Pediatric-type glioma findings

Here is a summary of the key findings from the review article by Chelsea Kotch, Katherine Green, Michael J Fisher & Darren Hargrave: *Pediatric-Type Diffuse Low Grade Glioma* (Adv Cancer Res. 2025;167:1-35; doi:10.1016/bs.acr.2025.08.006; Epub 2025 Sep 25). PubMed +1

Background & definitions

- The review addresses the family of **pediatric-type diffuse low grade gliomas** (pDLGGs) as newly recognized in the World Health Organization (WHO) 2021 classification of CNS tumours. PubMed +1
- This family comprises **four distinct entities**:
    1. Diffuse astrocytoma, MYB- or MYBL1-altered
    2. Angiocentric glioma
    3. Polymorphous low-grade neuroepithelial tumour of the young (PLNTY)
    4. Diffuse low grade glioma, MAPK-altered PubMed
- The review emphasizes that accurate diagnosis *requires* integrated histologic + molecular assessment, due to overlapping features among these entities. PubMed

Epidemiology / clinical & imaging features

- These tumours occur primarily in children and young patients (though may in some cases present in adolescents/young adults). PubMed
- They are typically supratentorial and may present with features such as seizures (especially when cortical) or other neurologic signs depending on location.
- Radiologically, many demonstrate features more favourable than adult-type diffuse gliomas: often less invasive appearance, sometimes non-enhancing, T2/FLAIR hyperintense masses, though heterogeneity remains. The review describes imaging features and challenges of distinguishing them. PubMed

Molecular/Pathologic findings

- A key point: These paediatric-type diffuse low grade gliomas are distinct biologically from adult-type diffuse gliomas (for example, IDH-mutant or H3-altered tumours). The review highlights that typical adult diffuse glioma alterations (IDH1/2, TERT promoter, H3K27M etc) are absent in many of these pDLGGs. read.qxmd.com

- Each of the four entities has characteristic molecular alterations:
    - Diffuse astrocytoma, MYB/MYBL1-altered: fusions or structural variants in MYB or MYBL1. old.pathologica.it +1
    - Angiocentric glioma: often MYB:QKI fusions (and part of that same spectrum) with astrocytic/ependymoma-like features. old.pathologica.it +1
    - PLNTY: oligodendroglioma-like components, CD34 expression, BRAF V600E or FGFR2/3 fusions, MAPK-pathway activation. Cureus +1
    - Diffuse low grade glioma, MAPK-altered: diverse MAPK pathway alterations (BRAF, FGFR1/2, etc) in infiltrative low-grade gliomas without IDH/H3 alterations. old.pathologica.it +1
- The review underscores that morphology alone is insufficient for diagnosis: because of overlapping histology (e.g., infiltration, glial phenotype, sometimes oligodendroglial appearance), one must incorporate immunohistochemistry, molecular genetics and, increasingly, methylation profiling. PubMed

Management & outcomes

- The authors summarise existing evidence (which remains limited) on management: surgical resection remains central, particularly when feasible for gross total resection of these low-grade tumours. However, infiltration and location can make surgery challenging. PubMed
- Because these tumours are biologically more favourable compared to adult diffuse gliomas, the prognosis tends to be better, with lower risk of malignant transformation (though data remain immature). The review emphasises that overtreatment should be avoided when possible. PubMed
- Important: The growing recognition of molecular targets (e.g., BRAF, FGFR) opens the possibility of targeted therapies in recurrent or residual disease. The authors review therapeutic implications of prevalent molecular alterations. PubMed

Key Implications / Take-Home Points

- For paediatric neuro-oncology practice: diagnosing these entities correctly is critical because they behave differently from adult-type diffuse gliomas — both in terms of natural history and therapeutic approach.
- The review supports a **tiered/integrated diagnostic algorithm**: clinical + imaging features → histology/immuno → molecular/genetic → consider methylation where needed.

- In the era of precision medicine, knowledge of the specific molecular alteration (e.g., MYB/MYBL1, MAPK pathway) is not just academic: it may guide prognosis, surgical planning, follow-up, and targeted therapy options.
- The review highlights areas of unmet need: more longitudinal outcome data, more trials of targeted therapies in these specific subgroups, consensus on follow-up and management of residual/infiltrative disease.

Limitations & gaps noted by the authors

- Because these entities are newly defined (WHO 2021) and relatively rare, the literature remains thin: many series are small, follow-up durations modest. The review calls for further multicentre studies. PubMed
- Heterogeneity remains (e.g., within MAPK-altered gliomas) and the boundaries between circumscribed low-grade gliomas, glioneuronal tumours, and these diffuse paediatric-type gliomas are still being refined.
- The role of adjuvant therapy (chemotherapy/radiotherapy) in these tumours is not well defined: because of the comparatively good prognosis, the risk–benefit of aggressive therapy is less clear.
- There is limited published evidence for targeted therapy in these specific pDLGG subtypes — many of the therapeutic implications remain speculative or based on case reports.

Added points to note

Given your special interest in pediatric neuro-oncology and drug delivery across the blood–brain barrier, some specific points to note:

- The review highlights that although these tumours are generally lower grade, their infiltrative pattern (especially for the MAPK-altered subgroup) may complicate achieving gross total resection and might impact microenvironment and BBB integrity.
- The presence of specific molecular drivers (for example BRAF, FGFR1/2 fusions) suggests that small-molecule inhibitors could be feasible, but in pediatric populations the drug delivery (crossing the BBB, intracranial penetration, pediatric dosing) remains a challenge. The review implies the need for more work on targeted therapy penetration in pediatric CNS.
- From a translational perspective, the biologic difference from adult gliomas (which often have IDH/H3 alterations) suggests that the microenvironment (including BBB, immune milieu) might differ; this has implications for delivery strategies, drug design, and potentially novel BBB modulation strategies specific to these paediatric tumour types.

Suggested annotated Vancouver-style citation

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