NEUROPATHOLOGY
NEOPLASIA, INFECTION

HAJNALKA RAJNAI
TUMORS OF THE CNS
INCIDANCE OF CHILDHOOD NEOPLASMS

- Leukemia: 32%
- CNS: 7%
- Lymphoma: 6%
- Neuroblastoma: 5%
- Kidney tumor: 7%
- Bone tumor: 3%
- Rhabdomyosarcoma: 3%
- Retinoblastoma: 4%
- Germ cell tumor: 3%
- Egyéb: 10%
PRIMARY TUMORS OF THE CNS

1. Gliomas
2. Neuronal or mixed glioneural tumors
3. Choroid plexus neoplasms
4. Embryonal tumors
5. Meningial tumors
6. Other parenchymal tumors
   • Haematologic malignancies
   • Germ cell tumors
**CHARACTERISTICS**

- Do not have premalignant or in situ stages
- Rarely spread outside of the CNS

**Symptoms**
- Epilepsy (focal or generalized)
- Focal neurologic deficits
- Signs of raised intracranial pressure
- Hydrocephalus

**Diagnosis**
- Age
- Sex
- Site of neoplasm
- Family history

**Grade**

- Predicting the biological behaviour
  - Grade I
    - Low proliferative potential
    - Possibility of curative resection
  - Grade II
    - Infiltrative
    - Often recur
    - Progression
  - Grade III
    - Histological evidence of malignancy
    - High mitotic activity, atypia
  - Grade IV
    - Cytologically malignant
    - Rapid disease evolution
I. GLIOMAS

- Oligodendroglia
- Astrocyte
- Ependyma
- Neuron
- Choroid plexus
1.1. Astrocytoma

1. Pilocytic astrocytoma (Grade I)

- Children and young adults
- Benign tumors
- Most commonly infratentorial – Cerebellum
II. Diffuse astrocytoma  (Grade II-IV)

- Fourth through the sixth decades of life
- Cerebral hemispheres – Focal signs, headache

Well-differentiated astrocytoma Grade II
- Atypia+ High cellularity

Anaplastic astrocytoma Grade III
- Atypia + High cellularity + High mitotic activity

Glioblastoma Grade IV
- Atypia + High cellularity + High mitotic activity + Necrosis/Endothel proliferation
Well-differentiated astrocytoma Grade II
Anaplastic astrocytoma Grade III
Normal brain
• IDH1 mutation

Well-differentiated astrocytoma
• Loss of 19 ch
• ATRX loss

Anaplastic astrocytoma
• 10 q loss

Glioblastoma
• Secunder

Glioblastoma
• Primer
• EGFR overexpr.
• 10q loss
• PTEN mutation
Glioblastoma Grade IV

Vascular proliferation

Necrosis
I. II. Oligodendroglioma

- Fourth and fifth decades of life
- Cerebral hemispheres – Seizure, headache
  - Frontal, temporal lobe
- 1p 19q codeletion
Well-differentiated oligodendroglioma
Grade II

Anaplastic oligodendroglioma
Grade III

Vascular proliferation
I. III. Ependymoma

- Intracranial – Childhood
  - IV. ventricle, III. ventricle
- Spinal ependymoma – 20-40 years of age
Ependymoma Grade II

Pseudorosettes

Anaplastic ependymoma Grade III

Necrosis
II. NEURONAL/GLIONEURONAL TUMORS

- Oligodendroglia
- Astrocyte
- Neuron
- Ependyma
- Choroid plexus
I. Central neurocytoma Grade II

- Intraventricular neoplasms located predominantly in the vicinity of the septum pellucidum
- Young adults
II. Gangliocytoma, ganglioglioma Grade I

- Mature appearing neurons ± Glial cells
- Glial component – with time anaplastic
III. Dysembryoplastic neuroepithelial tumor
Grade I

- Childhood tumor
- Superficial temporal lobe
III. CHOROID PLEXUS NEOPLASMS

- Oligodendroglia
- Astrocyte
- Neuron
- Ependyma
- Choroid plexus
Choroideus plexus papilloma

Plexus choroideus carcinoma
IV. EMBRIONAL NEUROEPITHELIAL TUMORS

- Predominance in children
- Disseminate through CSF pathways
- Small undifferentiated cells
- High mitotic index, widespread apoptosis
- Potential for divergent neuroepithelial differentiation
I. Medulloblastoma Grade IV

- 20% of pediatric brain tumor
- Infratentorial, IV. ventricle
II. Atypical teratoid/rhabdoid tumor (ATRT) Grade IV

- Most commonly <5 years
- Poor prognosis
- Anywhere in the CNS
V. MENINGIOMAS

- Benign tumors that arise from arachnoid meningotheelial cells
- External surfaces, or intraventricular
- Focal neurological deficits
I. Meningioma Grade 1.

- Incidence rises with age
- Primary CNS tumors ~30% meningioma
- Several histological variants

Psammoma body
II. Atypical Meningioma
Grade II.

III. Anaplastic Meningioma
Grade III.

Ki67

Necrosis
VI. PRIMARY CNS LYMPHOMA

- DLBCL type
- Most common CNS neoplasm in immunosuppressed persons
- Nearly always positive for the EBV
VII. CNS GERM CELL TUMORS

- Germinoma - 50%
- Teratoma - 20%
  - Mature teratoma
  - Immature teratoma
  - Teratoma with malignant transformation
- Yolk sac tumor
- Embryonal carcinoma - 5%
- Choriocarcinoma
- Mixed tumor - 25%
VIII. METASTATIC TUMORS

- Gray-white junction
- Sharply demarcated masses
- Perifocal edema

![Magnetic Resonance Imaging (MRI)](image1)
![Histology of Small Cell Lung Carcinoma (SCLC)](image2)
![Histology of Breast Carcinoma](image3)
INFECTIONS OF THE NERVOUS SYSTEM

Localisation:

1. Parenchyma: encephalitis, myelitis, encephalomyelitis.
SPREAD

1. Hematogenous spread
2. Direct implantation – Trauma, iatrogenic
3. Local extension – Otitis media, Congenital malformation
4. Peripheral nerves
1. Bacterial infection
   - Bakterial meningitis
   - Brain abscessus
   - Tuberculosis
   - Neurosyphilis

2. Virus infection
   - Viral meningitis
   - Herpesvirus
   - Cytomegalovirus
   - Poliovirus
   - Rabies
   - HIV
   - Progressive multifocal leukoencephalopathy

3. Fungal infection
   - Candida
   - Mucormycosis
   - Aspergillus
   - Cryptococcus

4. Protozoal infection
   - Toxoplasma

5. Parazite infection
   - Cystercosis
   - Echinococcus
I. Epidural abscess
   • Local spread – sinuitis, osteomyelitis
   • Bacterial, fungal
   • Spinal - spinal cord compression

II. Subdural empyema
   • Local spread – sinus
   • Arachnoid, subarachnoid space is unaffected
   • Thrombophlebitis in the bridging veins
MENINGITIS

I. Bacterial meningitis

1. Neronates
   • Escherichia coli
   • B Streptococcus
2. Children young, adults
   • Neisseria meningitidis
   • Streptococcus pneumoniae
3. Older individuals
   • Streptococcus pneumoniae
   • Listeria monocytogenes
II. Aseptic/Viral meningitis

- Echovirus
- Coxsackie B
- Coxsackie A
- Herpes simplex virus (HSV)-2
- Mumps
- Human immunodeficiency virus (HIV)
- Lymphohoriomeningitis virus
- Arbovirus
- Rubeola
- Parainfluenza virus
- Adenovirus
III. Chronic meningitis

III.I. Mycobacterium tuberculosis

- Meningitis – Fibrinous exudate
- Intraparenchymal mass (tuberculoma)
- Chronic tuberculotic infection - arachnoideal fibrosis - hydrocephalus
III.II. Spirochaetal infections

A. Neurosyphilis (3rd stadium) – Treponema pallidum
   • 10% of persons with untreated infection
     1. Chronic meningitis/meningovascular neurosyphilis
        • Involves the base of the brain
     2. Paretic neurosyphilis
        • Neuron loss – loss of mental, physical functions
     3. Tabes dorsalis
        • Sensory nerves in the dorsal roots
        • Sensory ataxia

B. Neuroborreliosis – Borrelia burgdorferi
   • Aseptic meningitis
   • Facial nerve palsies
   • Mild encephalopathy
   • Polyneuropathies
PARENCHYMAL INFECTIONS

I. Brain abscesses
   • Bacterial infections
   • Spread:
     • Direct implantation
     • Local extension
     • Hematogenous spread
   • Symptoms - Focal
II. Viral encephalitis

- Perivascular lymphoid infiltration
- Microglial nodules
- Neuronophagia
II. 1. Herpes virus

A. Herpes simplex-1
   • Children and young adults
   • Frontal, temporal lobe involvement
   • Necrotizing encephalitis

B. Herpes simplex-2
   • Adults
   • Viral meningitis
   • Primary HSV genital inf - neonates

C. Varicella zoster
   • Immunosuppressed patients
   • HZV encephalitis
II. II. Cytomegalovirus

A. Fetus
   • Periventricular necrosis
   • Microcephalia
   • Periventricular calcification

B. Adult
   • Immunosuppressed persons
   • Periventricular
   • Subacute encephalitis
II.III. Poliovirus

- Gastroenteritis – Secunder CNS spread
  - Poliomyelitis anterior acuta / Paralytic poliomyelitis
  - Damages motor neurons in the spinal cord and brain stem
  - Flaccid paralysis with muscle wasting and hyporeflexia

- 25 to 35 years – Postpolio syndrome
  - Progressive weakness, pain
II. IV. Rabies Virus

- Rabies
  - Rabid animals, usually by a bite

- Ascending along the peripheral nerves
  - the incubation period depends on the distance between the wound and the brain

- Symptoms:
  - Non specific
  - Signs of CNS excitability
    - Pain, hydrophobia
    - Mania-coma
II.V. Human Immunodeficiency virus

A. Aseptic meningitis
   • Within 1 to 2 weeks of onset of primary infection by HIV in about 10% of patients

B. HIV Encephalitis (HIVE)
   • Perivascular lymphoid infiltration
   • Myelin loss in the hemispheres (Leukoencephalopathy)
   • Microglial noduls
   • Giant cells

C. Opportunistic infections

D. Primary CNS lymphoma
II.VI. JC virus / Progressive multifocal leukoencephalopathy

- Polyoma virus
- Infects oligodendroglial cells
  - Demyelinisation
  - White matter – Hemispheres, Cerebellum
- Progressive neurologic symptoms
III. Fungal infections

A. Candida Albicans
   • Multiplex microabscessusok

B. Mucormycosis
   • Nasal cavity, sinus infection
   • Direct extension, Vascular invasion

C. Aspergillus fumigatus
   • Hemorrhagic infarctions
   • Vascular invasion

D. Cryptococcus neoformans
   • Meningitis, Meningoencephalitis
   • Fulminant
Candida albicans
Mucormycosis
Aspergillus fumigatus
Cryptococcus neoformans
IV. Protozoal infection - Toxoplasmosis

- Toxoplasma gondii
  - Humans intermedius hosts
  - Definitive host - Cat

A. Fetal infection/Congenital
  - Chorioretinitis
  - Hydrocephalus
  - Intracranial calcification

B. Adult infection
  - Immunosuppressed adults
  - Subacute symptoms
  - Evolving in 1 or 2 week period
  - Focal-diffuse
IV. Parazitic infection

I. Tenia solium - Cysticercosis

- End-stage infection
  - Larval organisms leave the lumen of the gastrointestinal tract
  - Encyst – Brain – subarachnoid space

- Symptoms
  - Focal symptoms
  - Epilepsy
2. Echinococcus /Hydatidosis/

- Childhood
- Contact with dogs
  - Encysts – Usually liver, lung rarely brain

- Symptoms
  - Focal signs
  - Epilepsy
- Robbins Basic Pathology, 9th Edition
- Neuropathology: A Reference Text of CNS Pathology, 3rd Edition