

Oligodendroglioma

IDH-mutant and 1p/19q-codeleted

Molecular neuropathology • morphology • grading • clinical correlation

Dr Abu Suraih Sakhri

MBBS, MD (Pathology)

www.abusuraihsakhri.com

Learning objectives

Define

- Recognize the integrated entity
- Identify its anatomic and clinical setting

Diagnose

- Explain the two required molecular findings
- Link typical architecture to pathology

Apply

- Distinguish grades 2 and 3
- Resolve astrocytic mimics with molecular results

Oligodendroglioma: The entity in one sentence

A diffusely infiltrating glioma with an IDH mutation and whole-arm 1p/19q codeletion.

- Defined by combined histologic and molecular assessment.
- Assigned CNS WHO grade 2 or 3.

Adult-type diffuse gliomas: Three molecular entities

Astrocytoma, IDH-mutant

- IDH mutation
- Often TP53 mutation and ATRX inactivation

Oligodendroglioma

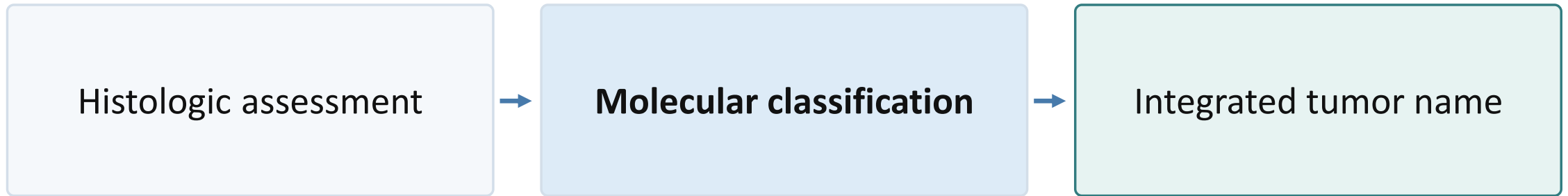
- IDH mutation
- Whole-arm 1p/19q codeletion

Glioblastoma, IDH-wildtype

- IDH-wildtype
- Common EGFR amplification, TERT alteration or +7/-10

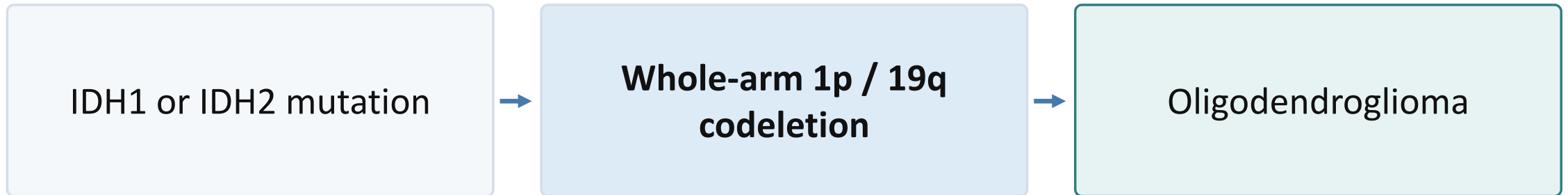
The genetic groups have different behaviors; The table is not a severity spectrum.

Integrated diagnosis requires two kinds of evidence



- Morphology establishes an infiltrating glioma phenotype.
- Genetics assigns the molecular entity; Morphology alone is insufficient.

Two indispensable molecular findings



- Both alterations are required for the named entity.
- Neither “fried eggs” nor delicate capillaries can substitute for molecular confirmation.

Histology and genetics answer different questions

Histomorphology

- What cellular architecture is present?
- Are there mitoses, anaplasia or necrosis?
- Is the process infiltrative?

Molecular profile

- Is an IDH1/IDH2 mutation present?
- Are 1p and 19q both lost as whole arms?
- Does the result support oligodendroglioma?

Frequency within the glioma family

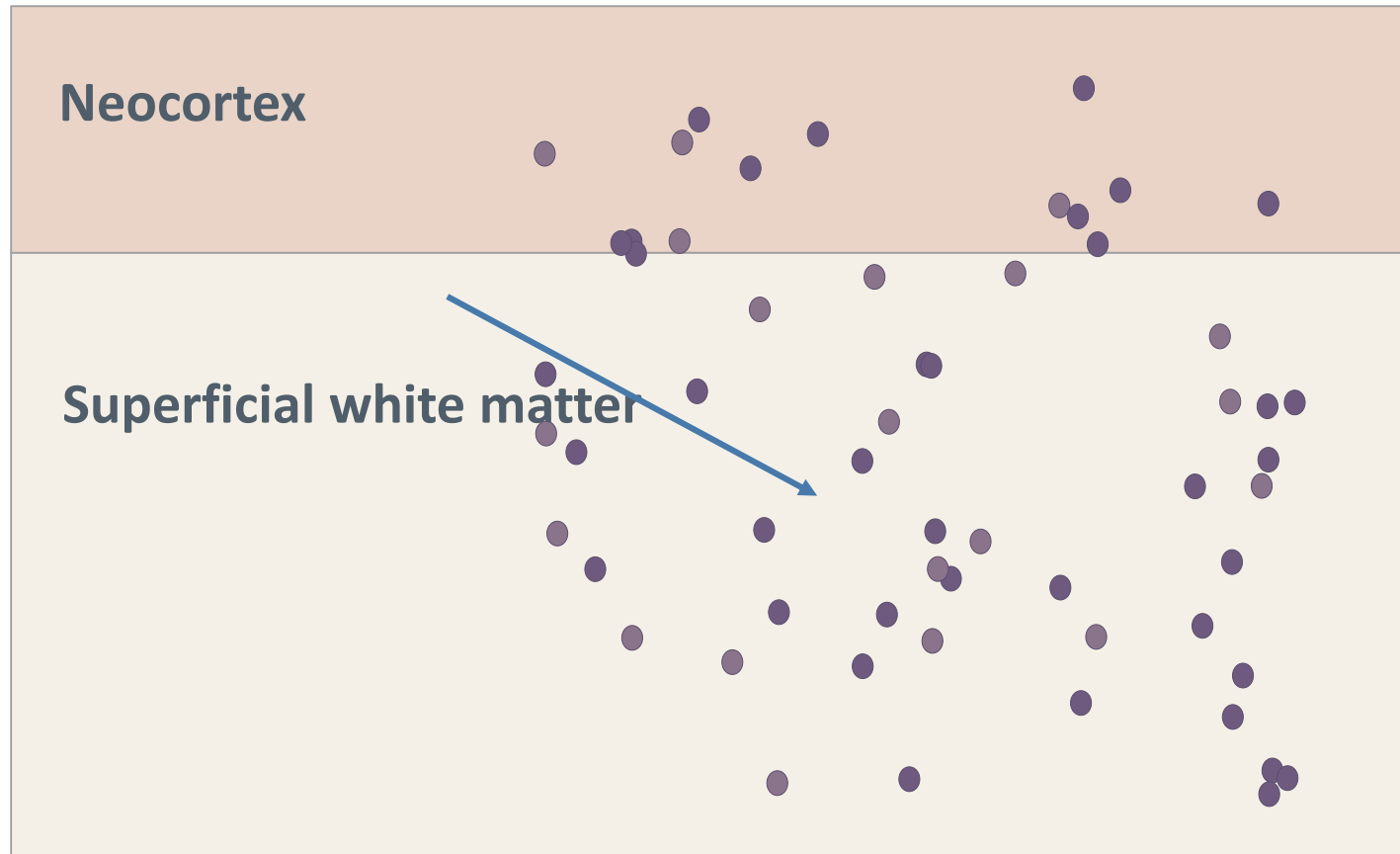
- Oligodendrogliomas represent approximately 5%–15% of gliomas.
- This percentage uses gliomas—not all brain tumors—as the denominator.
- Frequency estimates reflect the tumor category and its molecular redefinition.

Textbook frequency; Avoid applying this range to unselected CNS lesions.

The typical patient: Fourth to fifth decade

- Presentation is most common during the fourth and fifth decades of life.
- The age distribution overlaps other diffuse adult gliomas.
- Age therefore contributes clinical context but cannot establish the subtype.

Characteristic neuroanatomic location



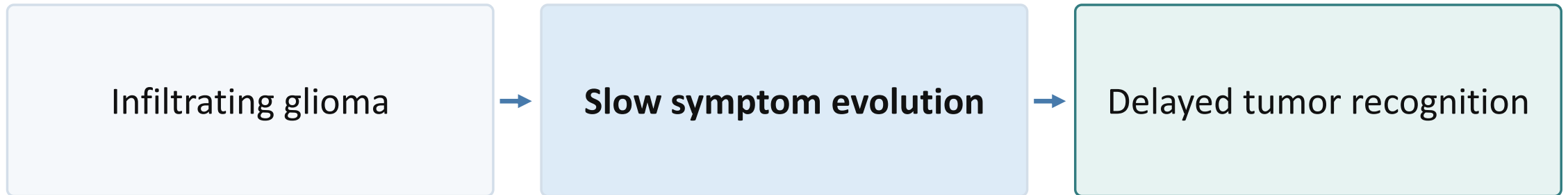
Schematic anatomic relationship

- Most lesions occur in the cerebral hemispheres.
- The neocortex and superficial white matter are favored.
- Cortical involvement provides a substrate for seizures.

A common clinical presentation: Seizures

- Seizures are a frequent manifestation of the superficial hemispheric distribution.
- Patients may have neurologic complaints for several years before diagnosis.
- A seizure presentation is suggestive of cortical disease, not specific for oligodendroglioma.

Why the clinical history may be prolonged



- Patients may report years of intermittent seizures or other neurologic complaints.
- Long duration does not establish grade 2; Pathology and molecular testing remain necessary.

The pathogenesis has a molecular foundation

An IDH mutation is necessary—but not sufficient—for oligodendroglioma.

- A second defining event is whole-arm 1p/19q codeletion.
- Molecular classification is stronger than oligodendrocyte-like cell morphology alone.

IDH mutation: Diagnostic implications

Gene

- Pathogenic IDH1 mutation
- Or pathogenic IDH2 mutation

Function

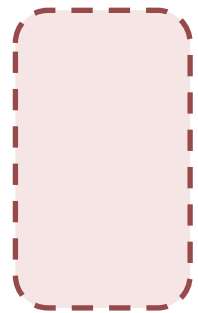
- Abnormal isocitrate dehydrogenase activity
- Associated altered metabolic signaling

Diagnosis

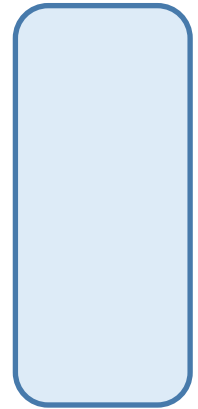
- Establishes IDH-mutant status
- Does not distinguish oligodendroglioma from IDH-mutant astrocytoma

What “whole-arm codeletion” means

Chromosome 1



1p deleted

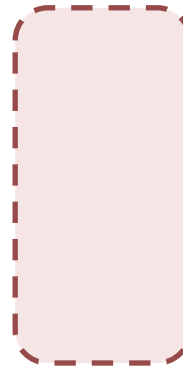


1q retained

Chromosome 19



19p retained



19q deleted

Whole-arm 1p + whole-arm 19q loss

Codeletion is a specific chromosomal pattern

Required finding

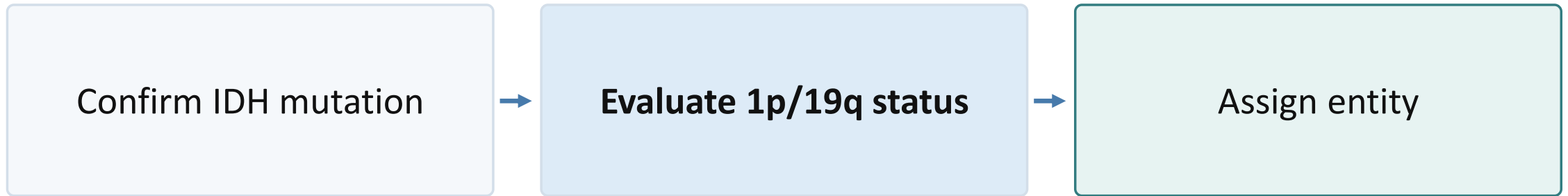
- Loss of the entire short arm of chromosome 1 (1p)
- Loss of the entire long arm of chromosome 19 (19q)
- Concordant losses in the same tumor

Not equivalent

- Isolated loss of 1p or 19q
- Focal or partial deletions alone
- Loss without evidence of the defining IDH mutation

Molecular method choice must be able to support whole-arm interpretation.

Molecular lineage: Two-step interpretation



- IDH-mutant plus whole-arm 1p/19q codeletion → oligodendroglioma.
- IDH-mutant without codeletion → assess astrocytoma-associated features.

TERT promoter mutations are common

- TERT-promoter mutations in the vast majority of oligodendrogliomas.
- TERT alteration is a frequent accompanying event—not one of the two defining criteria.
- TERT promoter status alone cannot separate all oligodendrogliomas from glioblastomas.

Additional changes and tumor progression



- Loss of chromosome 9p may delete the CDKN2A tumor-suppressor locus.
- This is less common than in IDH-mutant astrocytoma.

EGFR amplification: A useful contrast

Oligodendroglioma

- IDH-mutant, 1p/19q-codeleted
- TERT promoter mutation frequently present
- EGFR amplification not characteristic

Glioblastoma, IDH-wildtype

- IDH-wildtype by definition
- EGFR amplification can be present
- +7/−10 and TERT promoter alteration also occur

Diagnostic versus associated genomic findings

Essential

- IDH mutation
- Whole-arm 1p/19q codeletion

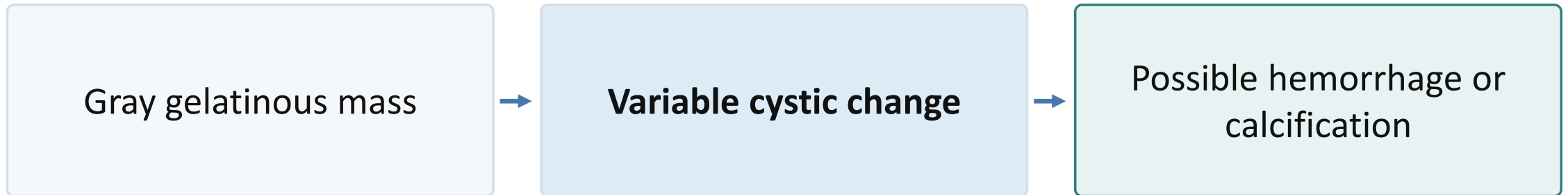
Frequent, associated

- TERT promoter mutation
- Supports the genomic context

Progression-associated

- Chromosome 9p/CDKN2A loss
- Not the fundamental entity definition

Gross morphology: An infiltrating gray lesion



- Gross features are characteristic but not molecularly specific.
- A seemingly circumscribed mass does not prove a noninfiltrative process.

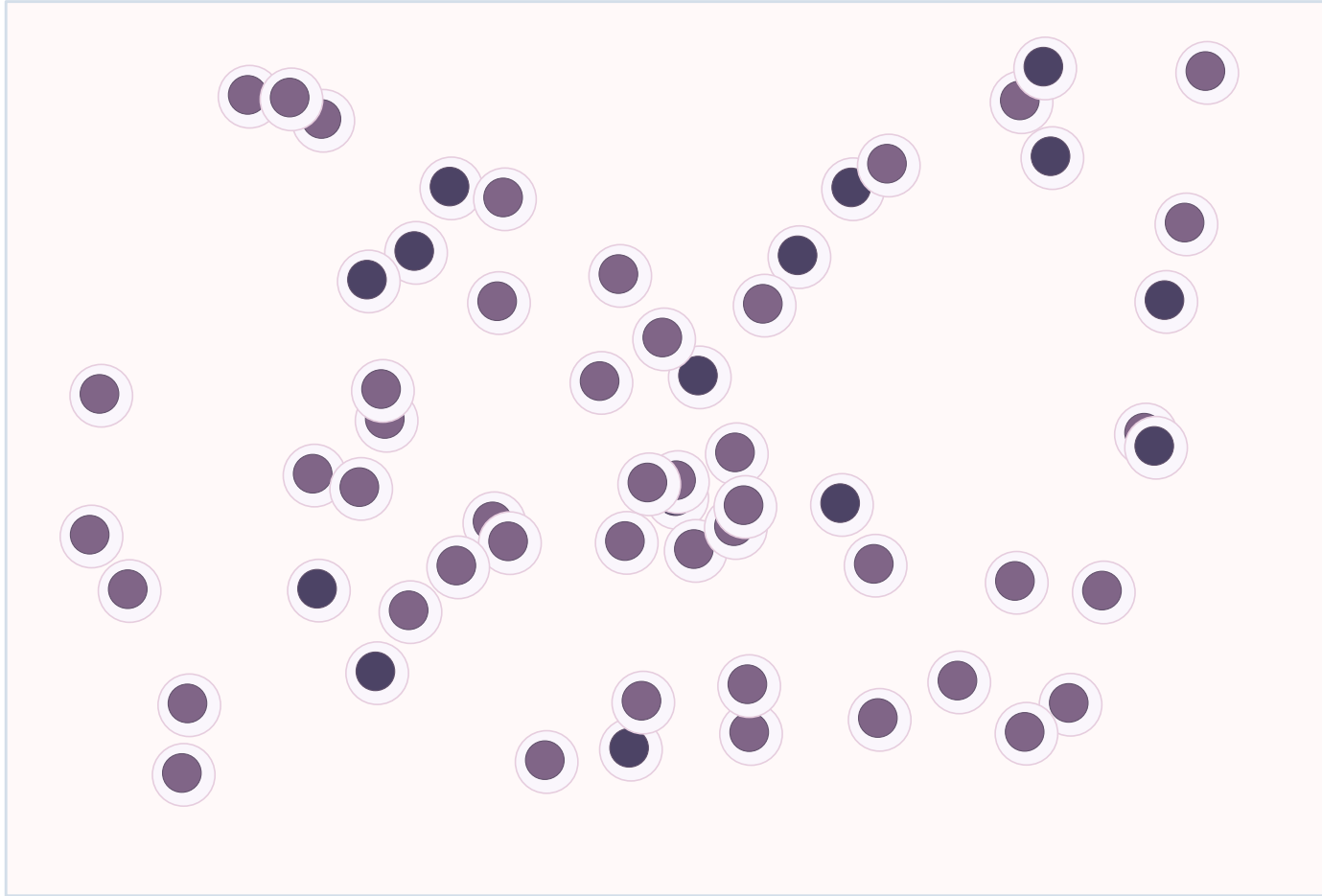
Macroscopic cystic and hemorrhagic areas

- Cysts and focal hemorrhage in some tumors.
- These findings may contribute to heterogeneous gross appearances.
- Neither is required for the diagnosis or provides a grading threshold.

Calcification is a characteristic feature

- Calcification may occur in as many as 90% of these tumors.
- The amount ranges from microscopic deposits to extensive calcified regions.
- Calcification supports recognition but is not diagnostic without molecular confirmation.

Classic oligodendroglial nuclear appearance



- Sheets of relatively regular cells.
- Round or spherical nuclei.
- Clear perinuclear halos may be present.

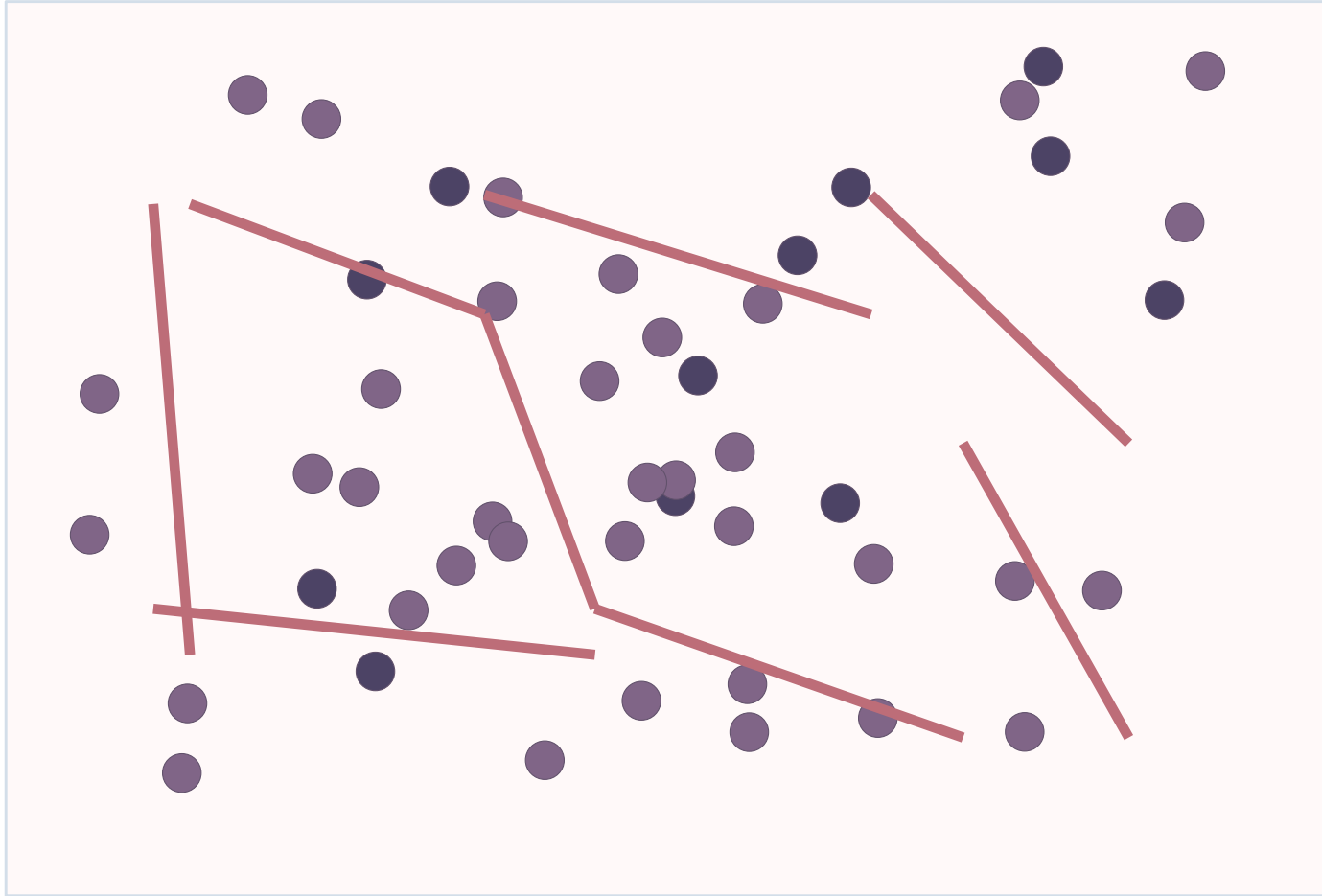
Original schematic — not a histologic specimen

“Fried-egg” cytology is a pattern, not a mutation test

The halo is a recognizable morphologic clue.

- Do not diagnose the molecular entity by halo appearance alone.
- Integrate tissue morphology with IDH and chromosome-arm status.

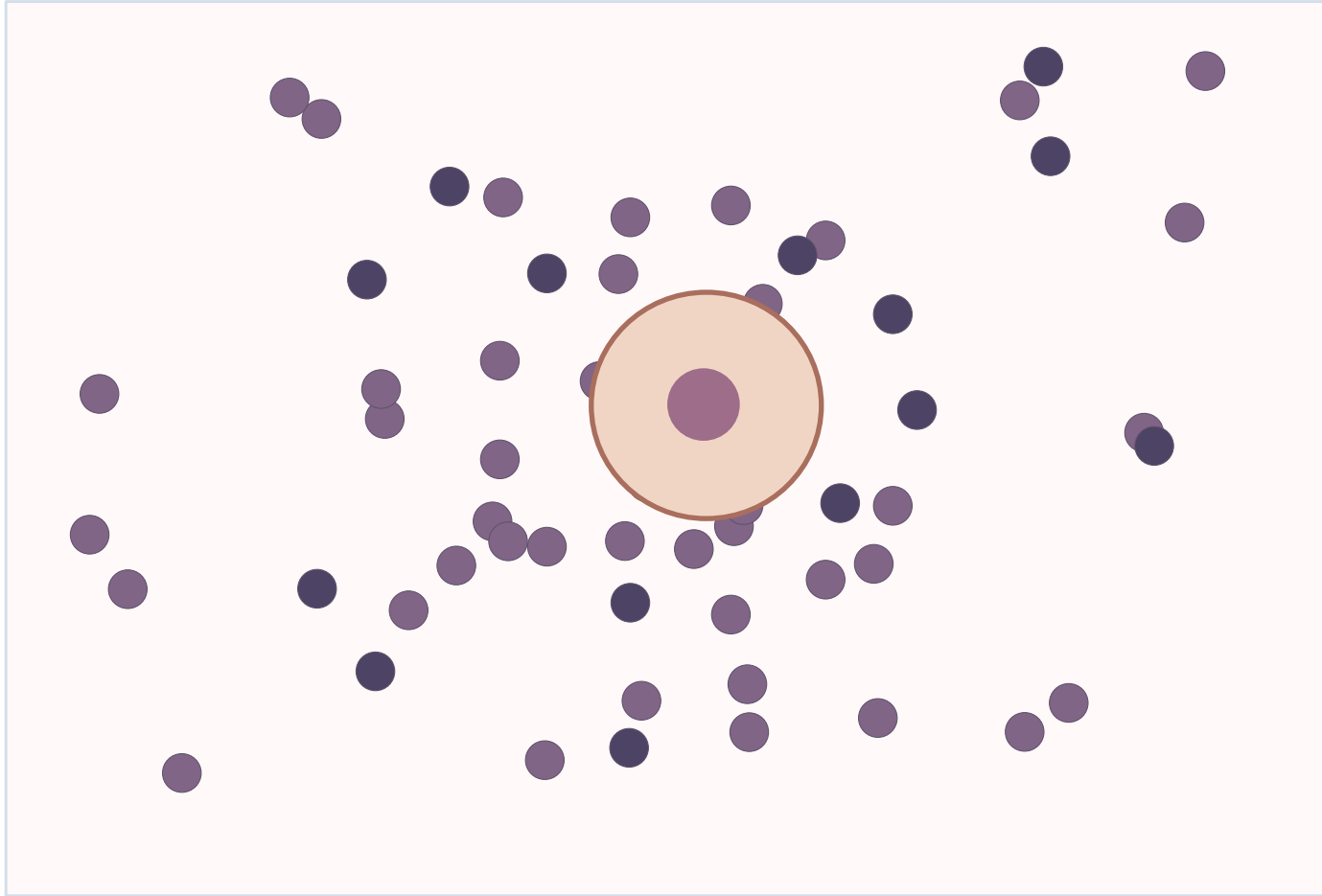
Delicate “chicken-wire” vasculature



- Branching fine-walled capillaries.
- Network traverses cellular tumor sheets.
- An architectural clue, not a genetic assay.

Original schematic — not a histologic specimen

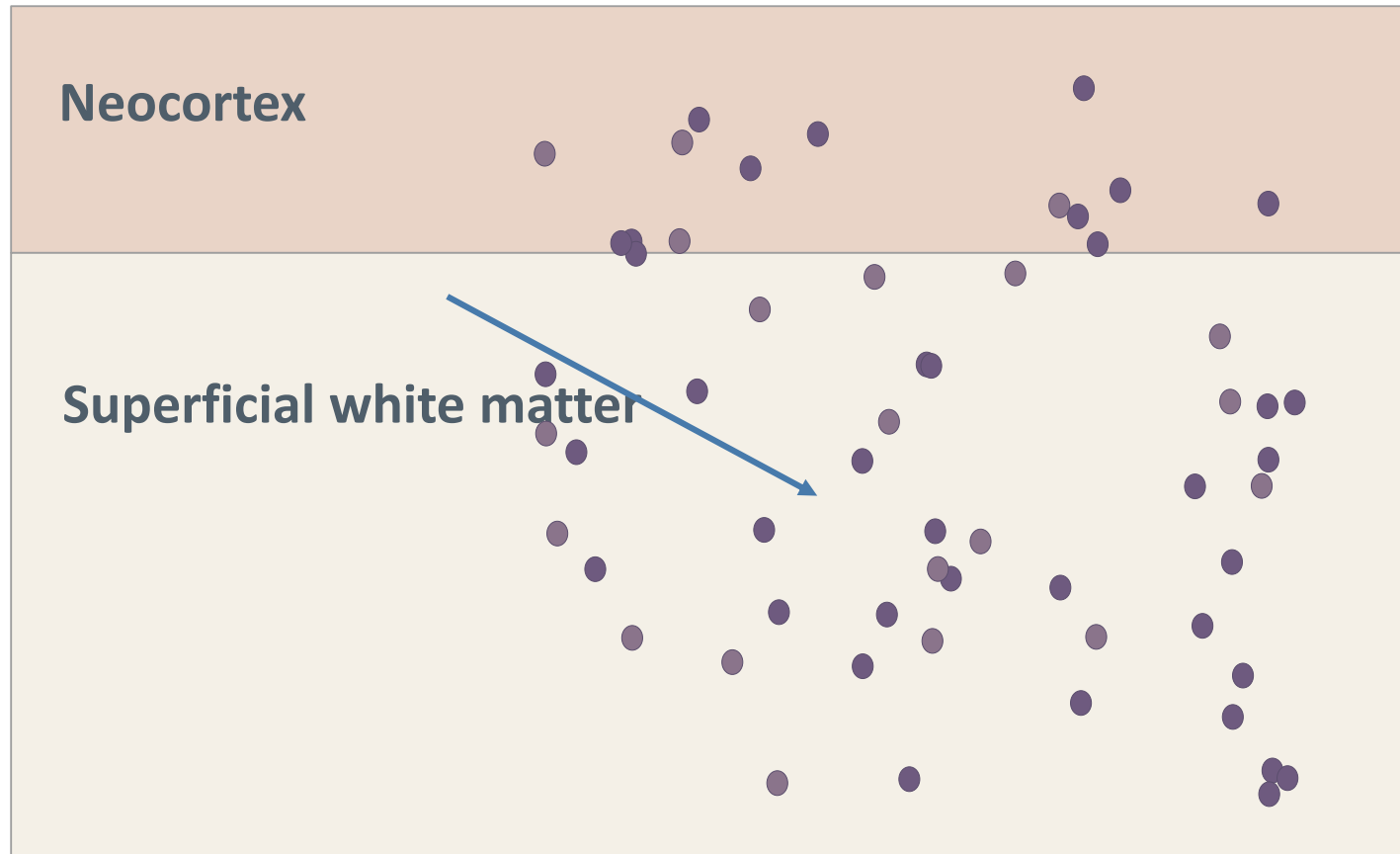
Perineuronal satellitosis in cortical tissue



Original schematic — not a histologic specimen

- Infiltrating tumor cells may collect around native cortical neurons.
- The pattern reflects cortical invasion.
- Recognize it as growth pattern rather than subtype-specific proof.

Infiltration beyond the apparent lesion



- Tumor cells can permeate adjacent cortex and white matter.
- Apparent borders do not equal the microscopic extent of disease.
- Anatomic growth pattern shapes surgical and sampling challenges.

Schematic anatomic relationship

Morphology: The three characteristic visual clues

Cytology

- Round nuclei
- Clear perinuclear halos

Vasculature

- Fine branching capillaries
- “Chicken-wire” arrangement

Infiltration

- Cortical involvement
- Perineuronal satellitosis

Any one clue may be absent; Molecular confirmation remains mandatory.

Grade 2: Relatively low proliferative activity

- CNS WHO grade 2 oligodendroglioma shows relatively low mitotic activity.
- Proliferation indices are low description.
- Morphologic low grade does not imply the absence of infiltrative growth.

Grade 3: Cellularity increases

- Grade 3 lesions have higher cellular density than grade 2 counterparts.
- Greater cellularity should be interpreted with other anaplastic features.
- No single universal numerical cellularity cutoff is supplied.

Grade 3: Nuclear anaplasia

- Grade 3 tumors may exhibit nuclear anaplasia.
- Changes may coexist with familiar round-cell oligodendroglial areas.
- Sampling multiple regions matters when the tumor is heterogeneous.

Grade 3: Increased mitotic activity

- An increase in mitoses is a key marker of grade 3 behavior.
- Distinguish true mitotic figures from apoptotic or pyknotic nuclei.
- Do not invent a mitotic-count cutoff; None is given in the primary excerpt.

Necrosis can occur in grade 3 tumors

- Necrosis in some grade 3 oligodendrogliomas.
- In oligodendroglioma, grade 3 is the highest WHO grade.
- Do not automatically apply the glioblastoma grade 4 category to a codeleted tumor.

Grade 2 and grade 3: Morphologic comparison

Feature	Grade 2	Grade 3
Cellularity	Lower	Increased
Nuclear appearance	Relatively uniform	More anaplasia
Mitotic activity	Low	Increased
Necrosis	Not typical	May be present
Integrated identity	IDH-mutant + 1p/19q-codeleted	Same molecular identity

Qualitative Robbins descriptions; Not numerical grading cutoffs.

Progression from grade 2 to grade 3



- High-grade lesions can appear de novo, but progression is more common.
- Clinical progression typically occurs over several years.

Sampling can miss a more aggressive component

- A limited sample interrogates only part of a spatially heterogeneous tumor.
- Grade assignment should reflect the most aggressive representative histology sampled.
- Molecular identity remains important even if the sampled morphology is deceptively bland.

Tumor type and tumor grade are separate axes

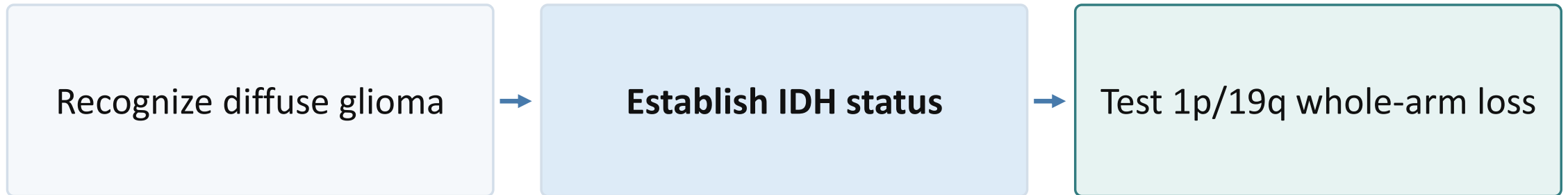
Type: Oligodendroglioma

- Requires IDH mutation
- Requires whole-arm 1p/19q codeletion
- Distinct molecular lineage

Grade: 2 or 3

- Uses histologic aggressiveness
- Mitoses, cellularity, anaplasia and necrosis
- Does not change molecular entity name

Practical integrated pathology workflow



- Integrate the microscopy, IDH result and copy-number findings into the report.
- Additional workup helps resolve discordant profiles.

IDH1 p.R132H immunohistochemistry

Purpose

- Detects a common IDH1 mutant protein
- Can highlight neoplastic cells in brain

Positive result

- Supports IDH-mutant status
- Does not prove 1p/19q codeletion

Negative result

- Does not exclude other IDH variants
- Sequencing may be necessary

When IDH1 R132H immunostaining is negative

- Other pathogenic IDH1 and IDH2 mutations remain possible.
- EANO recommends sequencing in relevant adult diffuse glioma settings.
- Interpret a negative antibody result as “R132H not detected,” not automatically IDH-wildtype.

How to interrogate chromosome-arm status

Copy-number methods

- Evaluate loss across chromosome arms
- Ensure coverage supports whole-arm status

Interpretation

- Both 1p and 19q arms must be deleted
- Partial deletion is not equivalent

Integrated result

- Combine with IDH mutation evidence
- Resolve discordant morphology and molecular testing

Supplementary testing framework: EANO molecular diagnostic guideline (2023).

ATRX and TP53: Discriminating context

Oligodendroglioma profile

- IDH-mutant + 1p/19q-codeleted
- ATRX nuclear expression usually retained
- TERT promoter alteration frequently present

Astrocytoma profile

- IDH-mutant without codeletion
- ATRX inactivation common
- TP53 mutation frequently present

Supportive markers do not replace defining chromosome-arm testing.

Key molecular contrast across adult diffuse gliomas

Feature	Oligodendroglioma	Astrocytoma, IDH-mutant	Glioblastoma, IDH-wt
IDH	Mutant	Mutant	Wildtype
1p/19q	Whole-arm codeletion	Not codeleted	Not defining
ATRX / TP53	Not characteristic axis	Often altered	Variable
TERT promoter	Common	Less defining	Often altered
CNS WHO grade	2 or 3	2, 3 or 4	4

Case: A cortical lesion with classic morphology

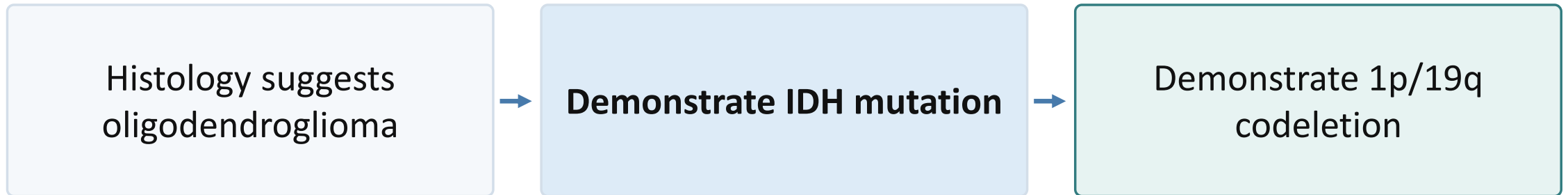
ILLUSTRATIVE TEACHING CASE

A middle-aged adult has a prolonged seizure history and a superficial hemispheric brain lesion.

Tissue: Round neoplastic nuclei, perinuclear clearing and delicate branching capillaries.

What is required before signing out oligodendroglioma?

Case interpretation: Confirm the genotype



- Only the integrated findings support the specific molecular entity.
- The vignette is illustrative; No actual patient data are shown.

Case: Greater cellularity and mitotic activity

ILLUSTRATIVE TEACHING CASE

An infiltrating hemispheric tumor has the molecular signature of oligodendroglioma.

The tissue shows conspicuous cellularity, anaplasia and increased mitotic activity.

Which grade is supported by these high-grade features?

Case interpretation: CNS WHO grade 3

The molecular entity remains oligodendroglioma.

- Greater cellularity, nuclear anaplasia and mitotic activity support grade 3.
- The grade is not converted to “glioblastoma” by high-grade morphology.

Case: A morphological mimic

ILLUSTRATIVE TEACHING CASE

A diffuse glioma has cells with round nuclei and apparent perinuclear halos.

IDH mutation is identified, but whole-arm 1p/19q codeletion is absent; ATRX nuclear loss is present.

Does the classic-looking cytology establish oligodendroglioma?

Case interpretation: Phenotype does not override genotype

No: Oligodendroglioma requires whole-arm 1p/19q codeletion.

- This molecular pattern directs evaluation toward IDH-mutant astrocytoma.
- Cell shape alone is inadequate for assigning tumor lineage.

Clinical prognosis: Relative—not absolute

Oligodendroglioma

- Better prognosis than astrocytic counterparts
- Long clinical course possible
- Grade still modifies outcome

Other diffuse gliomas

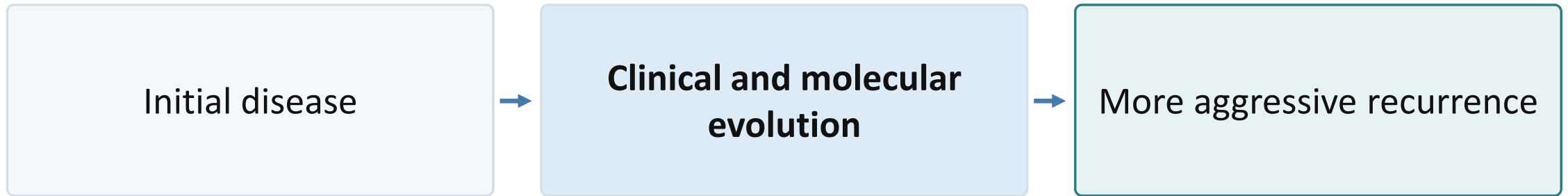
- Prognosis varies strongly by molecular type
- IDH-wildtype glioblastoma often behaves aggressively
- Grade alone is not a cross-entity comparator

Survival figures reported

Entity	Average survival in textbook
Oligodendroglioma, CNS WHO grade 2	15–20 years
Oligodendroglioma, CNS WHO grade 3	10–15 years

Textbook historical estimates under stated multimodal management; Not individualized prognosis or contemporary cohort data.

Progression occurs over years, not never



- Progression from lower to higher grade, typically over ≥ 5 years.
- Long survival does not mean cure or absence of recurrence.

Clinical management

Surgery

- Obtain diagnosis and reduce tumor burden
- Extent depends on anatomic feasibility

Radiation therapy

- Used in treatment strategies
- Part of multimodal management

Chemotherapy

- Used with surgery and radiotherapy
- Therapy details depend on clinical context

This is pathology-oriented context, not a treatment protocol or prescription.

Grading and prognosis require careful language

- Avoid treating textbook average survival as a personal prediction.
- Age, lesion location, extent of resection and treatment context may influence patient course.
- The molecular diagnosis informs interpretation of histologic grade.

Common diagnostic errors to avoid

Morphology only

- Assuming clear halos prove oligodendroglioma
- Ignoring genomic findings

Molecular shortcut

- Equating partial-arm loss with codeletion
- Treating R132H-negative as IDH-wildtype

Grading shortcut

- Automatically using grade 4 for necrosis
- Overinterpreting a limited sample

Oligodendroglioma versus pilocytic astrocytoma

Oligodendroglioma

- Diffuse infiltrating glioma
- IDH mutation + 1p/19q codeletion
- Typically adult hemispheric tumor

Pilocytic astrocytoma

- Relatively circumscribed architecture
- MAP kinase pathway alterations
- Commonly in younger patients and cerebellum

Oligodendroglioma versus ependymoma

Oligodendroglioma

- Diffuse cortical/subcortical infiltration
- Round nuclei and fine capillaries
- IDH-mutant and 1p/19q-codeleted

Ependymoma

- Often ventricular/spinal relation
- Perivascular pseudorosettes and true rosettes
- Classification also uses location and molecular subtype

Integrated diagnosis: How to phrase the report



- The name documents the molecular definition.
- The grade communicates the histologic aggressiveness within this entity.

Before finalizing the diagnosis

Check	Required interpretation
Histology	Infiltrating glioma; characteristic pattern and grade-relevant features
IDH testing	Pathogenic IDH1 or IDH2 mutation demonstrated
1p/19q testing	Whole-arm codeletion confirmed
Grade	CNS WHO grade 2 or 3 justified
Integrated wording	Entity, molecular status and grade internally consistent

Diagnostic checklist derived with EANO molecular-testing context.

Summary: Diagnosis, grade, outcome

Identity

- Diffuse glioma
- IDH mutation + whole-arm 1p/19q codeletion

Morphology

- Round nuclei and clear halos
- Delicate branching capillaries; Infiltration

Course

- Grades 2 and 3
- Relatively favorable among gliomas; May progress

Self-assessment: An apparently low-grade tumor

ILLUSTRATIVE TEACHING CASE

A diffuse cortical glioma contains regular round cells with low mitotic activity.

IDH1 p.R132H is positive. Cytogenetic testing shows no whole-arm 1p/19q codeletion.

Can this be diagnosed as oligodendroglioma, grade 2?

Answer: Absence of codeletion prevents the diagnosis

The defining molecular pair is incomplete.

- Evaluate the alternative adult-type diffuse glioma lineage.
- Assign entity and grade only after integrating molecular and histologic information.

Source references and classification context

Robbins, Cotran & Kumar. Pathologic Basis of Disease. 11th ed. (2026). Chapter 28, pp. 1177–1180.

WHO Classification of Tumours Editorial Board. Central Nervous System Tumours. 5th ed. (2021).

Sahm et al. Molecular diagnostic tools for WHO 2021 glioma classification: EANO guideline. Neuro-Oncology. 2023.

ASCO–SNO clinical practice guideline for diffuse astrocytic and oligodendroglial tumors in adults (2022).