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H3 G34-mutant high-grade gliomas: integrated clinical, imaging and pathological characterisation of a single-centre case series

José Pedro Lavrador [#] [1], Zita Reisz [#] [2], Naomi Sibtain [3], Kapil Rajwani [1], Asfand Baig Mirza [4], Francesco Vergani [1], Richard Gullan [1], Ranjeev Bhangoo [1], Keyoumars Ashkan [1], Cristina Bleil [1], Bassel Zebian [1], Barnaby Clark [5], Ross Laxton [2 5], Andrew King [2], Istvan Bodi [2], Safa Al-Saraj [2]

1 Department of Neurosurgery, King's College Hospital Foundation Trust, London, UK.
2 Department of Clinical Neuropathology, King's College Hospital Foundation Trust, London, UK.
3 Department of Neuroradiology, King's College Hospital Foundation Trust, London, UK.
4 Department of Neurosurgery, King's College Hospital Foundation Trust, London, UK. Asfand.mirza@nhs.net.
5 Molecular Neuropathology, Synnovis at King's College Hospital Foundation Trust, London, UK.
# Contributed equally.

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Abstract

Background: Diffuse hemispheric glioma, H3 G34-mutant, is a novel paediatric tumour type in the fifth edition of the WHO classification of CNS tumours associated with an invariably poor outcome. We present a comprehensive clinical, imaging and pathological review of this entity.

Methods: Patients with confirmed H3 G34R-mutant high-grade glioma were included in a single-centre retrospective cohort study and examined for clinical, radiological and histo-molecular data.

Results: Twelve patients were enrolled in the study - 7 males/5 females; the mean age was 17.5 years (10-57 years). Most patients presented with signs of raised intracranial pressure (8/12). The frontal lobe (60%) was the prevalent location, with a mixed cystic-nodular appearance (10/12) and presence of vascular flow voids coursing through/being encased by the mass (8/12), and all tumours showed cortical invasion. Nine patients had subtotal resection limited by functional margins, two patients underwent supra-total resection, and one patient had biopsy only. 5-ALA was administered to 6 patients, all of whom showed positive fluorescence. Histologically, the tumours showed a marked heterogeneity and aggressive spread along pre-existing brain structures and leptomeninges. In addition to the diagnostic H3 G34R/V mutation, pathogenic variants in TP53 and ATRX genes were found in most cases. Potential targetable mutations in PDGFRA and PIK3CA genes were detected in five cases. The MGMT promoter was highly methylated in half of the samples. Methylation profiling was a useful diagnostic tool and highlighted recurrent structural chromosome abnormalities, such as PDGFRA amplification, CDKN2A/B deletion, PTEN loss and various copy number changes in the cyclin D-CDK4/Rb pathway. Radiochemotherapy was the most common adjuvant treatment (9/12), and the average survival was 19.3 months.

Conclusions: H3 G34R-mutant hemispheric glioma is a distinct entity with characteristic imaging and pathological features. Genomic landscaping of individual tumours can offer an opportunity to adapt individual therapies and improve patient management.

Keywords: 5-Aminolevulinc acid; DNA methylation profiling; H3 G34-mutant; High-grade glioma; Sequencing; Tumour resection.

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