma (CEREBELLAR)
- Most common BENIGN tumor in **children** – astrocytoma of the cerebellum – more frequent than the medulloblastoma
- Very rare – meninges and schwann cells (meningiomas and schwannomas) – usu. found in adults
- In adults, metastatic tumors (most frequently from the lung) account for 25-30% of all brain tumors

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## GROWTH AND SPREAD OF NEUROECTODERMAL TUMORS

### *Forms of Growth*

- BY EXPANSION ONLY
  - good prognosis
  - ependymomas, choroid plexus papillomas
- BY EXPANSION AND INFILTRATION
  - oligodendrogliomas, many cerebellar astrocytomas, some glioblastomas
- MAINLY BY INFILTRATION
  - bad prognosis
  - glioblastomas, diffuse cerebral astrocytomas, medulloblastomas
  - gliomas are practically incurable because of their infiltrative growth pattern
  - **2<sup>o</sup> structures of Scherer**
    - indicate an underlying infiltrative tumor
    - can be subpial, perineuronal, or perivascular

### *Local spread of tumor across the pia*

- frequently seen in the “benign” forms – cerebellar astrocytomas and optic nerve gliomas
- some gliomas invade the Virchow-Robin spaces and the leptomeninges as a local phenomenon

### *Spread of the tumor through the ependyma*

- can lead to ventricular spread which leads to diffuse dissemination through the CSF pathways
- most common in midline cerebellar medulloblastomas
- less often in glioblastomas and oligodendrogliomas

### *Extraneural metastases*

- rare
- often follows operation

# Histological Typing of Brain Tumors

## TUMORS OF THE MENINGES - MENINGIOMAS

### *Meningioma (Grade I)*

- tumor composed of or differentiating toward arachnoid cells of the meninges
- Peak incidence – age 45
- Most frequent site of origin – parasagittal region
- may begin within bone or invade bone – osteoblastic or osteolytic lesions
- most are encapsulated, but projections may occur
- typically slow growing tumors
- malignant, metastatic, and invasive meningiomas do occur
- HISTOLOGICAL HALLMARK – “meningiothelial whorl”
- MICROLOGICALLY Identified subtypes
  - **Meningiotheliomatous (syncytial)**
    - consists of solid masses of cells with poor definition of the cell borders (syncytial)
  - **Fibrous (Fibroblastic)**
    - spindle-shaped cells resembling fibroblasts predominate
  - **Transitional (mixed)**
    - mixture of cells with syncytial appearance and fibroblastic features
    - tendency to form meningiothelial whorls, often around a capillary BV
    - some whorls contain hyaline cores or **psammoma bodies**
  - **Psammomatous**
    - psammoma bodies are the predominant feature
    - most often spinal

**Remember:** Meningiomas do not invade brain

### *Atypical Meningioma (Grade II)*

- erratic and unpredictable
- brain invasion permitted

### *Papillary (Grade II-III)*

- rare form of meningioma with a papillary pattern
- often associated with malignancy

### *Anaplastic (malignant)(Grade III)*

- any meningioma that displays anaplastic features

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## TUMORS OF THE CRANIAL AND SPINAL NERVES

### *Schwannoma (Grade I)*

- benign tumor composed entirely of Schwann cells
- encapsulated, sometimes cystic
- Characteristic biphasic pattern
  1. dense cellular areas (Antoni A pattern) with nuclear palisading (Verocay bodies)
  2. more loosely structured areas (Antoni B)
- can occur on any spinal or cranial nerve
- MOST COMMON
  1. vestibular portion of the VIIIth nerve – gradual and progressive hearing loss
  2. dorsal roots of spinal nerves – low back pain
- develops on the periphery of the nerve; nerve fibers on outside
- Resection is curable, if feasible

### ***Neurofibroma (Grade I)***

- localized (solitary) or diffuse (plexiform) tumor consisting predominantly of Schwann Cells and fibroblasts and perineural cells with loosely arranged collagen fibers.
  - develops from within the nerve
  - Characteristic appearance
    - waxy small bundles of neoplastic cells in a myxoid matrix
    - nerve fibers may be in the tumor
    - No Antoni A or B
  - Since it grows from within the nerve, resection is not possible without sacrificing the nerve
  - 5-10% become malignant
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## **TUMORS OF NEUROEPITHELIAL TISSUE (*Astrocytic, Oligodendroglial, Mixed Gliomas, and Ependymal*)**

### ***Astrocytic Tumors (fibrillary, diffuse)***

#### ***Astrocytoma (Grade II)***

- infiltrating tumor composed primarily of astrocytes
- Subtype
  - Gemistocytic
    - large, plump astrocytes w/ abundant cytoplasm (eosinophilic) and one or more, usually eccentric nuclei.
- HISTOLOGICAL CRITERIA FOR GRADING
  - slight hypercellularity
  - slight nuclear atypia
  - no vascular proliferation or necrosis

#### ***Anaplastic (malignant) Astrocytoma (Grade III)***

- HISTOLOGICAL CRITERIA FOR GRADING
  - moderate hypercellularity
  - moderate nuclear atypia
  - vascular proliferation permitted
  - no necrosis
  - mitoses

#### ***Glioblastoma Multiforme (GBM) – (Grade IV)***

- most frequent and malignant brain tumor (adults)
- mean survival – < 1 year
- most progress from lower grade astrocytomas (Grade II), they can arise de novo
- the 2° GBM arises in younger patients and has a better prognosis than the 1° GBM
- Most frequent genetic alteration – loss of heterozygosity on Chromosome 10 (80% of all cases)
- Most GBMs appear to have lost one entire copy of C – 10
- Different genetic alterations between 2° and 1°
  - 1° – EGFR amplification/overexpression
  - 2° – p53 mutations
- Variants: giant cell GBM, gliosarcoma
- HISTOLOGICAL CRITERIA FOR GRADING
  - vascular proliferation (not required)
  - **necrosis with or without palisading (REQUIRED)**
  - moderate to marked nuclear atypia
  - moderate to marked hypercellularity
  - mitoses

### ***Grading of Astrocytomas***

- some use grade I-IV
- some use three tier system (astrocytoma, anaplastic (malignant) astrocytoma, and glioblastoma)
- uses histological criteria mentioned above

### ***Special Astrocytomas***

#### ***Pilocytic (Grade I)***

- biphasic
- contains: compact areas with fusiform astrocytes and Rosenthal fibers and loose microcystic areas with eosinophilic granular bodies and stellate astrocytes
- Most occur in: children or young adults in cerebellum, hypothalamic region and optic nerve

#### ***Subependymal giant cell astrocytoma (with or w/o tuberous sclerosis) (Grade I)***

- young patients
- circumscribed intraventricular tumor that occludes the foramen of Monro

### ***Oligodendroglial Tumors***

#### ***Oligodendroglioma, low grade (Grade II)***

#### ***Oligodendroglioma, anaplastic (malignant)(grade III)***

- tumor composed primarily of oligodendroglia cells
- round, uniform in size nuclei, clear cytoplasm, well defined cytoplasmic membranes; “fried-egg”
- chicken wire partitioning with BV with varying degrees of endothelial hyperplasia is characteristic
- focal calcifications often found in or around tumor
- BAD prognosis – high cell density and necrosis
- structures of Scherer – produced by the affinity of the tumor cells for the cortical gray matter
- slow growth over a period of years
- **Prognosis better than astrocytomas of the same grade**
- **Anaplastic Oligodendrogliomas are better susceptible to chemotherapy than Astrocytic**
- usu. have loss of 9p and 19q chromosomes
- Loss of 9p and CDKN2A deletions are associated with progression from grade II to grade III

### ***Mixed Gliomas***

- oligo-astrocytoma (Grade II)
- Anaplastic (malignant) oligo-astrocytoma (Grade III)

### ***Ependymal neoplasms***

#### ***Ependymal, low grade (Grade II)***

- composed predominantly of ependymal cells
- form rosettes, canals, and most commonly, perivascular pseudorosettes
- Ependymal rosettes are diagnostic
- tumor typically projects from an ependymal surface
- slow growth over a period of years
- prognosis is better in adults than in children
- intraspinal have a better course than intra-cranial

#### ***Anaplastic (malignant) Ependymoma (Grade III)***

#### ***Myxopapillary Ependymoma (Grade I)***

- occurs virtually always in the region of the cauda equina and originates from the filum terminale or the conus medullaris
- ependymal cells arranged in a perivascular papillary pattern
- Perivascular and intercellular mucin deposition
- hemorrhages are frequent

### ***Subependymoma***

- tumor composed of nests of uniform ependymal cells in a stroma of dense acellular fibrillary processes
  - frequently, present as small asymptomatic nodules
  - others may present as small or large masses projecting into a ventricle, especially the 4<sup>th</sup> ventricle
  - typically slow growing
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## **CHOROID PLEXUS TUMORS**

### ***Choroid Plexus Papilloma (grade I) and carcinoma (grade III-IV)***

- papillary tumor composed of a single layer of cells covering a delicate vascular connective tissue core
- sometimes heavily calcified
- mitoses are rare
- malignant transformation – choroid plexus carcinoma – children (almost non-existent in adults)
- Pre-albumin (transthyretin) is present in choroid plexus tumors

### ***Colloid cyst of the 3<sup>rd</sup> ventricle***

- NOT A CHOROID PLEXUS TUMOR
  - mucus filled, epithelial-lined cyst occurring in the region of the 3<sup>rd</sup> ventricle in the region of the foramen of Monro, near the choroid plexus
  - benign
  - good prognosis if found early and surgically removed
  - Produces classic symptoms of headache, sudden transient paralysis of lower extremities, incontinence, personality changes, and occasionally dementia
  - affects mainly young to middle age adults
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## **NEURONAL TUMORS**

### ***Gangliocytoma (Grade I) and Ganglioglioma (Grade I-II)***

- tumor composed mainly of mature ganglion cells and glial cells
- non-neoplastic glial cells– gangliocytoma
- neoplastic glial cells- ganglioglioma
- mesenchymal stroma may be present
- often calcified and cystic
- slow growing tumors with benign potential
- malignancy may occur through transformation of glial elements
- Signs: seizures, ICP symptoms

### ***Central Neurocytoma***

- recently delineated discrete intraventricular tumor in the area of the foramen of Monro
- obstructs the flow of CSF
- ICP signs and symptoms
- looks like an oligodendroglioma
- young to middle age adults

### ***Other Defined mixed tumor entities***

#### ***Dysembryoplastic Neuroepithelial Tumor (Grade I)***

- exclusive symptom: partial complex seizure
- quasi-hamartomatous, intracortical multinodular mass composed of glioneuronal and other regions
- characteristic finding: mucoid background and “floating neurons”

## EMBRYONAL TUMORS

### *Medulloblastoma (Grade IV)*

- most frequent malignant tumor in children
- composed of small, poorly differentiated cells with ill-defined cytoplasmic processes
- tendency to form Homer-Wright rosettes
- differentiation into glial or neuronal elements may occur most characteristically in the midline of the cerebellum and in the roof of the 4<sup>th</sup> ventricle in children
- diffuse spread over the cerebellar folia often occurs early
- radiosensitive initially, but have a tendency to implant along the CSF pathways
- distant extraneural metastases occur infrequently
- member of the PNET (Primitive neuroepithelial tumors) – undifferentiated tumors

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## TUMORS OF THE PINEAL REGION

### *Germinoma*

- most frequent tumor in the pineal region
- biphasic
  - areas composed of large, primitive spheroidal cells
  - and stromal areas with a prominent lymphoid cell component
- indistinguishable from testicular seminoma and the ovarian dysgerminoma
- Radiosensitive
- Other germ cell tumors in the pineal region: embryonal carcinoma, yolk sac tumor, choriocarcinoma, and teratoma

### *Pineocytoma (Grade III)*

- uncommon tumor composed of pineal cells
- polar processes radiate towards the vascular stroma with club-like expansions at their tips
- Malignant tumor
- behaves as benign when it exhibits neuronal differentiation
- “pineocytomatous rosettes” common

### *Pineoblastoma (Grade IV)*

- rare, highly cellular pineal tumor
- consists of small, poorly differentiated cells (PNET cells)
- always a malignant tumor

### *Astrocytic tumors*

- benign and malignant astrocytic tumors may occur in the pineal gland

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## TUMORS OF UNCERTAIN HISTIOGENESIS

### *Hemangioblastoma*

- cystic, capillary-rich neoplasm containing variably lipidized stromal cells
- occurs either sporadically – 70% or occurs in association with the von Hippel-Lindau disease –30%
- Prototypic hemangioblastoma – cystic cerebellar mass with a contrast-enhancing mural nodule

## **CRANIOPHARYNGIOMA**

- tumor considered by some people to originate from remnants of the craniopharyngeal duct (Rathke's pouch)
  - calcified cystic suprasella mass filled with a dark brown fluid
  - first two decades of life
  - Histo: epithelial lobules exhibit peripheral palisading of nuclei abutting cyst-like spaces or connective tissue stroma and ?dehisce? to assume a stellate configuration
  - Common features: calcification, wet keratin, ossification, and inflammatory reaction
  - glial reactions and Rosenthal fibers in the vicinity
  - Variants:
    - Adamantinomatous
    - papillary (no nuclear palisades, microcystic degeneration, calcification, and wet keratin; better prognosis)
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## **PRIMARY CENTRAL NERVOUS SYSTEM LYMPHOMA**

- deep seated tumors
  - solitary in healthy people
  - multiple in immunocompromised patients
  - most are B-cell lymphomas
  - centered around arteries and angioinvasion are characteristic
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## **METASTATIC TUMORS**

- LOTS OF EDEMA!