Neuronal and Mixed Tumors

**Light microscopy**

- monomorphic small cells with evenly spaced, round, uniform nuclei (often mistaken for oligodendroglioma or ependymoma), and no anaplastic features.

### **(CENTRAL) NEUROCYTOMA**

- *benign* tumor of slowly growing well-differentiated neurons

- *young adults* (15-40 yrs).

### **Pathology**

**Light microscopy**

- monomorphic small cells with evenly spaced, round, uniform nuclei (often mistaken for oligodendroglioma or ependymoma), and no anaplastic features.

### **Clinical Features**

- Location
- Young adults
- Slowly growing
- No anaplastic features

### **Pathology**

- Well-differentiated neurons
- No anaplastic features

### **Genetics**

- Onc22
- No anaplastic features

### **Treatment**

- **Degree of differentiation**
- **Gradation**
- **Histology**
- **Clinical Features**
- **Diagnosis**

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Neuronal lineage must be confirmed:
1. Immunohistochemical stains for neurons (neuron-specific enolase, S100, synaptophysin).
2. Electron microscopy - true neuronal nature of neoplasm (neuritic processes, neurosecretory granules, neurofilaments, well-formed synapses).

**LOCATION**
- grow from septum pellucidum - 3rd or lateral ventricles (probably commonest lateral ventricular masses in this age group)
  • typical location - frontal horns and bodies of lateral ventricle, frequently attached to septum pellucidum and sometimes extending through foramen of Monro.

**CLINICAL FEATURES**
- ICP↑ caused by ventricular obstruction.

**DIAGNOSIS**
- CT - calcification and small cysts, obstructive hydrocephalus.
- MRI - isodense intraventricular mass, related to septum pellucidum, with variable cyst formation and contrast enhancement.

Contrast MRI - right lateral ventricular neurocytoma producing obstruction of foramen of Monro:

Contrast MRI - partly cystic, multi-septated, enhancing mass, related to septum pellucidum, fills bodies of both lateral ventricles, causes hydrocephalus.

**TREATMENT**
Surgical resection is often curative (± radiotherapy).

**DYSEMBRYOPLASTIC NEUROEPITHELIAL TUMOR (DNET)**
- extremely slow-growing benign mixed glial-neuronal tumor (neurons, astrocytes, and oligodendrocytes).
- may have germinal origin.
- patients' ages range 3-35 years (mean 21.5 yrs).

Vignette: kid with seizures + bubbly lesion in temporal lobe

**PATHOLOGY**
- **intracortical nodular-appearing neoplasm (features similar to CORTEX DYSPLASIS) enlarging gyrus** (forming megagyrus).
- 2/3 (62%) in **temporal cortex**, 1/3 (31%) in frontal cortex.
- cystic changes, frequent association with dysplastic cortex.
- hypocellular lesion - well-differentiated normal neurons "floating" in pool of mucopolysaccharide-rich fluid (stains with alcian blue) and surrounded (but NOT tightly*) by neoplastic oligodendroglial-like cells without anaplastic features.

*main difference from OLIGODENDROGLIOMA (perineurial satellitosis)

Note absence of perineuronal satellitosis (i.e. neurons are NOT tightly surrounded by other cells), which is typically seen in oligodendrogial tumors;

Perivascular and perineuronal satellitosis is characteristic of OLIGODENDROGLIOMA spread into grey matter:
NEURONAL AND MIXED TUMORS

Clinical Features
- Often presents as intractable partial seizures.
  - No neurological deficits (or stable congenital deficit).

Diagnosis
MRI - Variable signal and enhancement characteristics (= low-grade astrocytomas).

T2-MRI - Right-sided temporal abnormality (arrow) with thickened cortex, poorly demarcated from white matter.

T1-MRI - Well-circumscribed neoplasm originating in cortical region (arrow); inner table of skull has been remodeled (suggesting slow-growing neoplasm).

Treatment
- Good prognosis after surgical extirpation.
  - Rare postoperative complication - schizophreniform psychosis, paranoia, and depression.
  - Radiation and chemotherapy have no clear benefit.

Ganglioglioma, Gangliocytoma
- Rare benign slowly growing CNS tumors:
  - Ganglioglioma (95%) - Contains both astrocytic and neuronal components. Glial component is most commonly astrocytic, but it may be oligodendrogial.
  - Gangliocytoma (5%) - Only neuronal component without glial component.
    (Its counterpart in PNS is ganglioneuroma.)

- 1.3% brain tumors; 1% intramedullary spinal neoplasms.
- 10% primary brain tumors in children.
- Age: 2 months - 70 years (most < 30 yrs).
**GENETICS**
- BRAF V600E mutation can be detected in up to 50% of gangliogliomas

**PATHOLOGY**
- Biphasic: neoplastic mature ganglion cells + neoplastic glial cells
  1) neoplastic ganglion cells: large dysplastic/dysmorphic-appearing neurons, often binucleated (important diagnostic feature!!), irregularly clustered; apparently random orientation of neurites.
  2) neoplastic astrocytes (in GANGLIOGLIOMA)
  3) relatively acellular fibrovascular stroma.
- DERMOSPATIC INFANILE GANGLIOGLIOMA and closely related DERMOSPATIC INFANTILE ASTROCYTOMA have abundant mesenchymal component; predilection for infants and young children; good prognosis.
- anywhere in CNS (esp. superficial temporal cortex; rarely, in spinal cord).
- 50% are located in temporal lobes, and only 3.7% and 3.5% located in brainstem and spinal cord, respectively.
- firm grayish tumor that may have cystic components and calcification.
- mild-to-moderately cellular, slightly pleomorphic with rare mitotic figures.
- biological behavior is not predicted by histology (many anaplastic GANGLIOGLIOMAS do not demonstrate clinically aggressive behavior).
- metastatic spread is extremely rare (isolated report of leptomeningeal spread).
- glial component occasionally becomes frankly anaplastic → rapid progression (MALIGNANT GANGLIOGLIOMA).

**CLINICAL FEATURES**
- as DNET — often presents as intractable partial seizures.
- most GANGLIOGLIOMAS are nonaggressive.
- no neurological deficits (or stable congenital deficit).

**DIAGNOSIS**
- CT — nonspecific: hypo- or iso-dense, well circumscribed mass located superficially.
  - ≈ 50% show cystic areas (esp. in cerebellum; single large cyst ± cyst with mural nodule ± multicystic mass).
  - ≈ 50% show contrast enhancement (solid tumors have more contrast enhancement).
  - punctate or fleck-like calcification is seen in ≈ 35-50% tumors.
  - surrounding edema is unusual.
  - no mass effect.
- MRI — nonspecific.
- MR spectroscopy — choline-to-creatinine ratio is lower and N-acetyl aspartate-to-creatinine ratio* is higher than in gliomas.
  - *N-acetyl aspartate↑ is due to neuronal component

![Solid enhancing tumor in temporal lobe with no surrounding edema in younger patient with intractable seizures](image-url)
N EURONAL AND M IXED TUMORS

Gadolinium-enhanced T1-MRI - enhancing tumor involving hippocampus, uncus, and amygdala:

Exophytic temporal lobe ganglioglioma (T1-MRI with contrast) - large mass originating from medial aspect of left temporal lobe, both solid and cystic components; large exophytic component extends through tentorial incisura into superior cerebellar cistern; tumor has also compressed atrium of left lateral ventricle.
NEURAL AND MIXED TUMORS

TREATMENT

- complete resection is generally curative (radiation is rarely indicated); may have good prognosis even when untreated (but incomplete removals are associated with local recurrence).
- use of chemotherapy has not been reported.

PROGNOSIS

- poor prognosis factors – age < 1 yr, brainstem involvement.

LHERMITTE-DUCLOS disease (s. dysplastic gangliocytoma of cerebellum)

- rare (221 known cases), benign, slowly growing tumor of cerebellum, sometimes considered as hamartoma
- described by Jacques Jean Lhermitte and P. Duclos in 1920.
- most common in the third and fourth decades.
- often associated with Cowden syndrome (mutations of PTEN gene) and is pathognomonic for this disease (also includes multiple growths on skin).
- histology: diffuse hypertrophy of stratum granulosum of cerebellum

- 1) enlarged circumscribed cerebellar folia
- 2) internal granular layer is focally indistinct and is occupied by large ganglion cells
- 3) myelinated tracks in outer molecular layer
- 4) underlying white matter is atrophic and glotic

Right cerebellar mass with linear striations. No pathological enhancement.

Desmoplastic Infantile Ganglioglioma and Astrocytoma (DIG/DIA)

DIAG first described in 1982 by Taratomuto et al (J Neurosurg. 1987;66:58)
DIG first described in 1987 by VandenBerg et al

- rare (< 0.1% of CNS tumors) supratentorial neuroepithelial tumors of infancy (most < 1 year).

PATHOLOGY

- WHO grade I

- cystic with solid area/mural nodule
- large – usually involve more than one lobe.

- well-delineated from normal brain
- calcification common, chronic inflammatory cells uncommon.
- exceptionally, frank anaplastic features are encountered (high mitotic rate, vascular proliferation, palisading necrosis, and high proliferation index)

1. Desmoplastic leptomeningeal component

- involve the subarachnoid space and extends into Virchow-Robin spaces
- Neoplastic neuroepithelial cells in desmoplastic spindled stroma arranged in fascicular and storiform patterns with pericellular reticulin deposition lending a mesenchymal appearance
- Neoplastic neuroepithelial cells:
  1) Astrocytic cells - the only component in DIA; spindled or gemistocytic neoplastic astrocytes
  2) Neuronal component - seen in DIG in addition to neoplastic astrocytes; small ganglion cells, uncommonly large ganglion cells or areas resembling ganglioglioma

2. Immature small cell component (unclear prognostic significance)

- hypercellular poorly differentiated neuroepithelial cells
- no desmoplasia
- may show mitoses, vascular proliferation, or necrosis

DIA.
CLINICAL FEATURES

- hydrocephalus, seizures

Infant with rapidly progressive macrocephaly

DIAGNOSTICS

- Large cystic and solid mass (enhancing):
- **Treatment**: gross total resection
  - chemotherapy if infiltrative or progressive
  - residual disease may not grow and may spontaneously regress
- despite large size and poorly differentiated cells, prognosis is excellent (but multiple cerebrospinal metastases have been reported).

**BIBLIOGRAPHY** for ch. “Neuro-Oncology” → follow this [LINK] >>