

## News Release

### Imaging Features and Consideration of Progression Pattern of Diffuse Hemispheric Gliomas, H3 G34-mutant

#### Key Points

- Diffuse hemispheric glioma H3 G34-mutant (DHG) is a newly defined pediatric-type high-grade glioma, according to the World Health Organization (WHO) 5th edition classification of central nervous system tumors. Its pathophysiology remains largely unknown, and prognosis is poor despite widely accepted treatment with surgery, radiation, and chemotherapy.
- Previous studies have reported that a high extent of resection (EOR) improves prognosis in malignant gliomas in general. However, the efficacy of the surgical resection in DHG remains unclear.
- Image analysis using MRI and PET scans revealed deep white matter infiltration from the early stage in DHGs. The extent of white matter infiltration in tumor resection cases was significantly negatively correlated with the EOR. In addition, cases with EOR of less than 90% had significantly worse prognosis.
- Patients with an extent of resection (EOR) of 90% or more had significantly longer survival, but achieving this was difficult in cases with extensive white matter involvement. Our analysis revealed the natural progression of DHGs where residual lesions extensively infiltrate the white matter and eventually invade the brainstem and contralateral brain, thereby contributing to mortality.

#### Summary

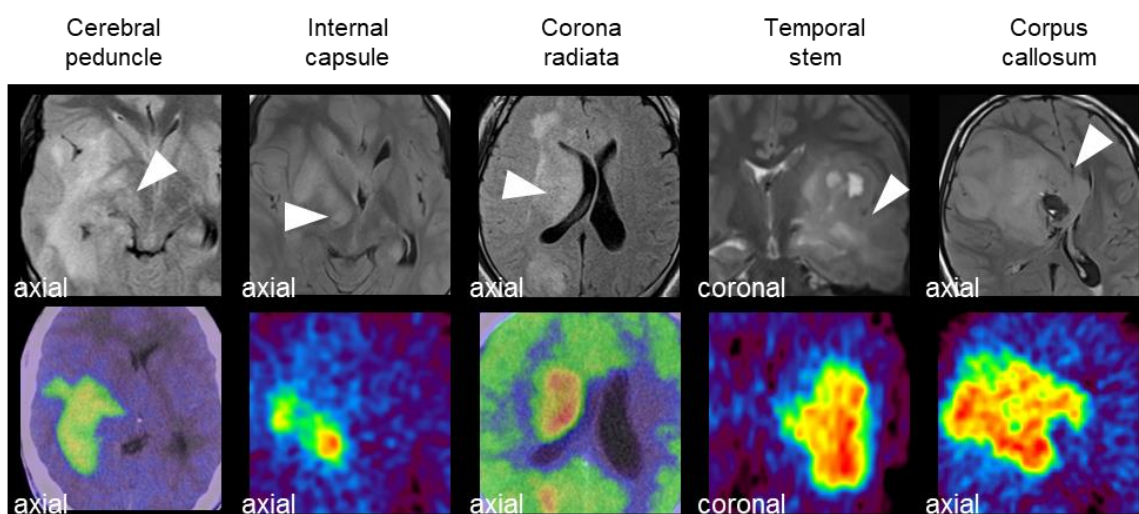
Diffuse hemispheric glioma H3 G34-mutant (DHG) has been identified as a distinct pediatric-type high-grade glioma, according to the World Health Organization (WHO) classification of central nervous system tumors. This study analyzed 9 cases of this rare tumor to better understand its imaging features and progression patterns. MRI findings revealed early deep white matter infiltration, which complicates surgical resection. While achieving an extent of resection (EOR) of 90% or more was associated with longer survival, this was only feasible in cases with limited white matter involvement. Histopathological analysis confirmed extensive infiltration, with some tumors eventually invading the brainstem. These findings highlight the challenges of surgical treatment and emphasize the need for further research into effective therapeutic strategies for DHGs.

## Research Background

Diffuse Hemispheric Glioma, H3 G34-mutant (DHG), is a rare and aggressive pediatric-type high-grade glioma newly classified by the WHO, primarily affecting adolescents and young adults. Despite a relatively better prognosis than other high-grade gliomas, DHGs inevitably recur under current treatment strategies, and the role of surgical resection remains unclear. This study retrospectively analyzes nine DHG cases, focusing on imaging features and tumor progression patterns to better understand its clinical characteristics and improve treatment approaches.

## Research Results

In this study, we retrospectively studied 9 cases of diffuse hemispheric glioma, with H3 G34R mutation detected by Sanger sequencing in all tumors. Initial MRI revealed T2/FLAIR high lesions with poor contrast enhancement in all cases. The tumors demonstrated restricted diffusion on MRI, high accumulation of methionine (MET) and low or partial accumulation of FDG. The MET-accumulated area corresponded to areas of diffusion restriction and T2/FLAIR high lesions, suggesting that all T2/FLAIR high lesions were tumor components infiltrating the deep white matter, including the internal capsule, corona radiata, temporal stem, and corpus callosum from early stage (Fig.1).

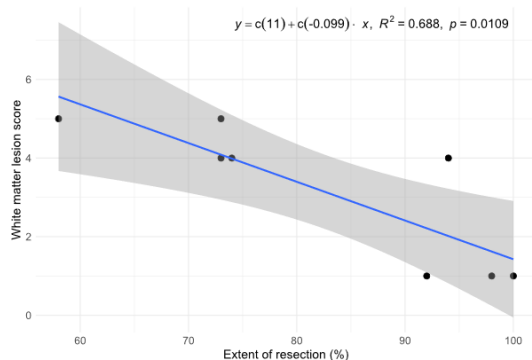


The white matter lesion (WML) score in cases with tumor resection showed a statistically significant negative correlation with the extent of resection (EOR) (Fig. 2A).

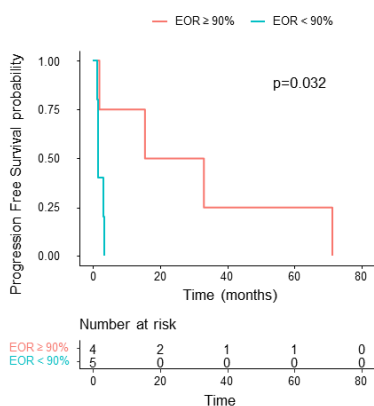
Median progression free survival (PFS) in cases with an EOR of 90% or more was significantly longer than in cases where EOR was less than 90% (24.4 months vs 1.6 months,  $p=0.032$ ) (Fig.2B). Overall survival in cases with an EOR of 90% or

more was also significantly longer than in cases with EOR of less than 90% (37.3 months vs 13.4 months,  $p=0.01$ ) (Fig. 2C).

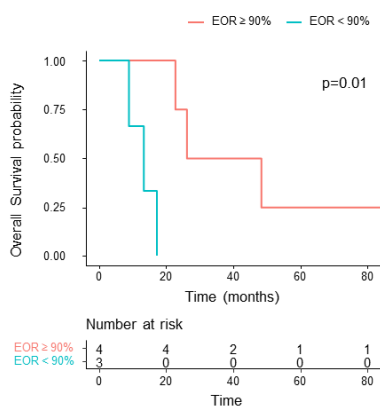
**A**



**B**



**C**



Imaging findings and autopsy showed that the residual tumor invaded along the deep white matter, and that the tumor extended to the brainstem and contralateral brain in all cases in the terminal state.

## Research Summary and Future Perspective

Diffuse Hemispheric Glioma, H3 G34-mutant (DHG) is an aggressive and infiltrative pediatric-type high-grade glioma with a strong tendency for early deep white matter infiltration. Surgical resection remains challenging, as white matter infiltration negatively impacts the extent of resection (EOR). While EOR may influence survival to some extent, improving prognosis through surgical strategies alone may not be practical. Therefore, further research into the molecular characteristics of these tumors appears essential for enhancing patient outcomes.

## Publication

Imaging Features and Consideration of Progression Pattern of Diffuse Hemispheric Gliomas, H3 G34-mutant

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