

Neuronal and Glioneuronal Tumors

Ganglioglioma and dysembryoplastic neuroepithelial tumor

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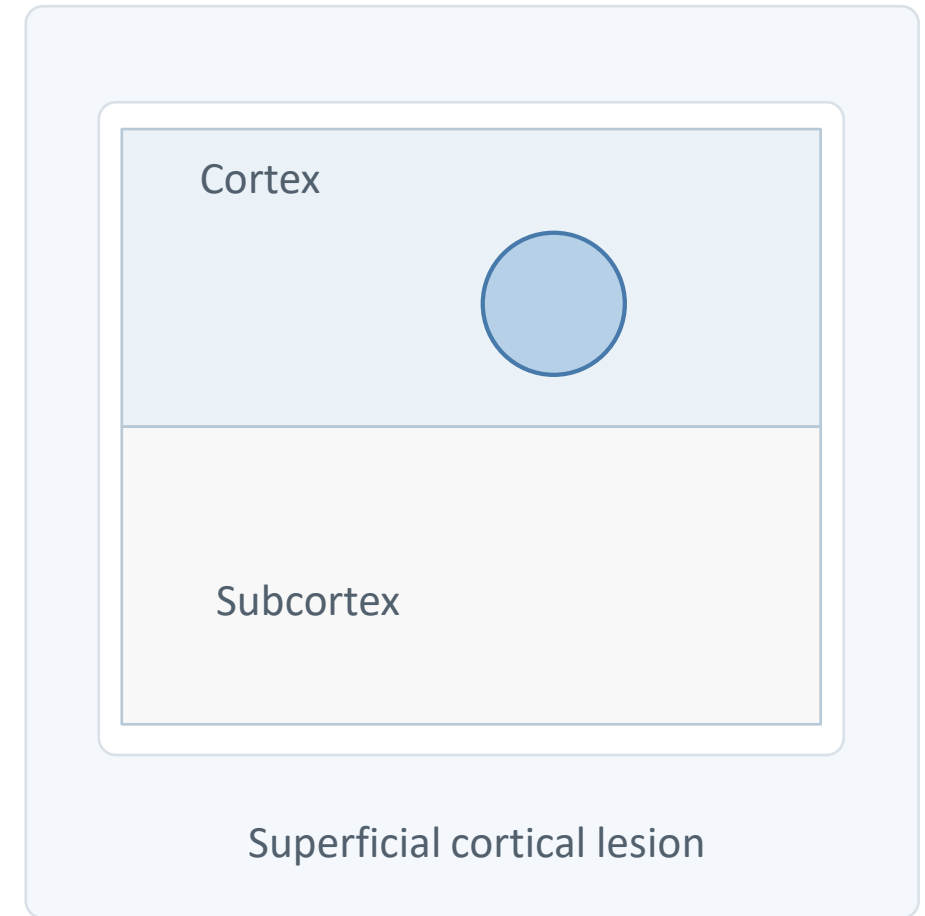
Learning objectives

- Recognize the clinical setting in which neuronal or glioneuronal tumors are suspected.
- Distinguish the mixed cellular composition of ganglioglioma from the specific glioneuronal architecture of DNET.
- Explain the significance of CNS WHO grade 1, surgical control of epilepsy, and selected molecular findings.
- Apply morphologic criteria in focused differential diagnoses.

A small but distinctive CNS tumor category

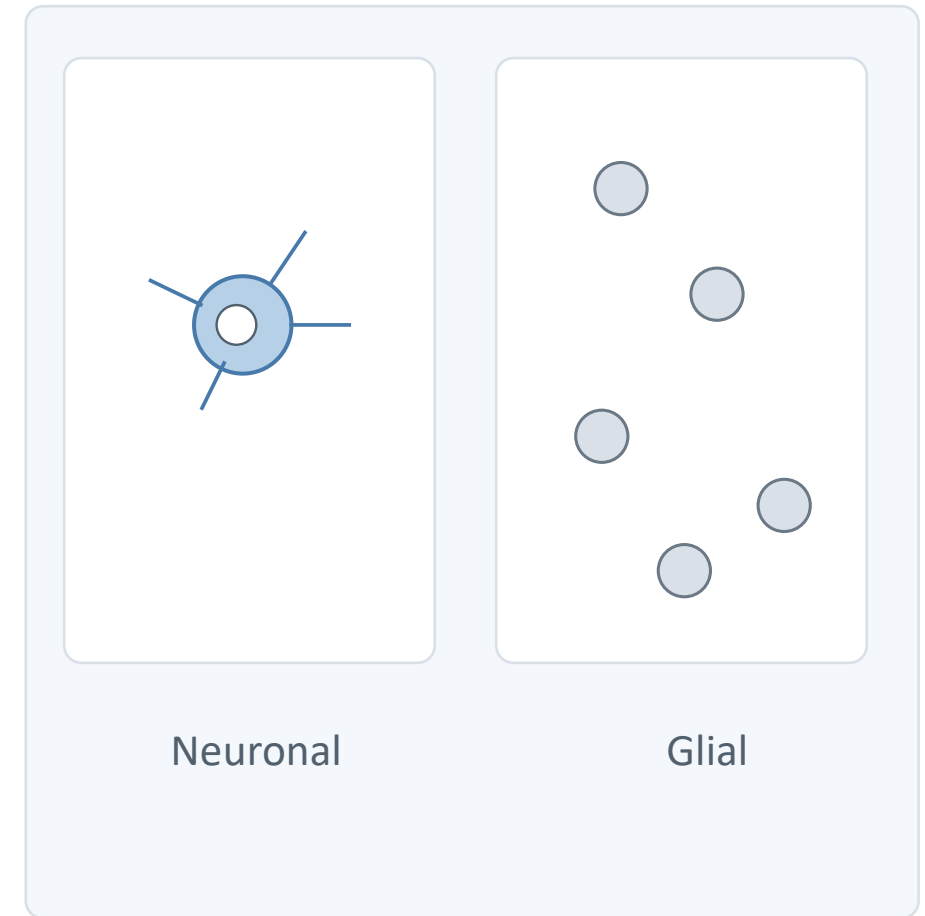
- Tumors with neuronal differentiation are less common than glial tumors.
- The patients emphasized are children and young adults.
- Epilepsy is a prominent presenting context for this group.

The clinical clue is important, but it does not replace tissue-based classification.



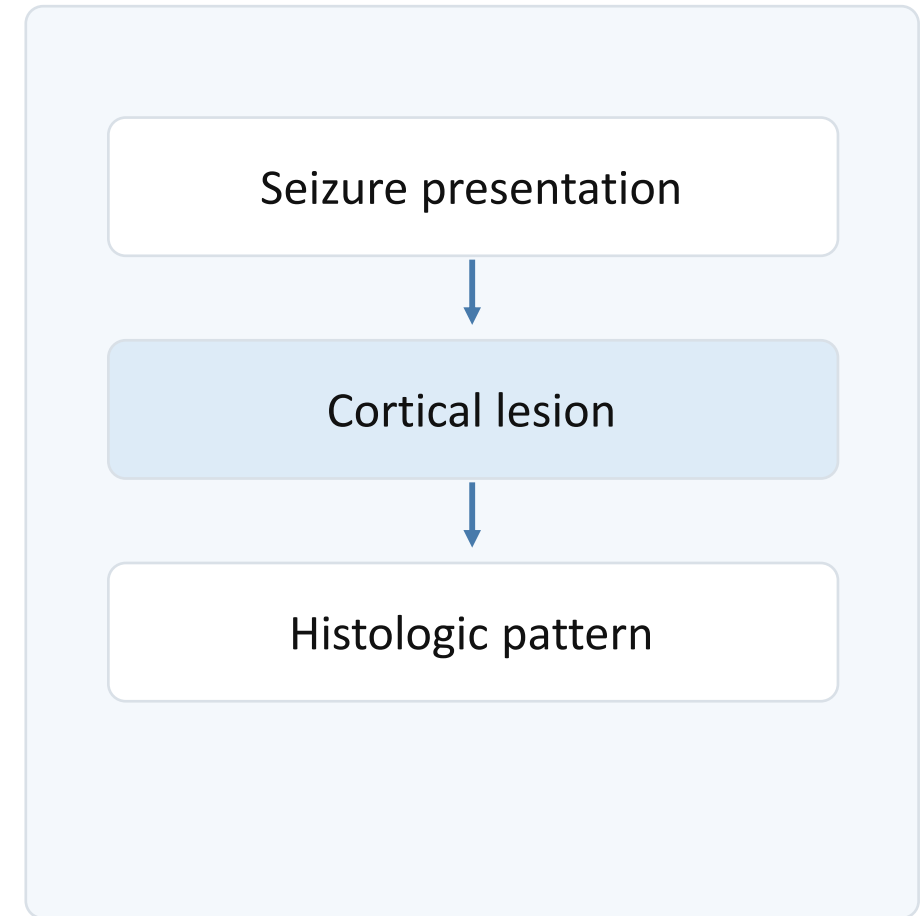
What “glioneuronal” describes

- The term signals neuronal and glial differentiation in the tumor.
- Ganglioglioma contains a conspicuous mixture of mature neuronal and glial components.
- DNET shows a characteristic glioneuronal architectural pattern.



Why these tumors commonly enter an epilepsy work-up

- Seizures prompt evaluation of a cortical brain lesion.
- Many described lesions are superficial or intracortical.
- Pathology interprets the lesion using its specific architecture—not seizure history alone.



CNS WHO grade 1: Meaning within this lecture

- Robbins assigns CNS WHO grade 1 to ganglioglioma and DNET.
- Grade 1 here accompanies generally slow or benign behavior.
- Extent of resection and seizure outcomes are clinically relevant, particularly in epilepsy-associated presentations.

Do not equate grade 1 with “requires no clinical management.”

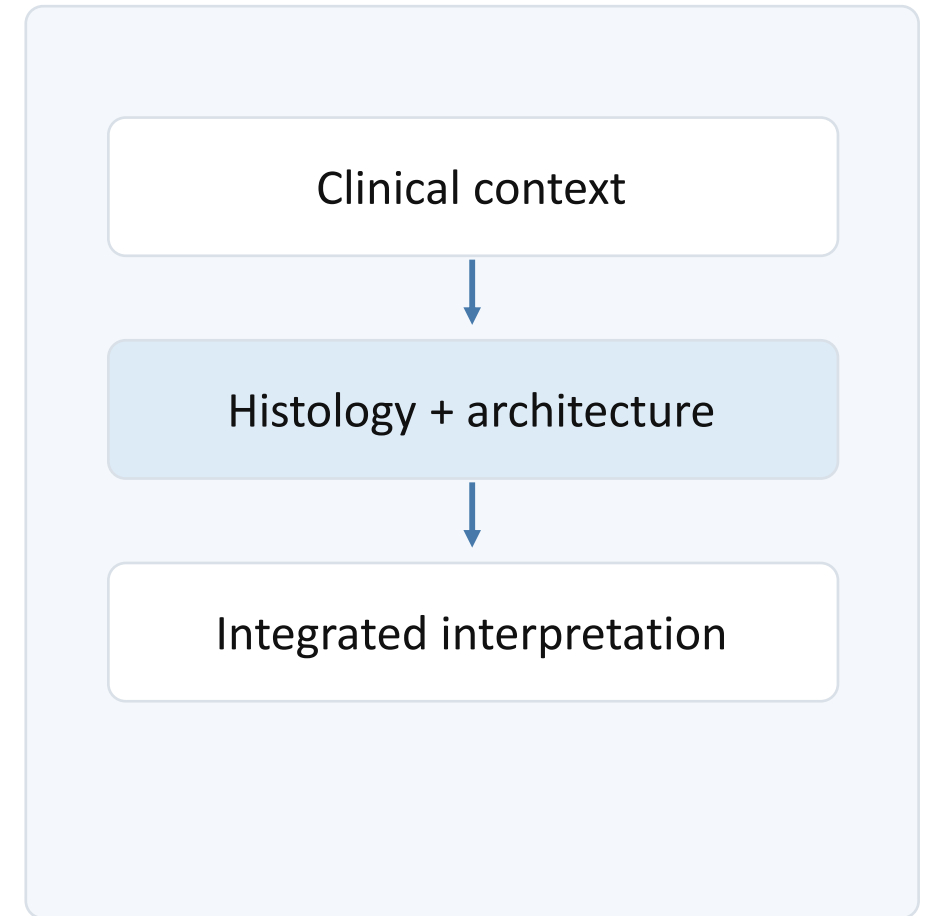
The two core entities

Ganglioglioma	Dysembryoplastic neuroepithelial tumor
Mixed neuronal and glial cells	Specific glioneuronal nodules
Commonly temporal; Often cystic	Superficial temporal cortex; Other sites possible
Dysmorphic / binucleate neurons	Floating neurons in mucin-rich pools
BRAF V600E in a subset	FGFR1 alterations are a molecular adjunct*

*FGFR1: EANO / WHO CNS5 supplementary context; Not stated in the Robbins topic excerpt.

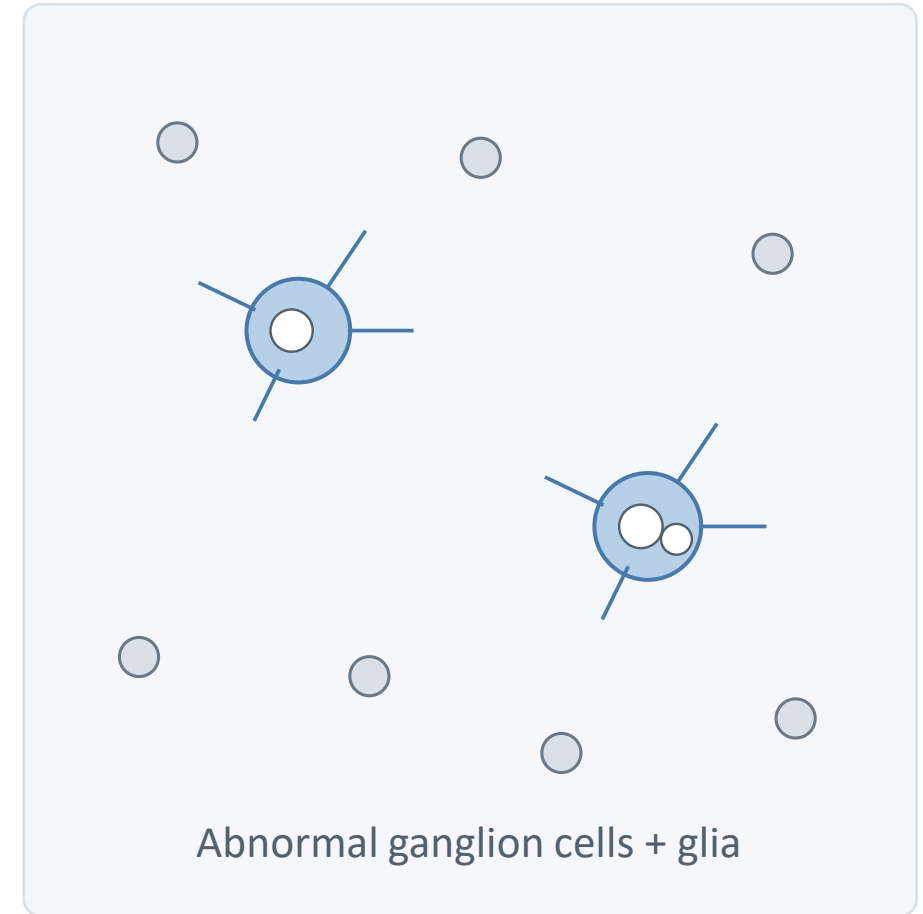
Clinical and diagnostic lens

- Age and epilepsy history provide the clinical context.
- Anatomic relationship to cortex guides lesion sampling.
- Microscopic pattern establishes the key discriminators.
- Molecular testing can be an adjunct when clinically indicated.



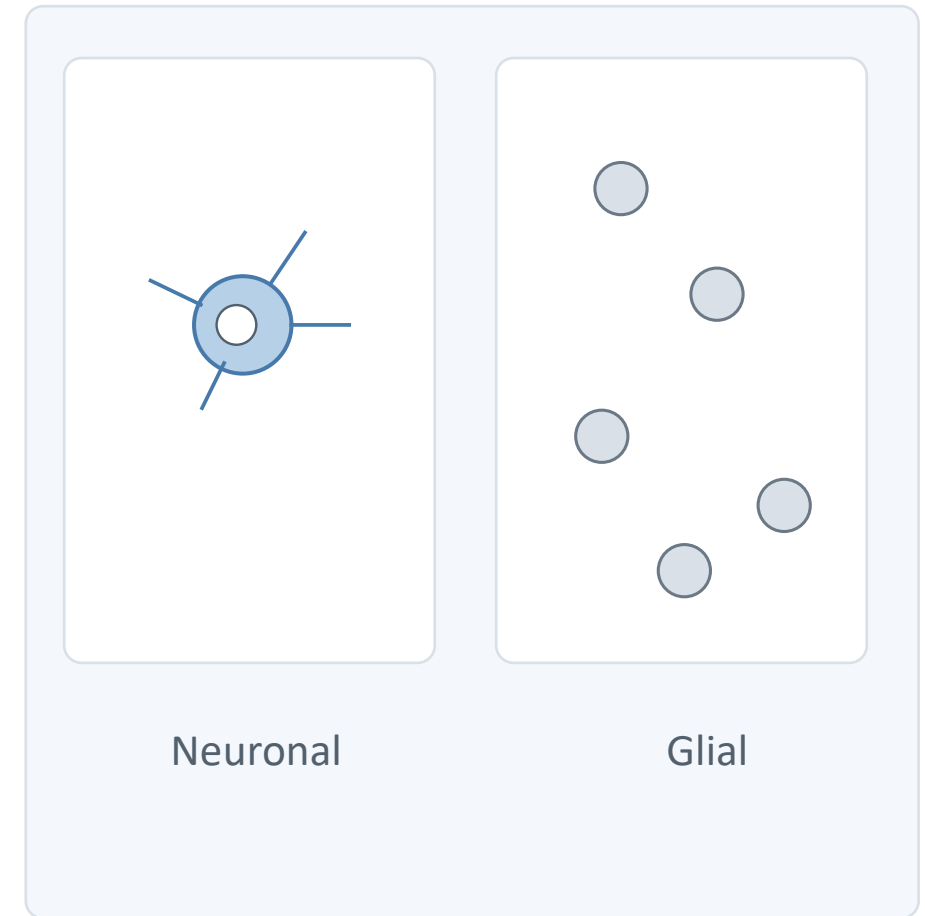
Ganglioglioma: Defining lesion

- Composed of mature neuronal and glial tumor cells.
- Typically superficial and associated with seizures.
- Robbins calls it the most common neuronal tumor in the CNS.



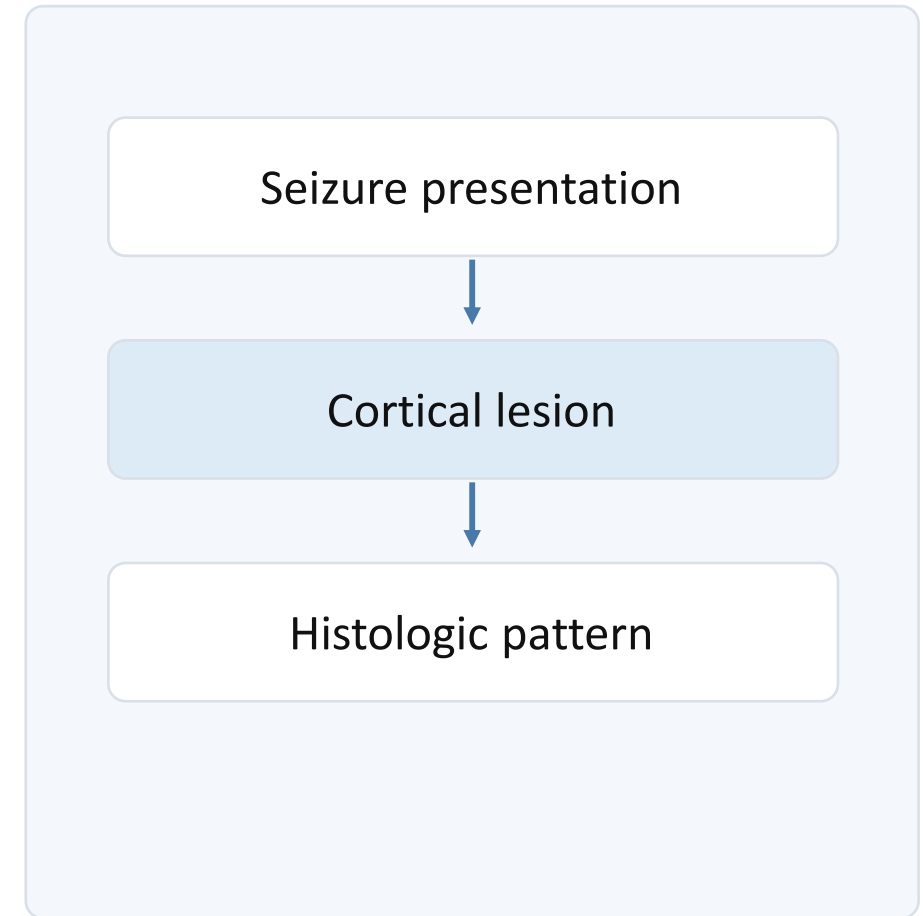
Two cellular compartments in ganglioglioma

- The neuronal compartment contains abnormal ganglion cells.
- The glial compartment often resembles pilocytic astrocytoma.
- Both are interpreted in the context of the same lesion.



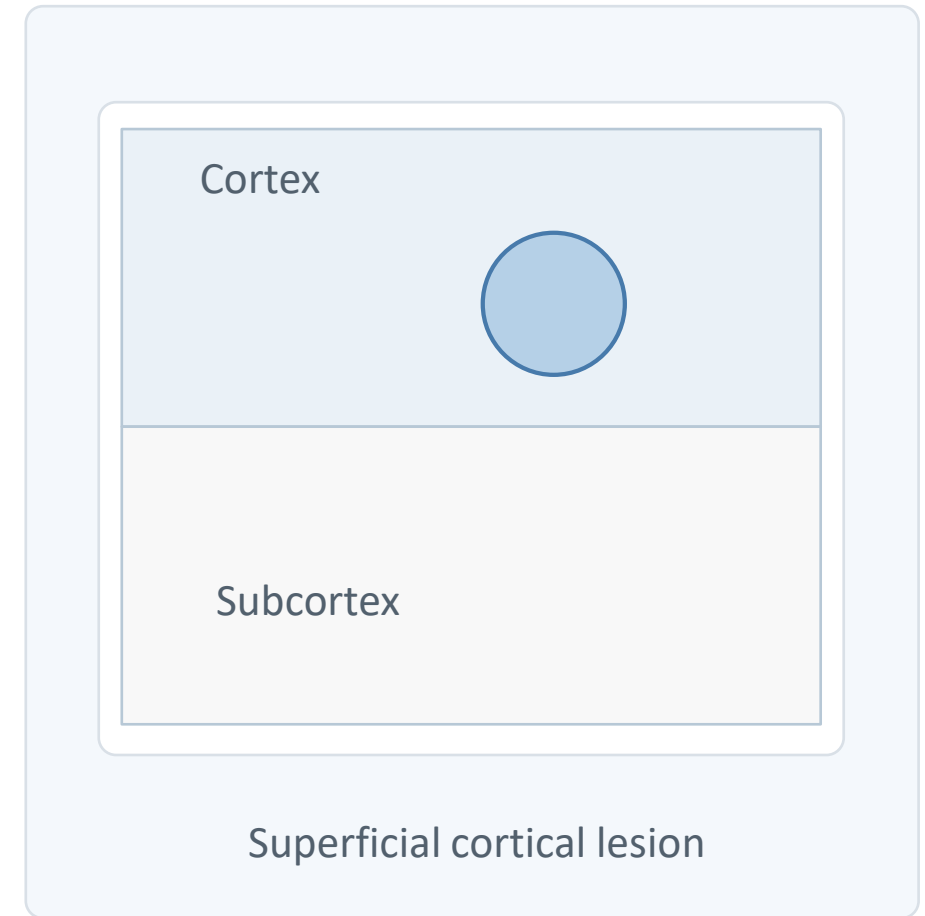
Age and clinical setting of ganglioglioma

- Neuronal tumors as a group predominantly affect children and young adults.
- Gangliogliomas often come to attention through seizures.
- Medically refractory epilepsy is one important surgical presentation.



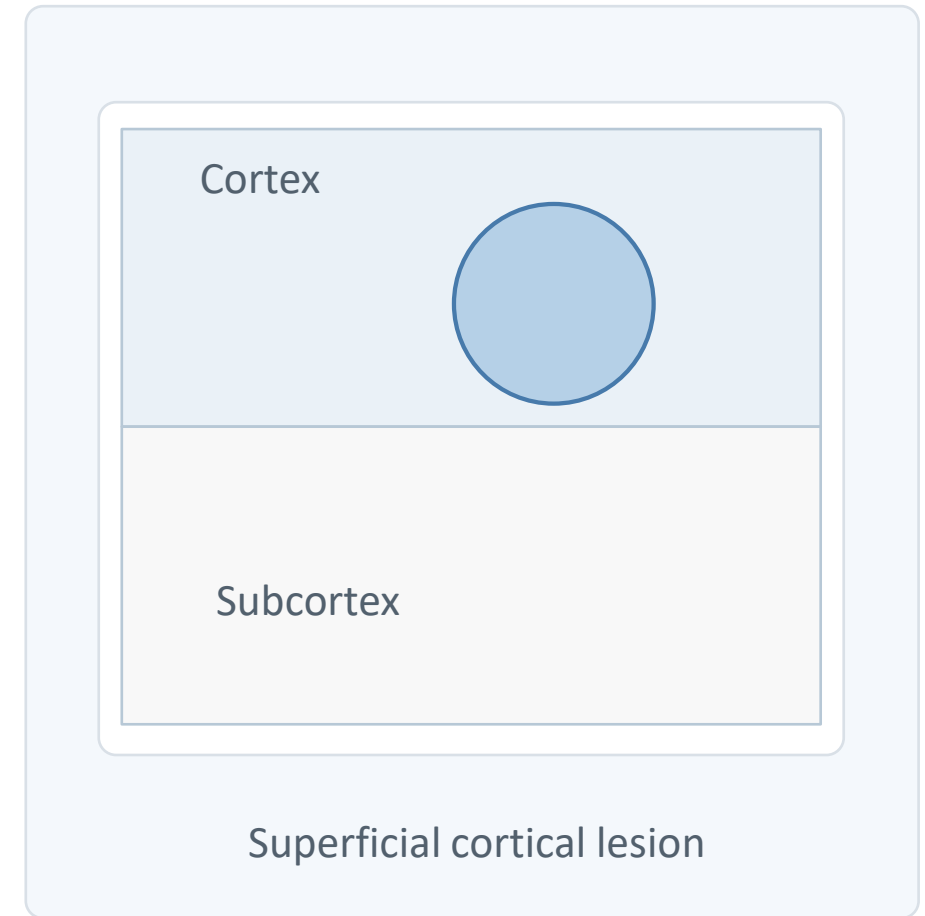
Temporal lobe predominance in ganglioglioma

- The temporal lobe is the most common site.
- The lesion is often close to the cerebral surface.
- Location is a clue, not a standalone histologic diagnosis.



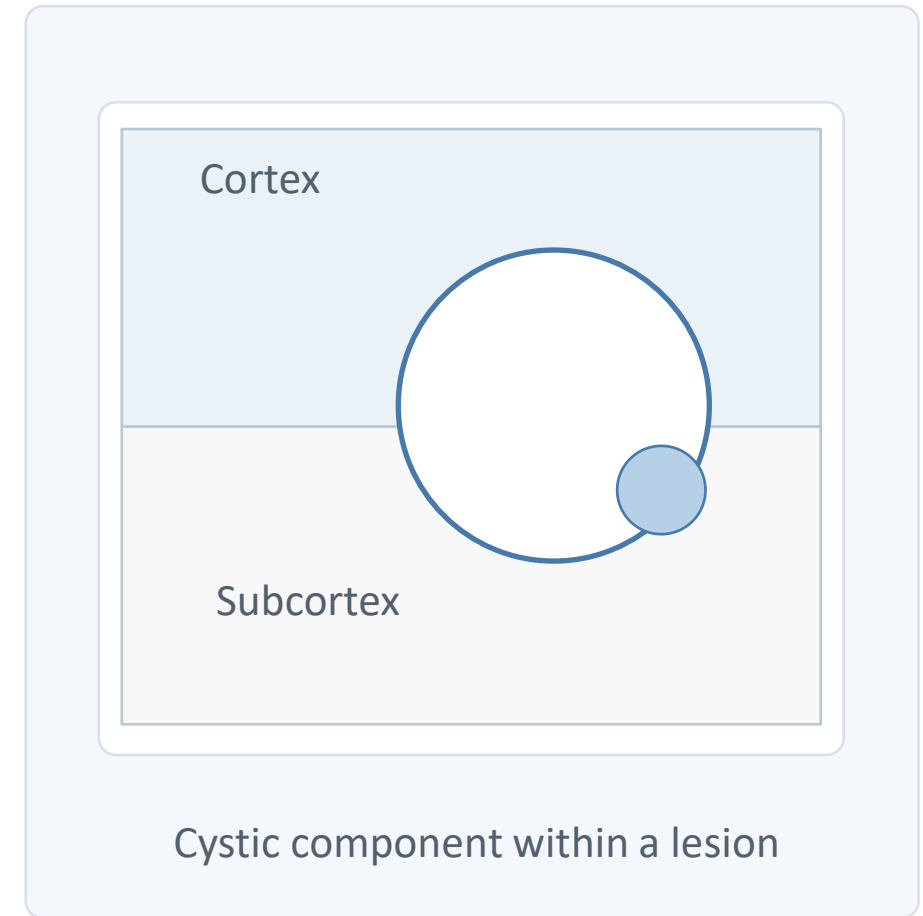
Superficial growth pattern

- Gangliogliomas are typically superficial.
- A lesion near cortex can be evaluated in an epilepsy-directed work-up.
- Assess the neuron–glia relationship in the tissue sample.



Cystic components in ganglioglioma

- A cystic component is frequently present.
- This is an anatomic feature, not the defining microscopic criterion.
- The diagnosis still requires evaluation of the neuronal and glial cells.



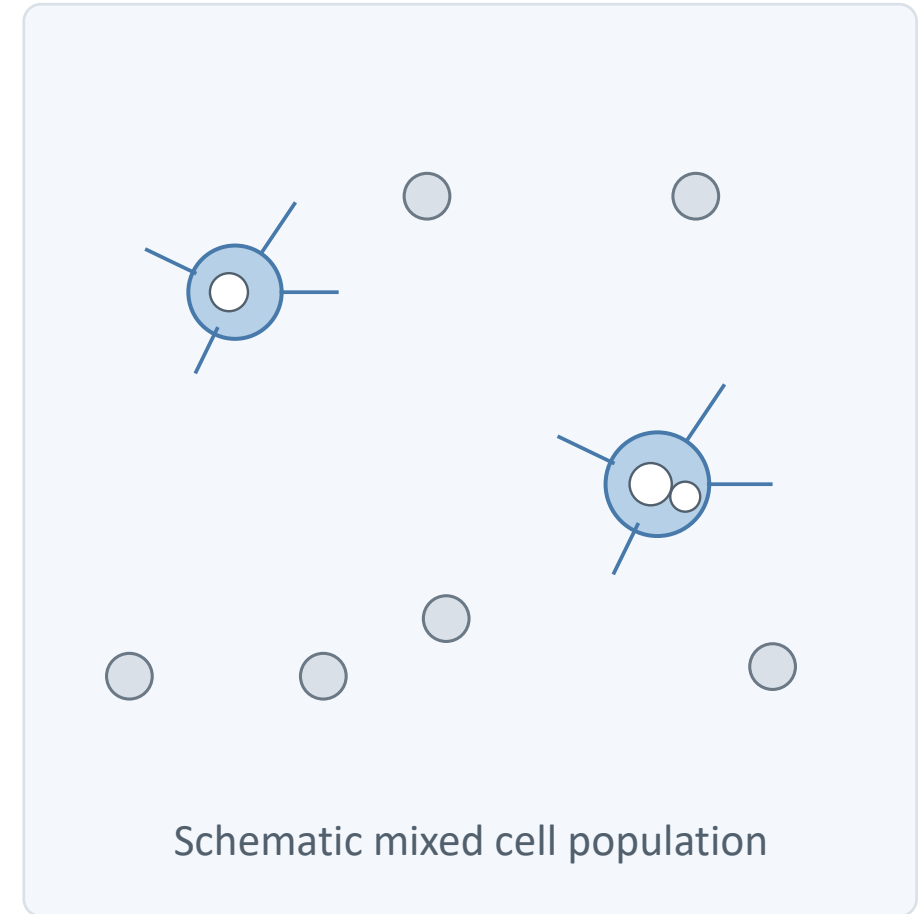
Slow growth and symptom burden

- Most gangliogliomas grow slowly.
- Nevertheless, their seizure burden can be substantial.
- Clinical impact is not determined by proliferative tempo alone.

A slow-growing cortical tumor may still motivate surgery because of epilepsy.

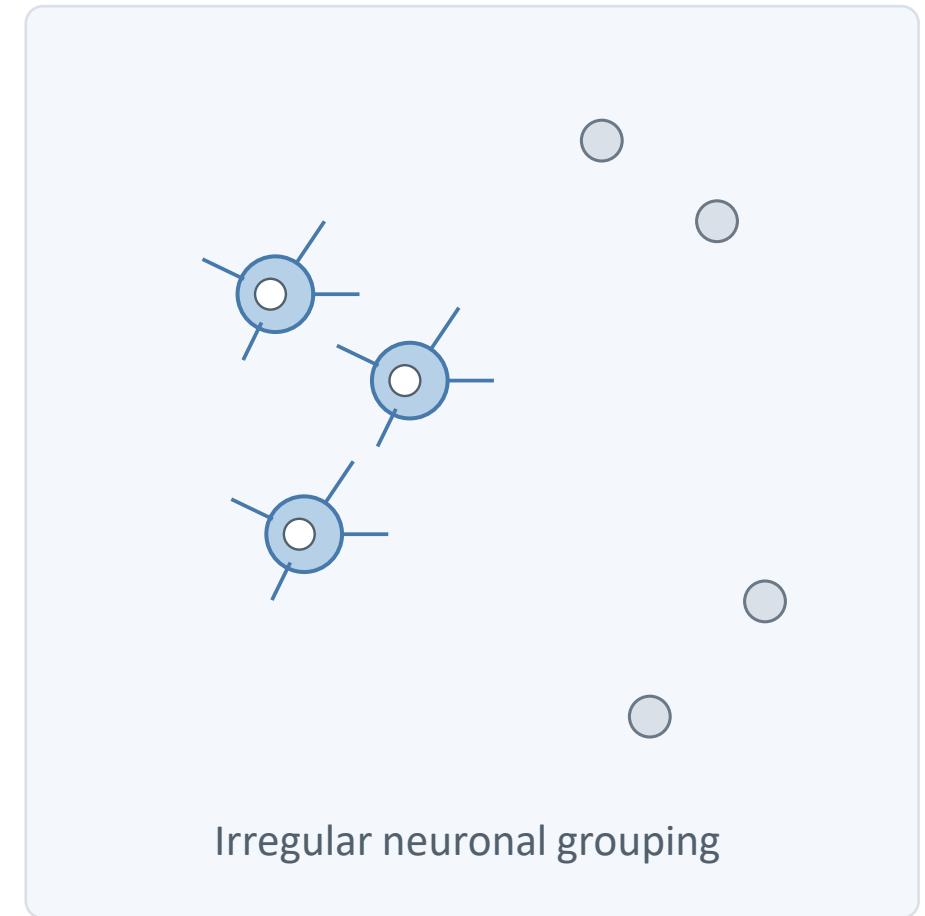
Recognizing neoplastic ganglion cells

- Ganglion cells appear atypically clustered in the lesion.
- Cellular dysmorphism supports the neuronal component.
- Aberrant orientation of neuronal processes is another feature noted by Robbins.



Irregular neuronal clustering

- Normal cortical neurons are arranged in an ordered tissue context.
- Ganglioglioma neurons may form irregular clusters.
- Read the clustering alongside cytologic dysmorphism and the associated glial component.



Dysmorphic neuronal forms

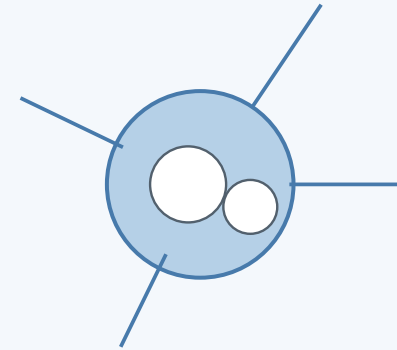
- Some neoplastic neurons have conspicuously abnormal shapes.
- Dysmorphism is a feature of the neuronal population.
- Its significance rests on the overall lesion pattern.



Variation in neuronal form

Binucleate ganglion cells

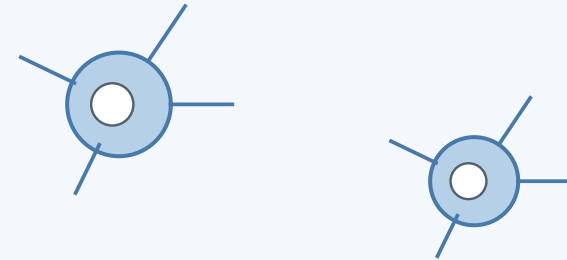
- Binucleate neuronal forms are specifically described in ganglioglioma.
- These coexist with other dysmorphic neuronal forms.
- No single cytologic feature should substitute for an integrated interpretation.



Illustrative binucleate neuron

Random orientation of neuronal processes

- Neuronal processes can show disordered directionality.
- The finding contrasts with the expected organization of surrounding parenchyma.
- Interpret process orientation together with cell distribution and glial morphology.



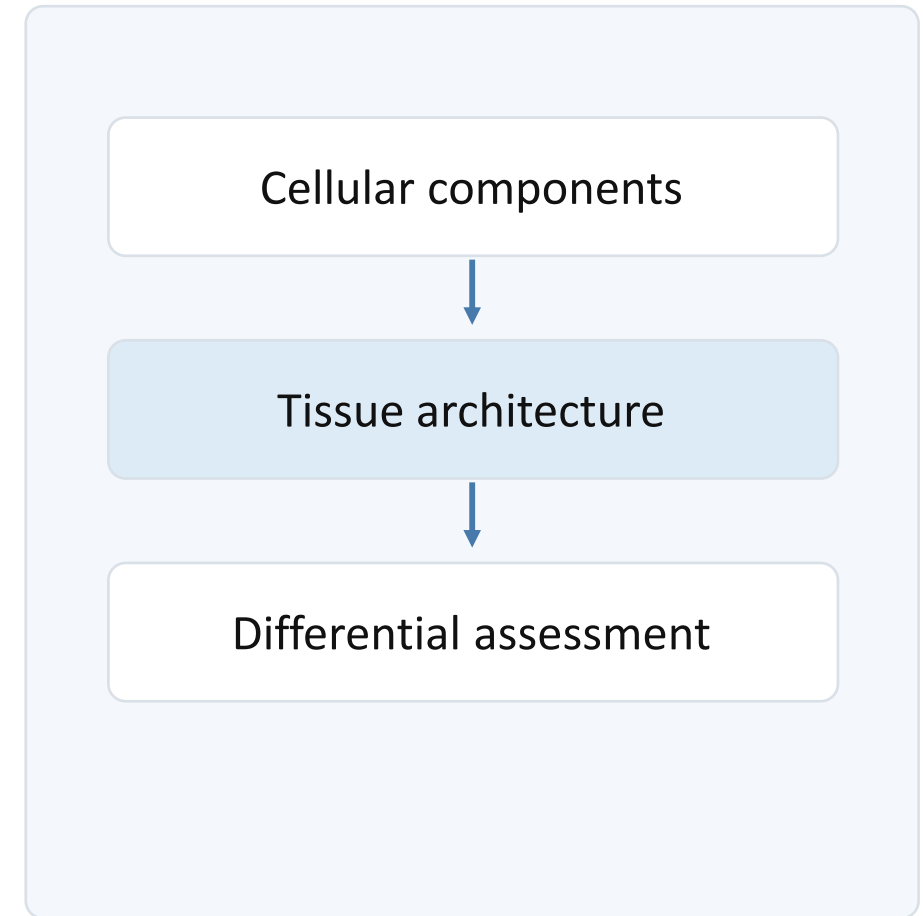
Disordered process directions

The glial component often looks pilocytic

Ganglioglioma: Glial component	Pilocytic astrocytoma: Nearby context
Frequently pilocytic-like in morphology	Fibrillary, bipolar “hairlike” astrocytic cells
Intermixed with abnormal neurons	Distinct circumscribed astrocytic tumor
Dual differentiation is decisive	Typical biphasic pattern, Rosenthal fibers / granular bodies

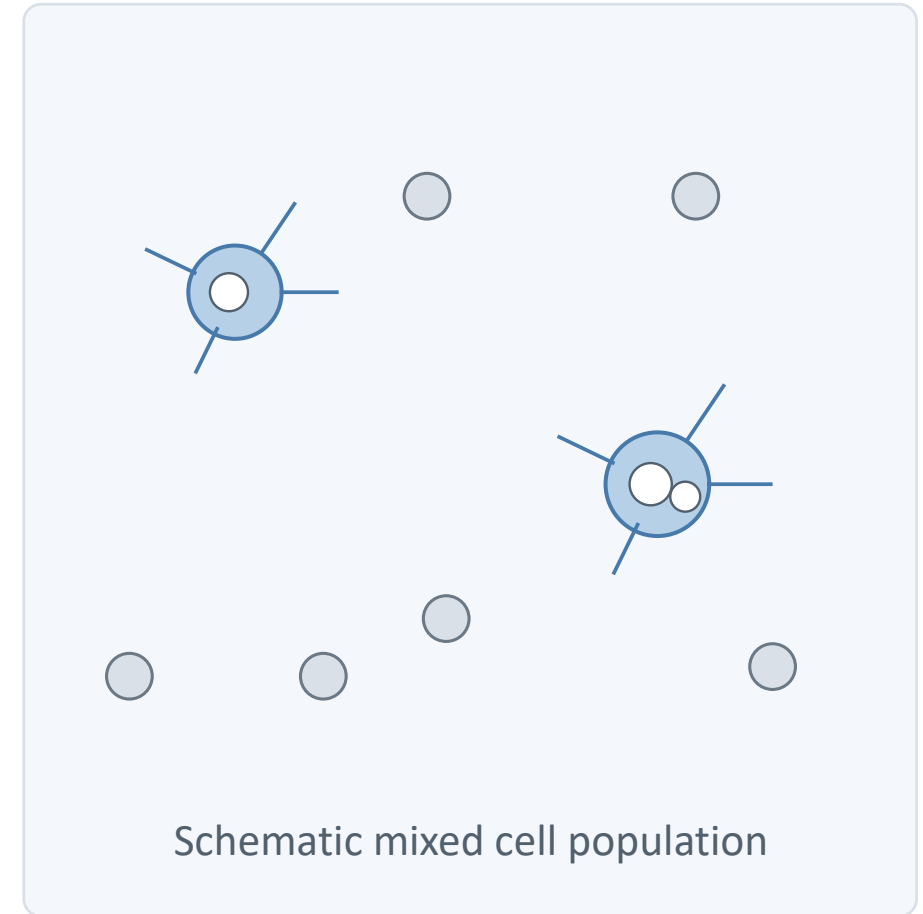
Why “pilocytic-like” does not equal pilocytic astrocytoma

- Similar-looking glial tissue can appear in both settings.
- Ganglioglioma diagnosis requires attention to the neuronal population.
- A specimen that samples only one compartment can limit confidence.



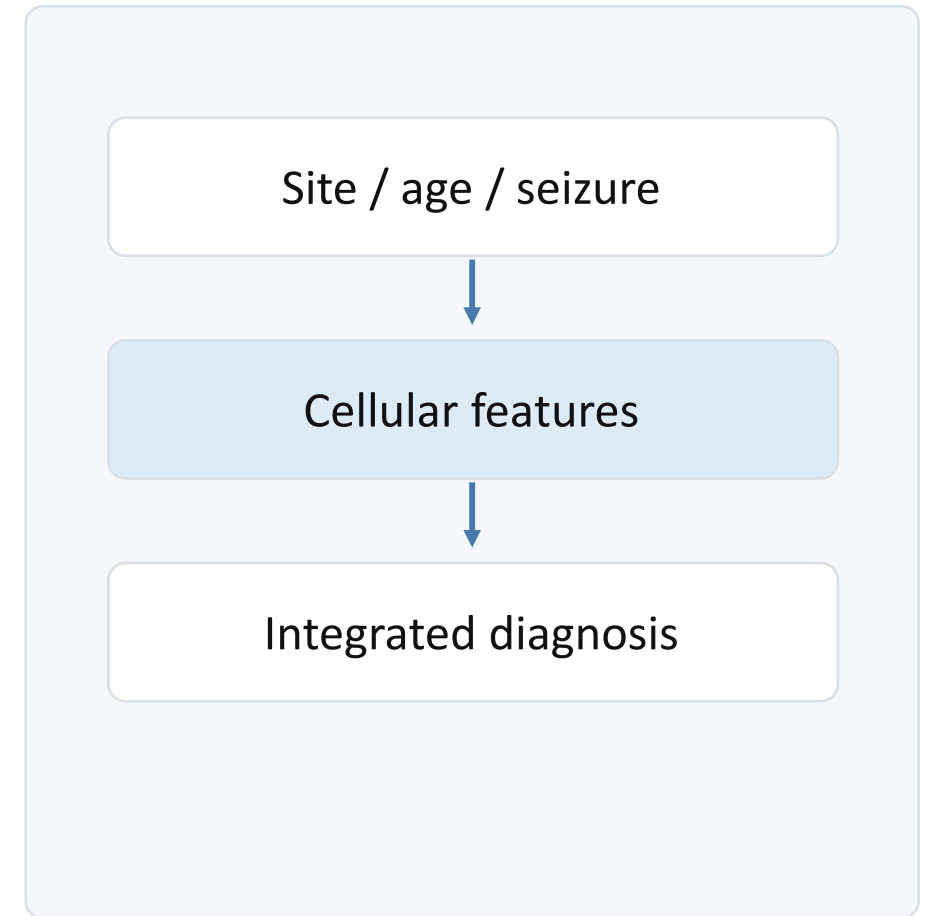
The mixed morphology in one field

- Large abnormal neurons appear amid a smaller glial population.
- Irregular distribution matters as much as individual cell appearance.
- This diagram is a simplified model, not an H&E micrograph.



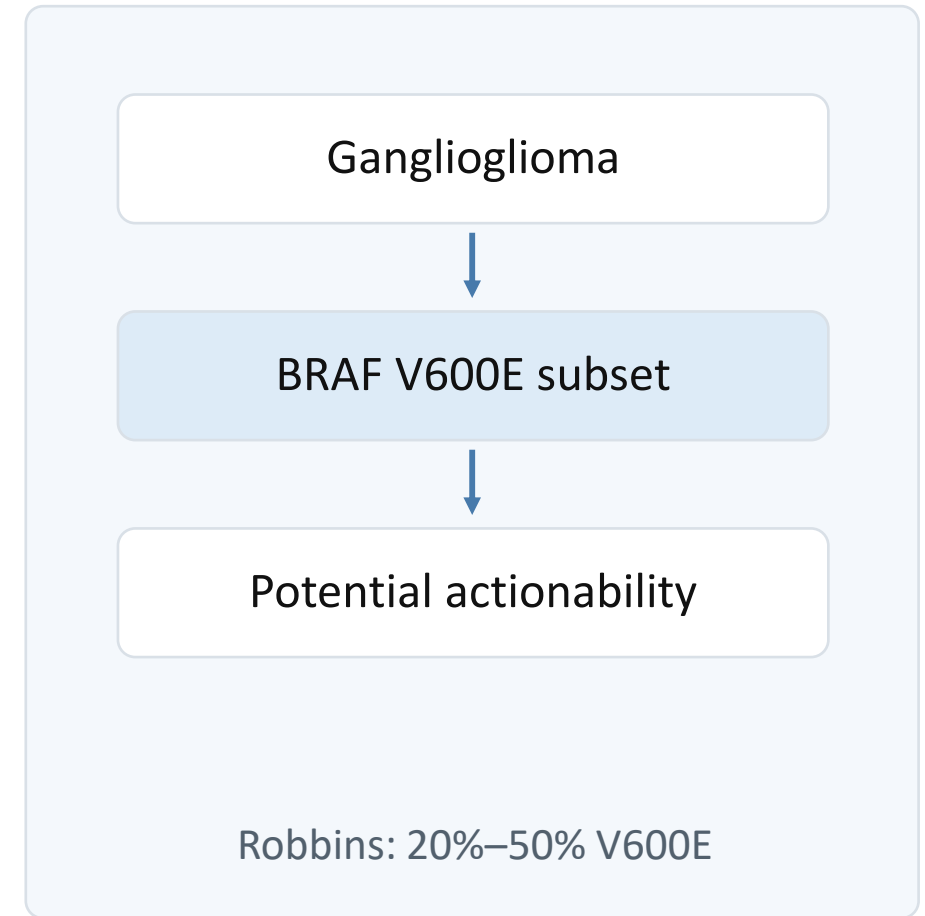
A practical ganglioglioma morphology checklist

- Look for abnormal mature-appearing ganglion cells.
- Examine clustering and orientation of neuronal processes.
- Assess dysmorphic and binucleate forms.
- Characterize the accompanying glial component.



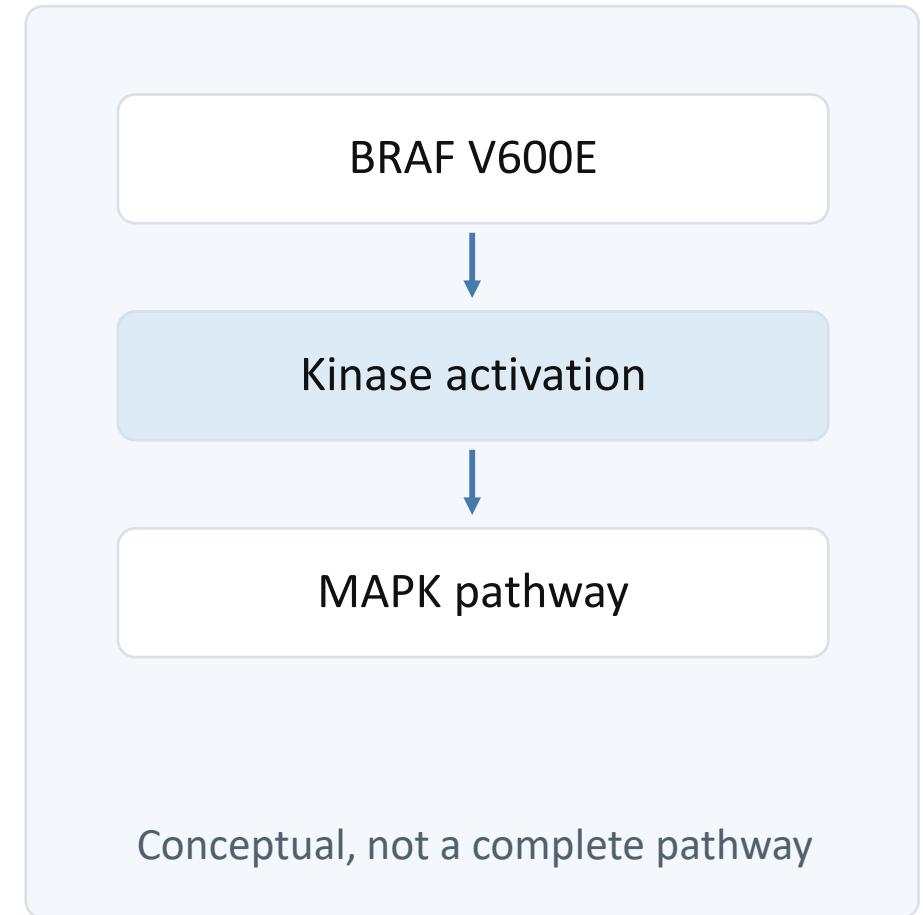
BRAF V600E occurs in a subset

- An activating BRAF V600E mutation in approximately 20%–50% of gangliogliomas.
- A negative result does not exclude the entity.
- This is a molecular feature in a fraction of tumors, not a universal defining lesion.



An activating BRAF alteration: Conceptual significance

- BRAF is a signal-transduction kinase.
- The V600E alteration is an activating mutation.
- Molecular results complement histomorphology rather than replacing it.

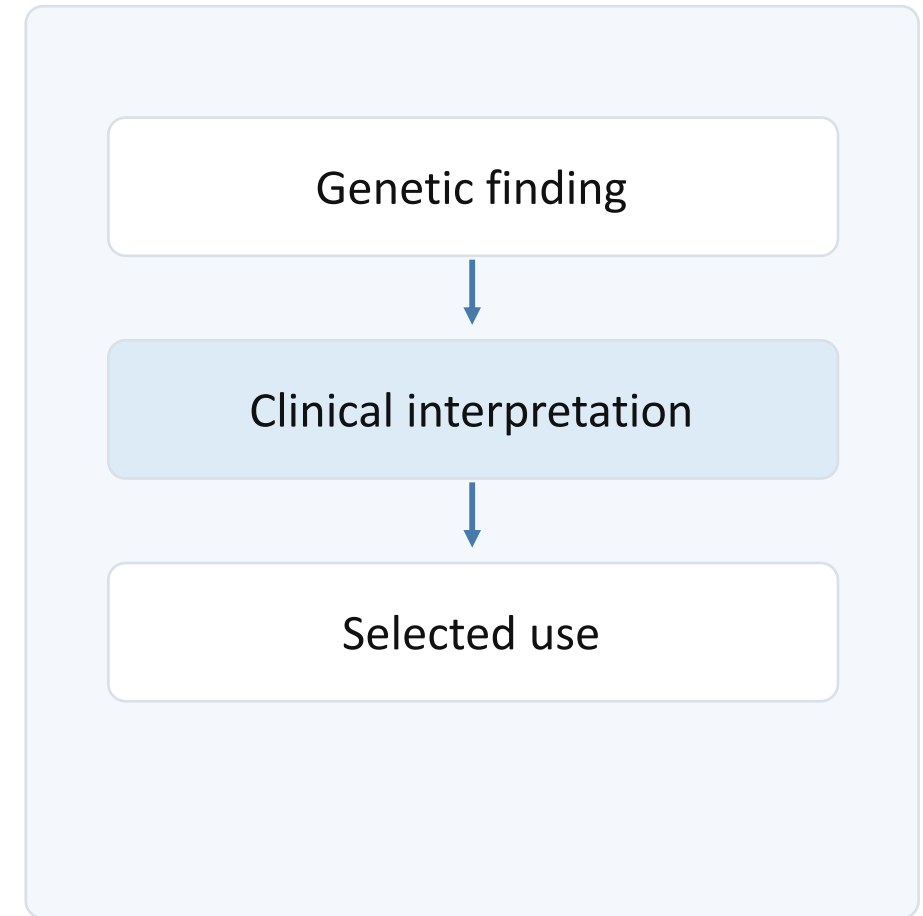


When molecular information is clinically relevant

- Identify whether the tumor has a therapeutically relevant molecular alteration.
- Keep diagnostic classification distinct from an actionable therapeutic finding.
- Use the integrated diagnosis and clinical context when interpreting a result.

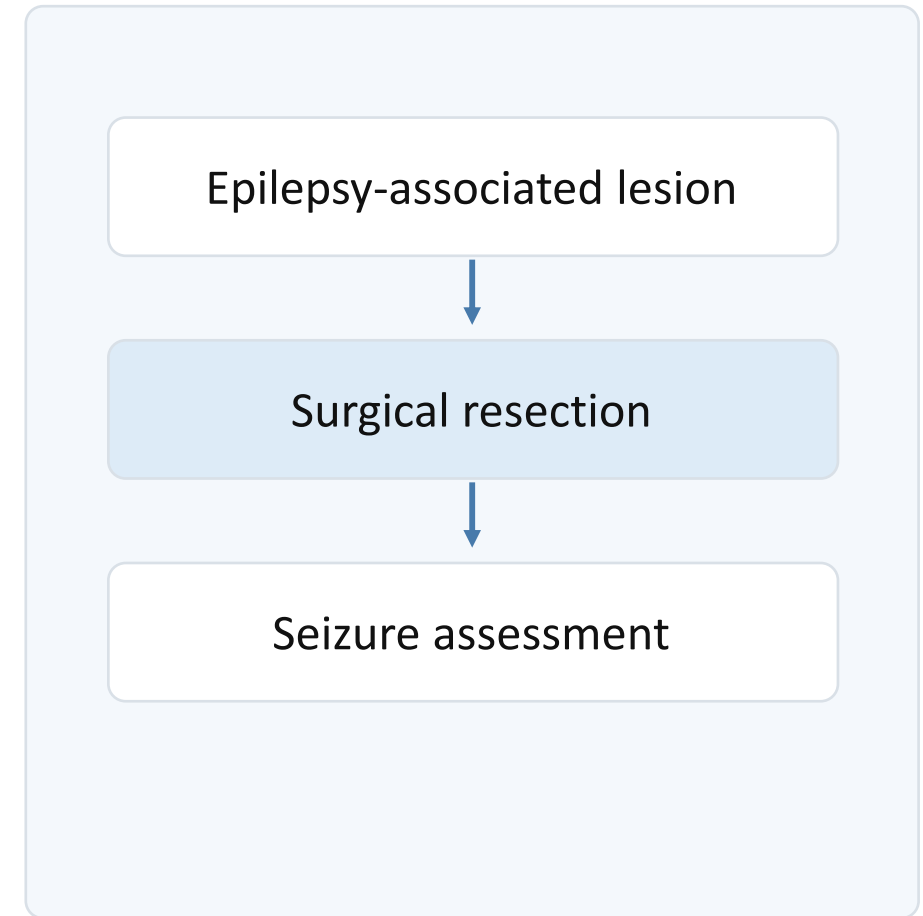
Targeted therapy is a selected use of BRAF status

- BRAF V600E occasionally provides a basis for targeted therapy.
- This does not imply that every ganglioglioma needs targeted treatment.
- The source excerpt does not establish a universal treatment algorithm or drug regimen.



Resection and epilepsy control

- For medically refractory epilepsy, surgery is frequently effective in controlling seizures.
- This reflects a clinically important consequence of treating the lesion.
- Individual outcomes should not be inferred from the general source statement.



Ganglioglioma: Clinicopathologic signature

Clinical clue	Tissue discriminator
Young person with epilepsy	Mixed neuronal + glial tumor
Temporal / superficial location	Irregular neuronal clusters
Often a cystic component	Dysmorphic or binucleate neurons
Usually slow growth	Glia often pilocytic-like

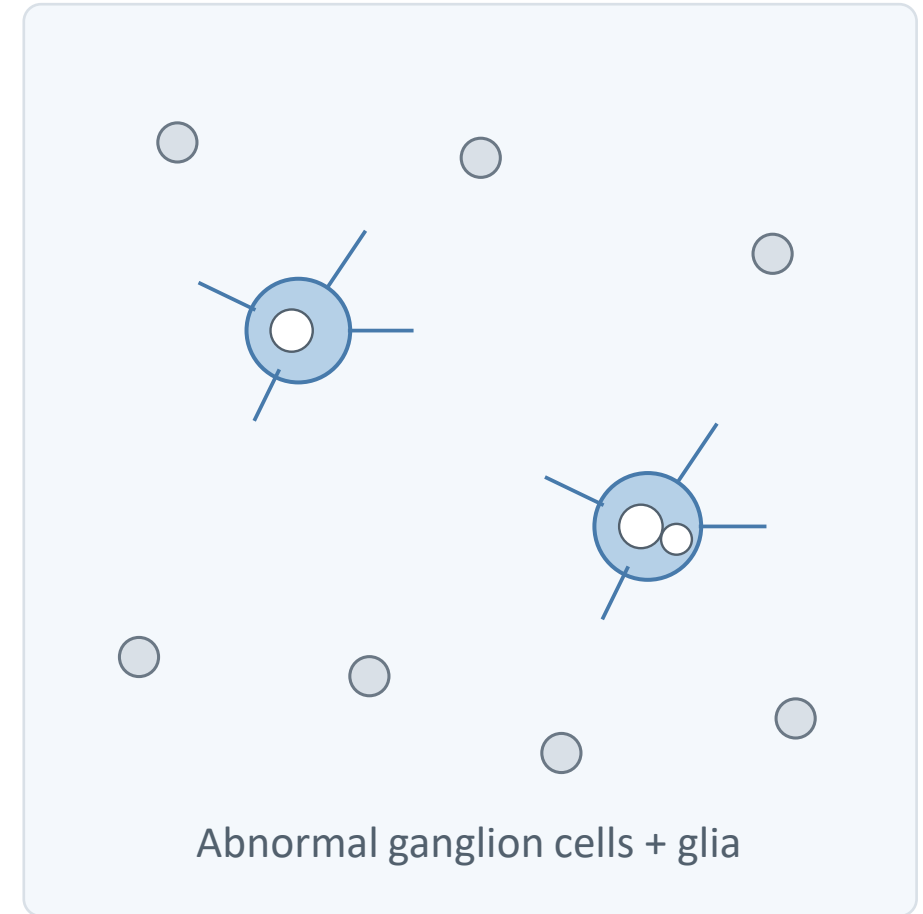
Case 1: Seizure-associated superficial temporal lesion

- Illustrative case: A young adult has medically refractory seizures and a superficial temporal lesion.
- Resection shows mature-appearing neurons in irregular clusters mixed with glial cells.
- Several abnormal neurons are binucleate.

What diagnosis best explains the combined pattern?

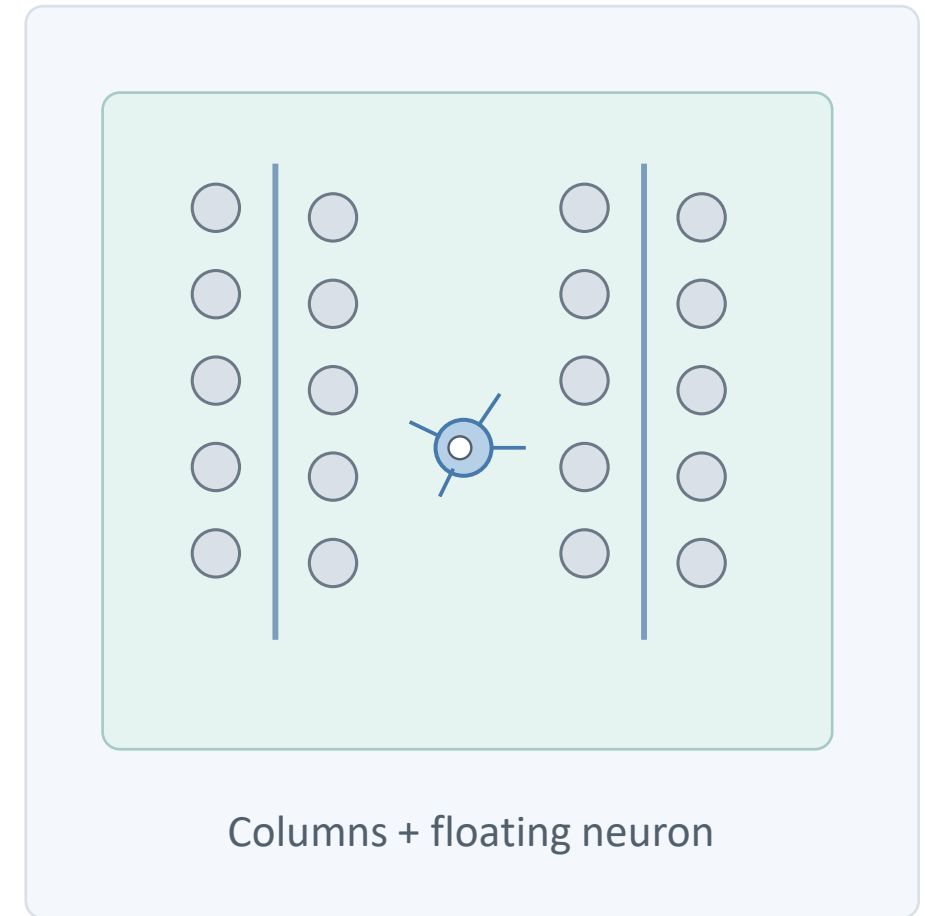
Case 1: Resolving the evidence

- Ganglioglioma is supported by the combined neuronal and glial populations.
- Irregularly clustered, dysmorphic / binucleate neurons are defining clues.
- Clinical site and seizure association strengthen the fit but do not prove the diagnosis.



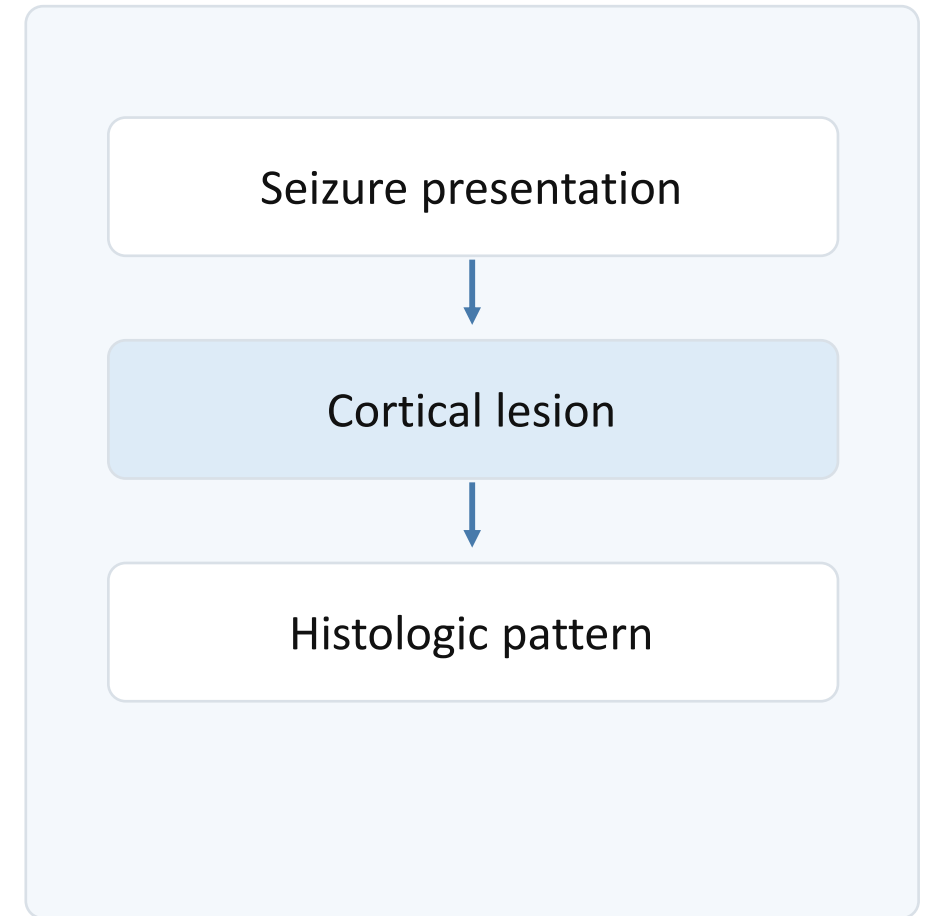
DNET: The essential concept

- Dysembryoplastic neuroepithelial tumor is a rare, benign CNS WHO grade 1 lesion.
- It is strongly linked clinically with epilepsy.
- Its characteristic finding is a glioneuronal architecture in a mucin-rich cortical tumor.



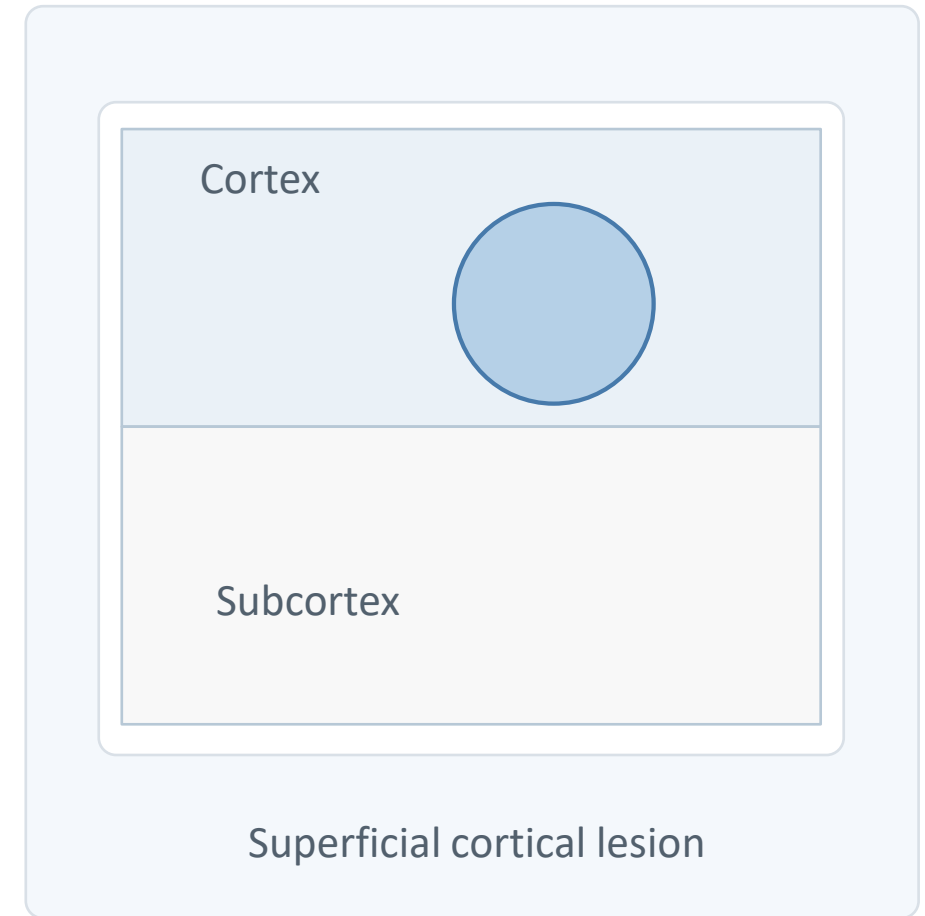
An epilepsy-associated low-grade cortical tumor

- DNET is frequently identified in patients with seizures.
- Good prognosis after surgical resection.
- The combination of seizure presentation and characteristic tissue architecture is diagnostically useful.



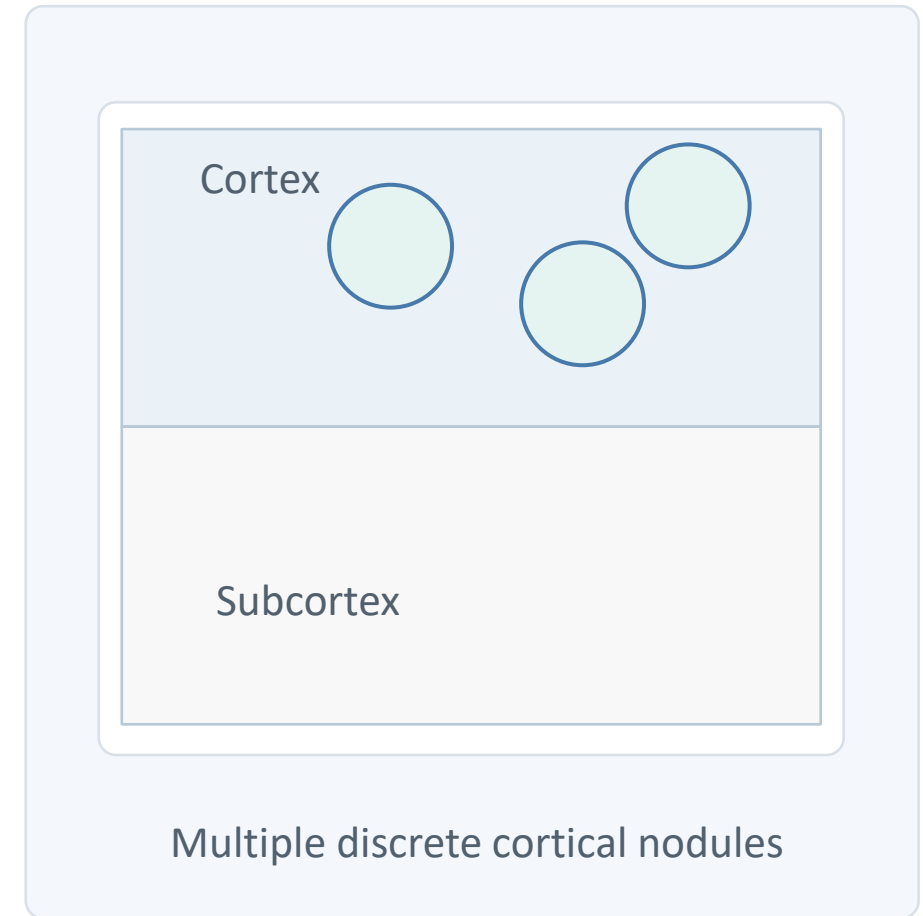
DNET most often arises in superficial temporal cortex

- The usual site is the superficial temporal lobe.
- Other locations can occur.
- A superficial cortical site supports, but does not establish, the diagnosis.



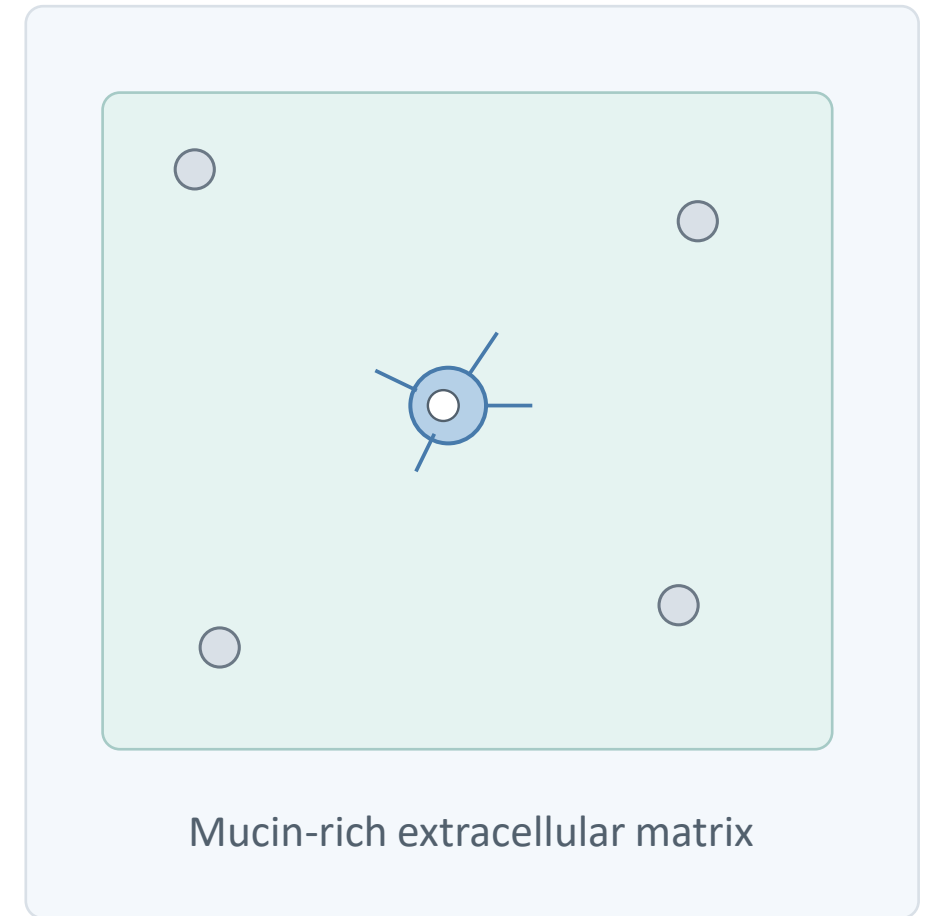
Multiple discrete intracortical nodules

- DNET typically consists of multiple discrete nodules.
- The nodules are located within cortex.
- This low-power organization is important before examining individual cells.



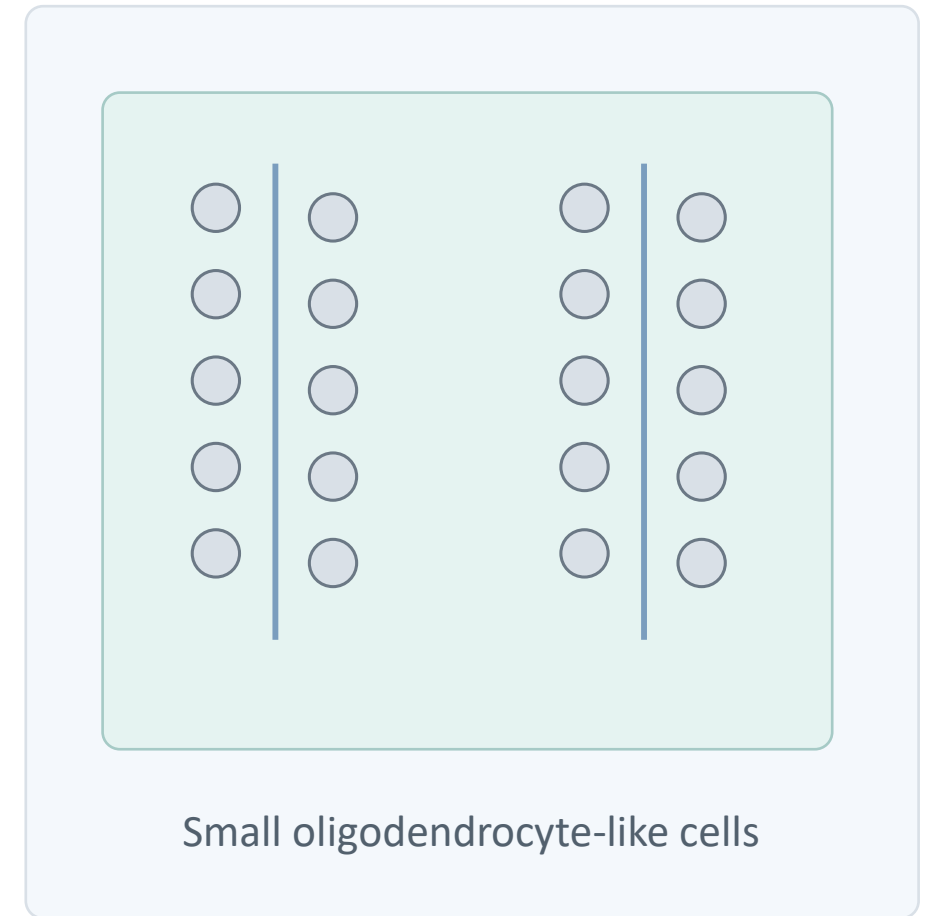
The nodules have a mucin-rich matrix

- The tumor is characterized by abundant mucin-rich areas.
- Basophilic mucin-rich pools.
- The matrix forms the setting for the characteristic “floating neurons.”



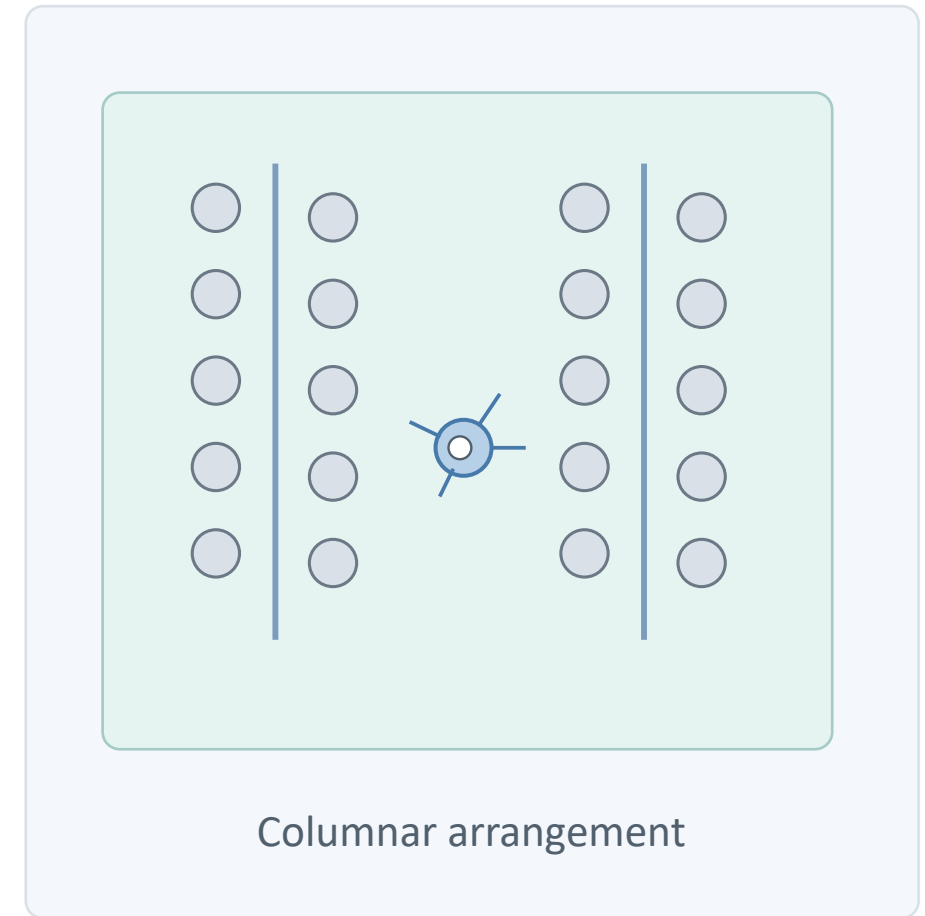
Small oligodendrocyte-like cells

- A small, round-cell population has oligodendrocyte-like appearance.
- These cells participate in the special glioneuronal architectural arrangement.
- Cell appearance alone should not lead to an oligodendroglioma diagnosis.



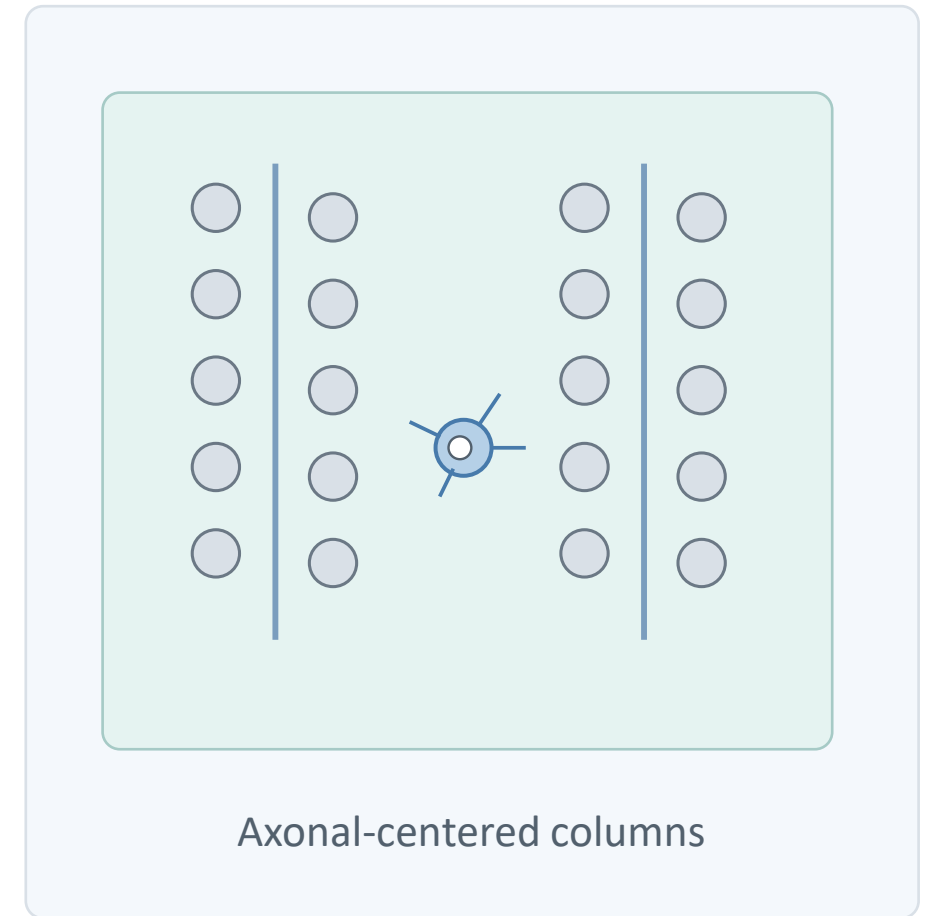
Columns of small cells are a key architectural clue

- Oligodendrocyte-like cells form columns.
- The columns organize around central axonal bundles or capillaries.
- The low-power columnar pattern is integral to recognizing DNET.



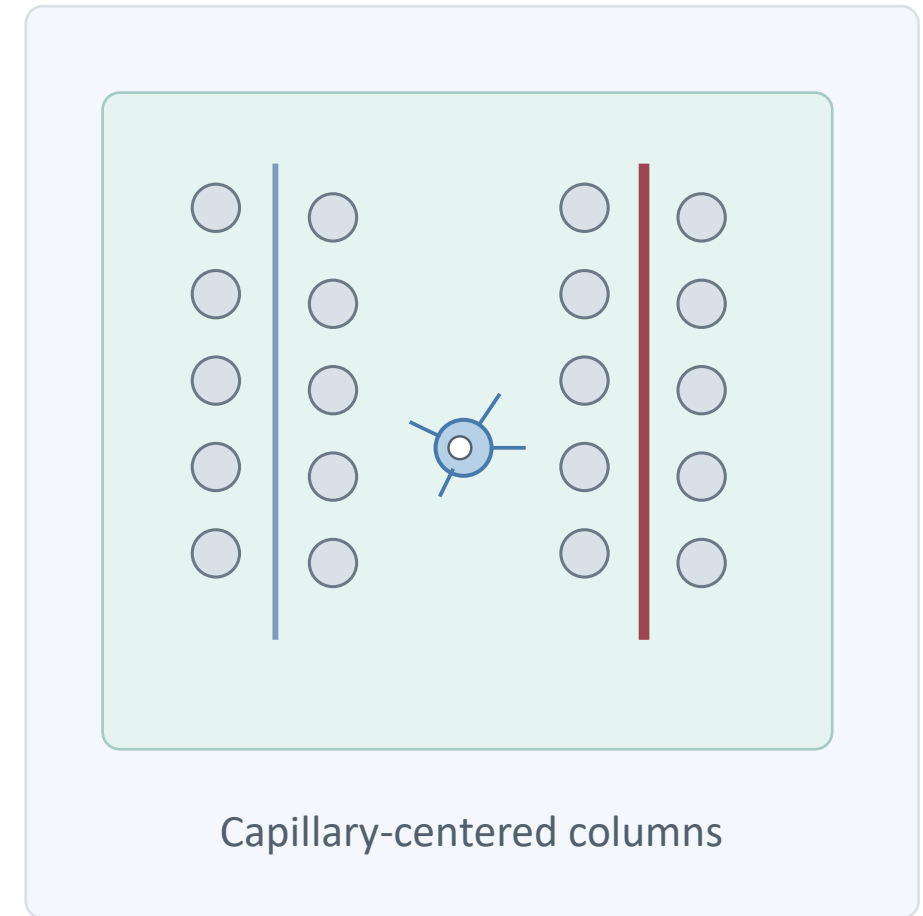
Axonal bundles may form the column centers

- A central axonal bundle may provide the axis of a column.
- Small oligodendrocyte-like cells flank the bundle.
- The relationship is architectural and must be interpreted on histologic tissue.



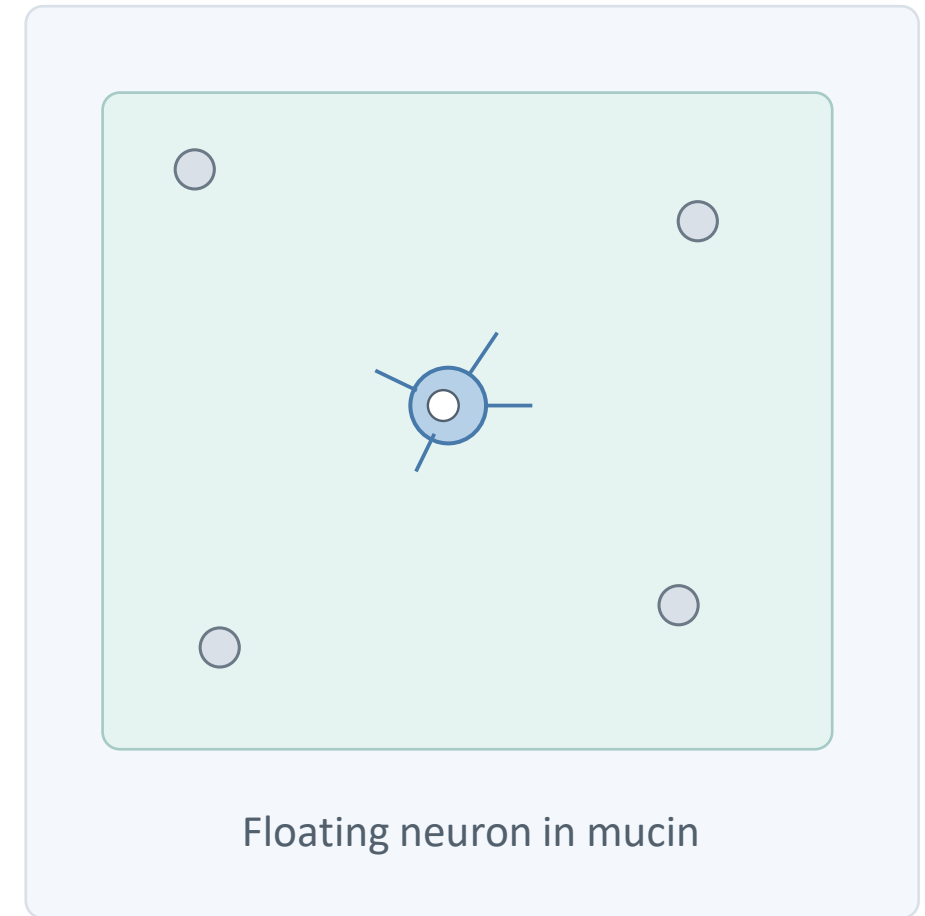
Capillaries are an alternative column center

- Robbins also describes columns around capillaries.
- The columnar arrangement is not restricted to axonal bundles.
- Compare multiple tumor fields to understand the pattern.



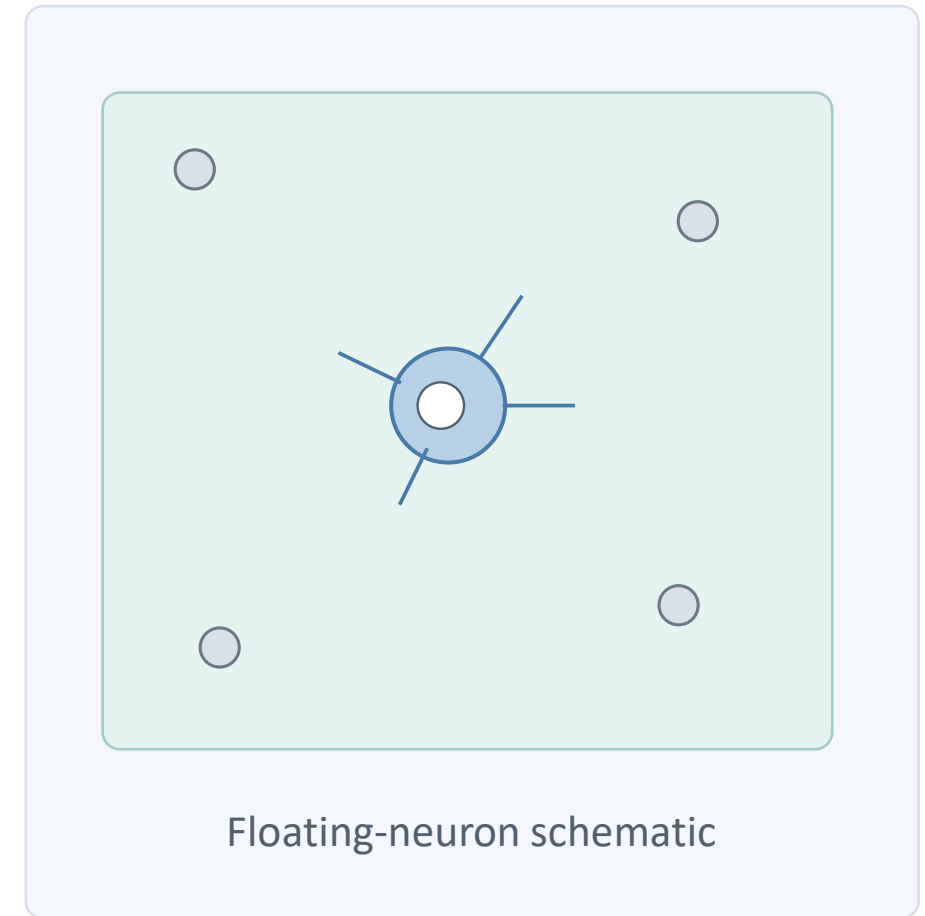
Floating neurons in mucin-rich pools

- Neurons appear suspended within the basophilic mucinous matrix.
- This is the “floating neuron” appearance.
- It is a major diagnostic clue when paired with the other DNET architectural features.



Why the floating-neuron pattern is distinctive

- The neuron is within a pale, mucin-rich space rather than a dense cellular cluster.
- The surrounding small cells and columnar elements provide architectural context.
- Do not interpret one isolated neuron without assessing the entire lesion.

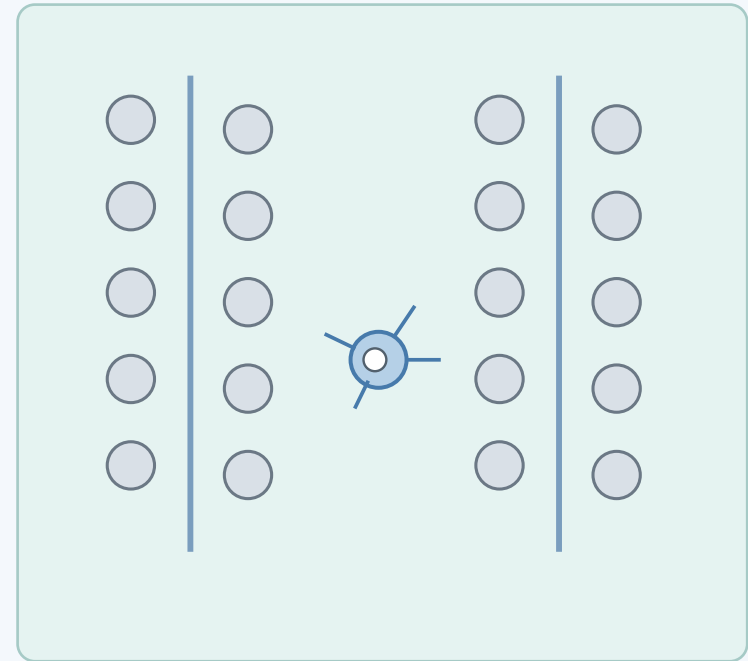


DNET at low and higher conceptual magnification

Low-power question	Higher-power question
Are there discrete intracortical nodules?	Are oligodendrocyte-like cells present?
Is the material mucin-rich?	Do small cells form columns?
Where are the nodules distributed?	Are floating neurons present?

Combining the DNET diagnostic features

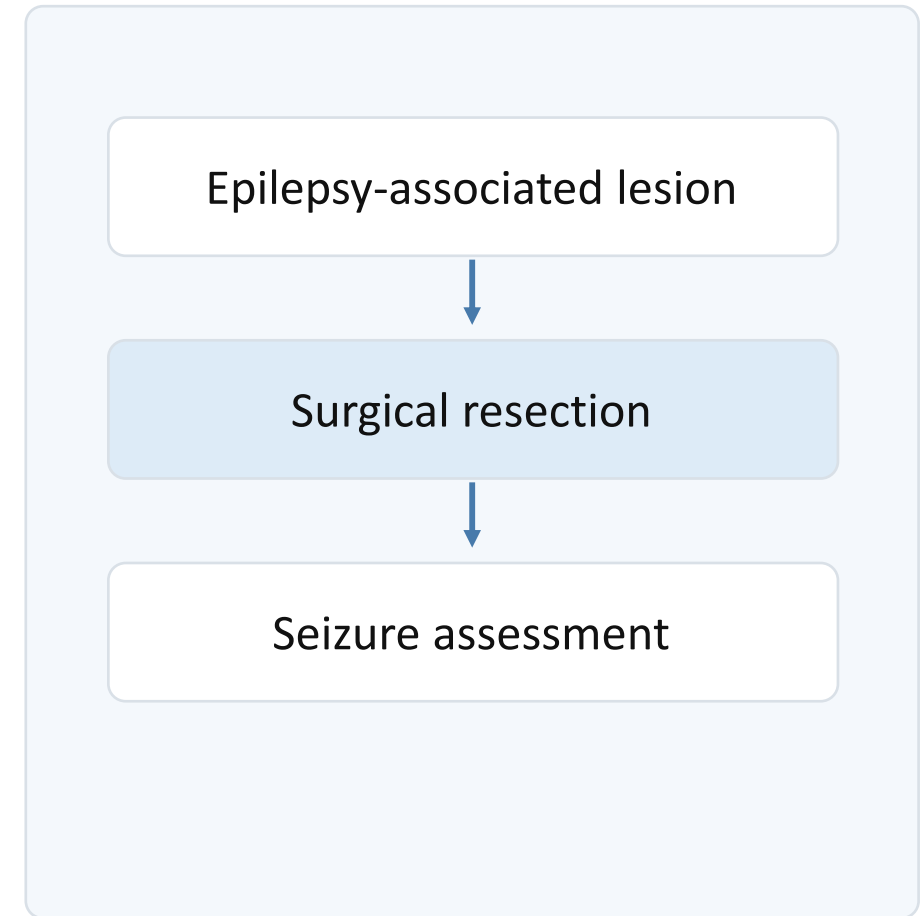
- Intracortical, discrete mucin-rich nodules.
- Oligodendrocyte-like cells in columns around axonal bundles / capillaries.
- Floating neurons within basophilic mucinous pools.



Integrated specific glioneuronal pattern

DNET behavior after resection

- Low recurrence rates.
- Seizure control is generally favorable after surgical removal.
- The grade 1 assignment is consistent with the favorable overall course described.



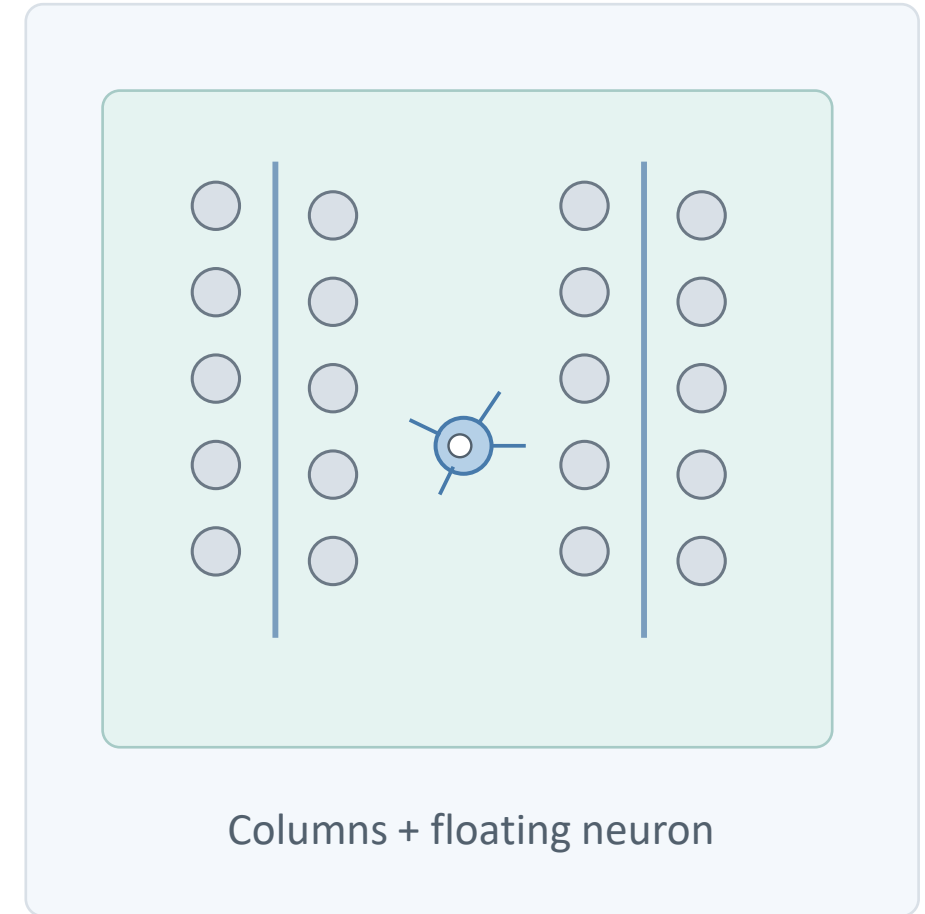
Case 2: Cortical lesion with mucin and floating neurons

- Illustrative case: Epilepsy in a young patient with a superficial temporal cortical lesion.
- The specimen has multiple mucin-rich nodules.
- Small cells form columns around central structures; Neurons appear suspended in mucin.

Which entity fits the architecture best?

Case 2: Interpreting the pattern

- DNET is favored by the combination of cortical nodules, columnar oligodendrocyte-like cells and floating neurons.
- The site and epilepsy are compatible.
- The diagnosis is supported by the integrated architecture rather than by mucin alone.



Ganglioglioma versus DNET: Primary discriminators

Ganglioglioma	DNET
Mixed ganglion + glial cells	Intracortical, mucin-rich nodules
Dysmorphic / binucleate neurons	“Floating” neurons
Irregular neuronal clustering	Oligodendrocyte-like cells in columns
Glia often resemble pilocytic astrocytoma	Columns centered on axons or capillaries

Shared features must not collapse two diagnoses

What both can share	What separates them
Temporal / superficial association	Distinct cellular / architectural patterns
Epilepsy in young patients	Ganglion-cell dysmorphism vs floating neurons
CNS WHO grade 1	Mixed tumor vs specific mucin-rich nodules
Potential benefit from resection	Histology remains indispensable

Molecular context: BRAF and FGFR1

Ganglioglioma	DNET
BRAF V600E in ~20%–50% (Robbins)	FGFR1 alterations (WHO CNS5 / EANO)
Activation may occasionally inform targeted therapy	Molecular adjunct to DNET classification
Mutation absence does not erase morphology	Do not substitute a single marker for histology

Molecular profiling: What a result can and cannot do

- A molecular result can support classification in the appropriate morphology.
- Ganglioglioma may carry BRAF / MAPK pathway changes (EANO).
- DNET is associated with FGFR1 alterations (EANO).
- No molecular result should be treated as isolated proof without integrated evaluation.

Differential: Glial tumor with pilocytic morphology

Pilocytic astrocytoma	Ganglioglioma
Circumscribed astrocytic tumor	Neuronal–glial tumor
Often biphasic microcystic / compact architecture	Neoplastic dysmorphic ganglion cells present
Rosenthal fibers and eosinophilic granular bodies	Glial tissue can itself look pilocytic

Differential: Small round cells are not sufficient

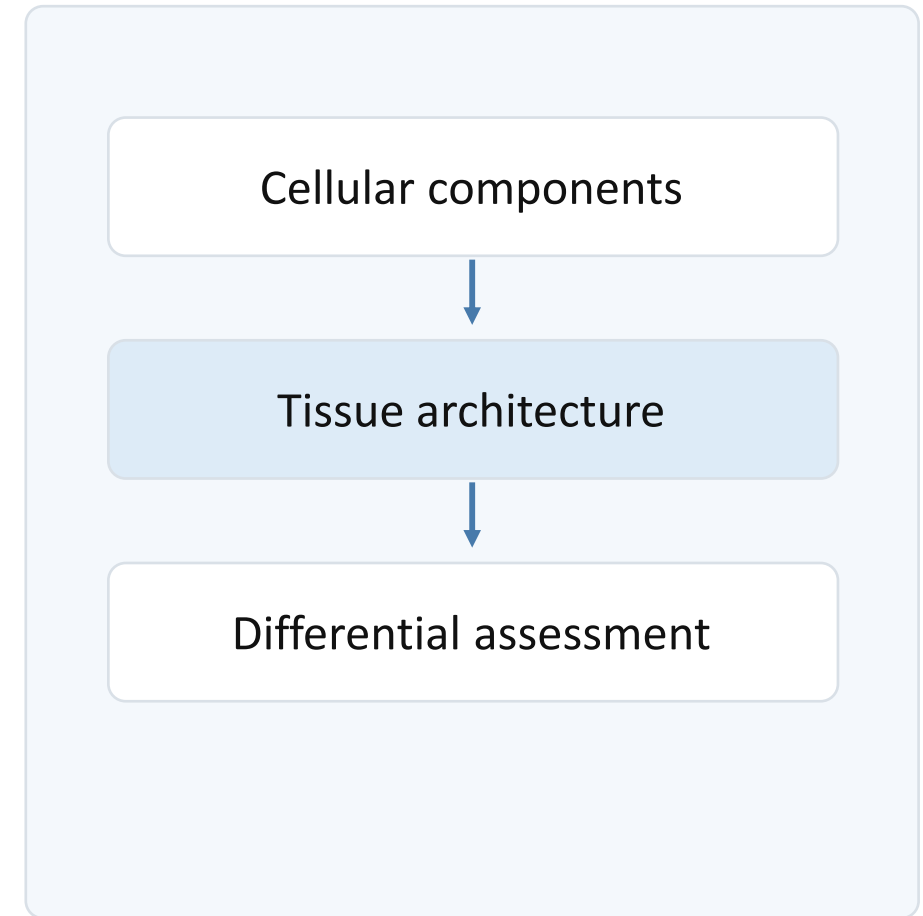
DNET	Oligodendroglioma, IDH-mutant / 1p19q-codeleted
Oligodendrocyte-like cells in columns	Typically uniform clear-halo cells; Infiltrative glioma
Mucin-rich nodules with floating neurons	Characteristic delicate branching capillary network
CNS WHO grade 1	Requires IDH alteration and whole-arm 1p/19q codeletion

Differential: Avoid confusing ependymal rosettes with DNET columns

DNET architecture	Ependymoma architecture
Mucin-rich cortical nodules	Often associated with ventricular / spinal system
Small-cell columns around axons / capillaries	Perivascular pseudorosettes with fibrillary nuclear-free zones
Floating neurons may occur	True rosettes may surround a lumen

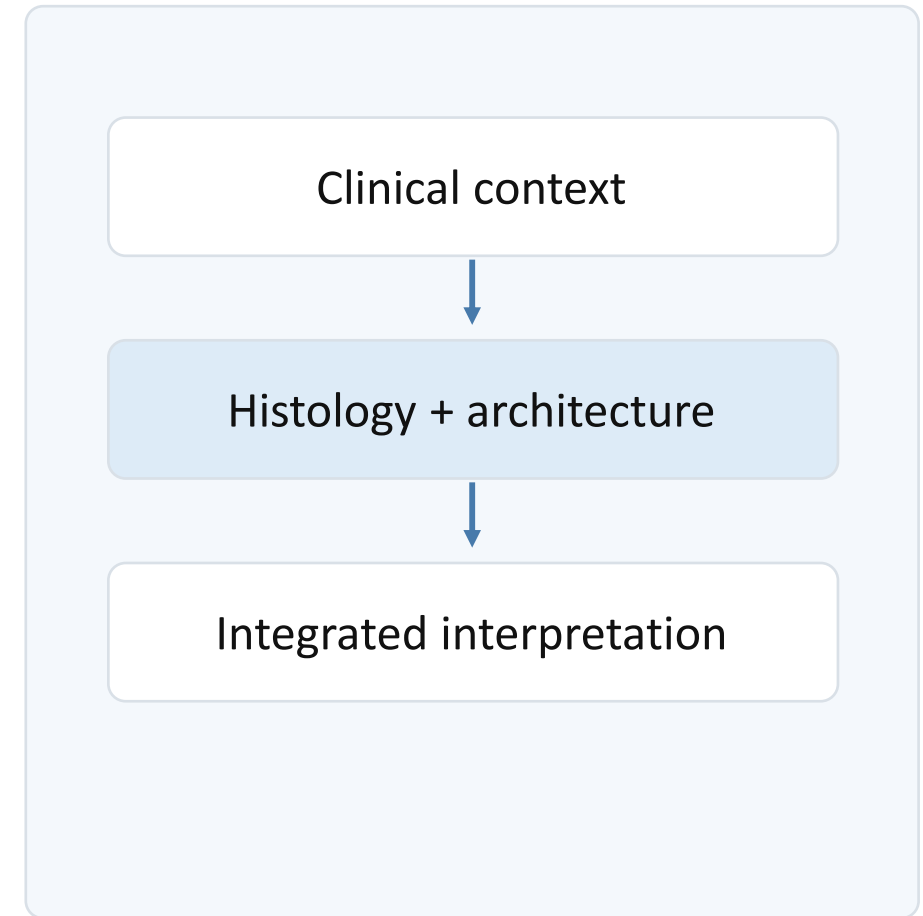
Diagnostic sampling: Seek the defining compartment

- For suspected ganglioglioma, identify abnormal neuronal cells as well as the glial component.
- For suspected DNET, assess low-power nodules and the specific glioneuronal element.
- The decision should integrate clinical, anatomic, microscopic and selective molecular findings.



Pattern-based diagnostic synthesis

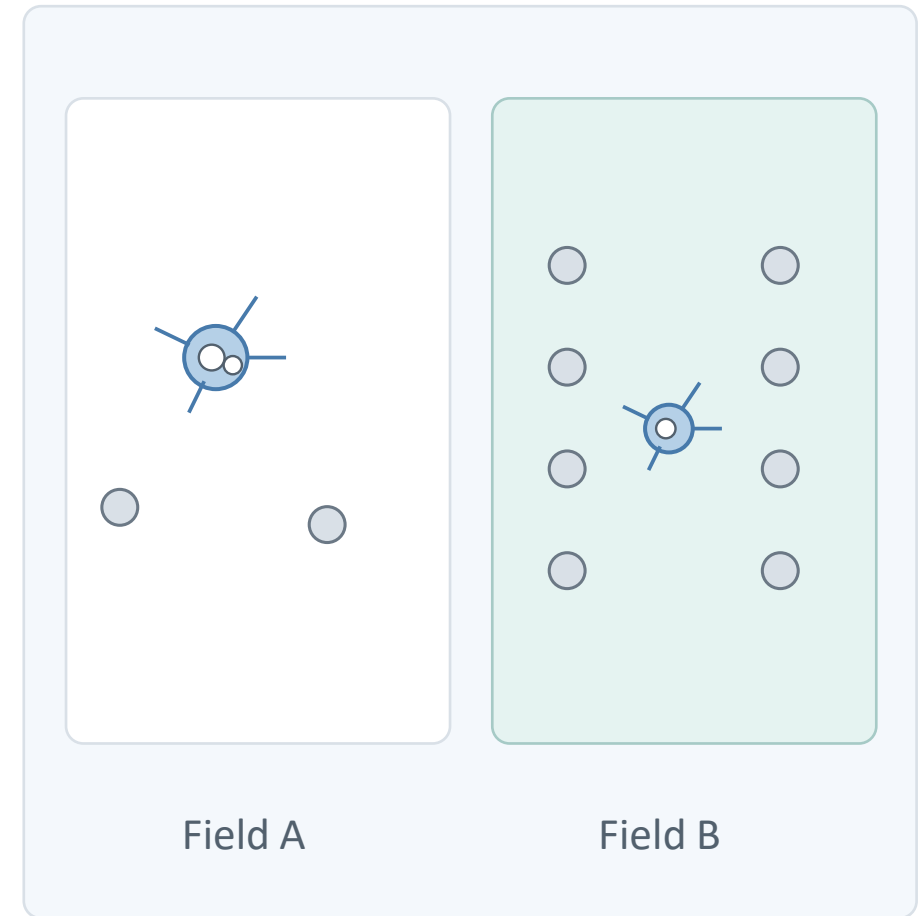
- Start with cortical location and seizure-associated clinical context.
- Ask whether the dominant signature is dysmorphic ganglion cells plus glia, or mucin-rich nodules with floating neurons.
- Consider relevant glial/ependymal mimics if the expected architecture is missing.



Morphology challenge: Two schematic fields

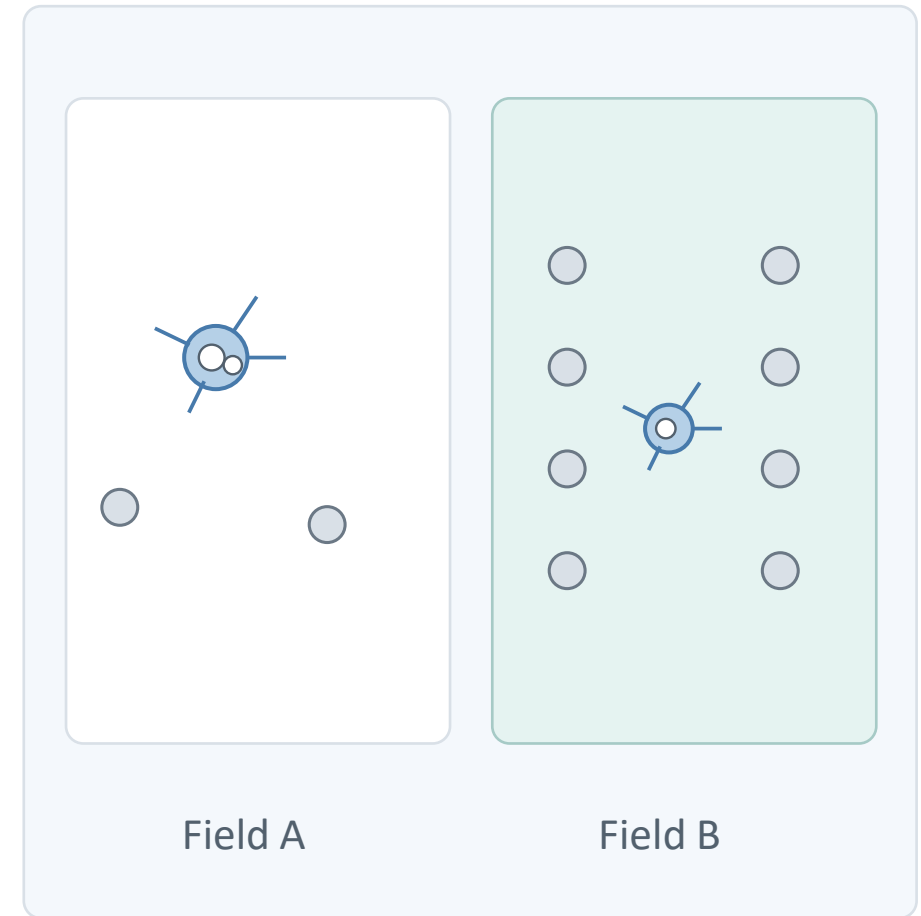
- Field A: Irregularly clustered, enlarged abnormal ganglion cells mixed with glia.
- Field B: Cortical mucin-rich nodules with columnar small cells and floating neurons.

Assign the most likely entity to field A and field B.



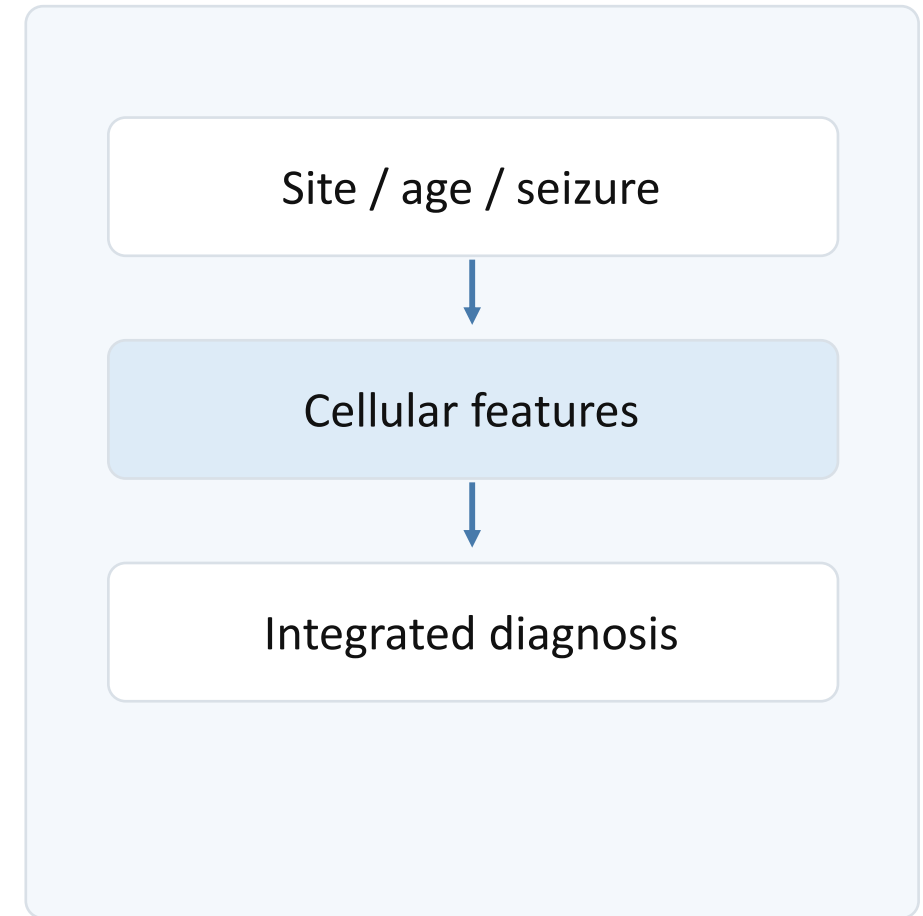
Morphology challenge: Answers

- Field A → Ganglioglioma: Abnormal mature ganglion cells with a glial component.
- Field B → DNET: Distinctive mucin-rich nodules, columnar elements and floating neurons.
- Clinical context reinforces—but does not replace—these patterns.



Five distinctions to retain

- Ganglioglioma and DNET are CNS WHO grade 1 tumors.
- Both often occur in young patients presenting with epilepsy.
- Ganglioglioma: Mixed glia plus irregular, often dysmorphic or binucleate ganglion cells.
- DNET: Mucin-rich cortical nodules, columns of small cells and floating neurons.
- BRAF V600E can have treatment relevance in some gangliogliomas; Molecular findings require context.



Selected primary and supplementary references

- Robbins, Cotran & Kumar. Pathologic Basis of Disease. 11th ed. 2026. Chapter 28, pp. 1181–1182.
- Louis DN et al. The 2021 WHO Classification of Tumors of the Central Nervous System: a summary. Neuro-Oncology. 2021.
- Sahm F et al. Molecular diagnostic tools for WHO 2021 classification: EANO guideline. Neuro-Oncology. 2023.