

# Pediatric Gliomas– a case-based, practical approach to using the WHO 2021 classification

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## Case-Based Questions (please see page 3 for answers)

1.	You receive a thalamic tumor biopsy from a 12-year-old boy. Morphologically this appears to be a low-grade glioma. Which of the following would be an appropriate integrated diagnosis?
a.	Diffuse low-grade glioma, MAPK pathway altered <ul style="list-style-type: none"><li>- WHO grade 2</li><li>- H3K27M and BRAFV600E mutant</li></ul>
b.	Diffuse midline glioma, H3 K27-altered <ul style="list-style-type: none"><li>- WHO grade 4</li><li>- H3K27me3 retained</li><li>- PDGFRA mutant</li></ul>
c.	Diffuse low-grade glioma, MAPK pathway altered <ul style="list-style-type: none"><li>- EGFR mutant</li><li>- H3K27me3 lost</li></ul>
d.	Diffuse midline glioma, H3K27-altered <ul style="list-style-type: none"><li>- WHO grade 4</li><li>- EGFR mutant</li><li>- H3K27me3 lost</li><li>- H3K27 wildtype</li></ul>
e.	Glioblastoma, IDH-wildtype <ul style="list-style-type: none"><li>- WHO grade 4</li><li>- P53 and H3K27M mutant</li></ul>
2.	You receive a resection specimen from a large hemispheric mass from an 8-month-old girl. Microscopically this shows features of a high-grade glioma. Which of the following is most likely to be found on molecular testing
a.	H3.3 p.G34R
b.	H3.3 p.K27M
c.	FGFR1 fusion
d.	BRAF fusion
e.	NTRK fusion
3.	You receive molecular results from a biopsy from a 5-year-old boy with a pontine lesion. The tumor is positive for a <i>KIAA1549-BRAF</i> fusion. Which histology is most likely to be seen on microscopic examination?
a.	Diffuse astrocytoma
b.	Ganglioglioma
c.	Glioblastoma
d.	Pliocytic astrocytoma
e.	Pleomorphic xanthoastrocytoma

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Question 1: Correct answer and rationale: D is the correct answer. The DMG category has been expanded to include both H3K27M mutant cases as well as those diffuse gliomas with loss of H3K27me3 through expression of EZHIP, or in the context of EGFR mutations. Neither the term glioblastoma nor diffuse low-grade gliomas should not be used for H3K27M mutant tumors.

Question 2: Correct answer and rationale: (e) NTRK fusion. In infant hemispheric high-grade gliomas, fusions in NTRK, ROS1, ALK or MET are more likely to be encountered. FGFR1 and BRAF fusions are found in low grade gliomas of childhood. H3.3 p.G34R mutations are found in hemispheric high-grade gliomas in the adolescent, young adult age group. H3.3 p.K27M is found in midline gliomas and are uncommon in infants.

Question 3: Correct answer and rationale: (d) pilocytic astrocytoma is the most frequent morphology encountered in BRAF fusion positive brain tumors.