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Clinical, molecular, and surgical predictors of outcome in non-DIPG pediatric diffuse midline gliomas: A collaborative retrospective analysis

Sara Iglesias [1], Victoria Becerra [2], Pablo Miranda [3], Trinidad Márquez [4], Lara Galbarriatu [5], Pablo M Munarriz [6], Jorge Gimenez [7], Javier Saceda [8], Francisca Rius [9], José Hinojosa [2]

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Abstract

Purpose: To review a multicentric series of non-pontine diffuse midline glioma (DMG), describing clinical and histomolecular variability, surgical planning and complications, treatment strategies and factors related to outcome.

Methods: A retrospective multicentre study promoted by the Spanish Society of Paediatric Neurosurgery (SENEP) was conducted including paediatric patients with non-pontine DMG who underwent surgery and were diagnosed between 2016 and 2025, with a minimum follow-up of 1 month. Associations between clinical variables and survival were explored using Kaplan-Meier curves and Cox regression analyses.

Results: Thirty-five paediatric patients (aged 2-17) were included. Tumour location was unilateral thalamic in 48.6%, bithalamic in 25.7%, and less frequently involved the hypothalamus, pineal region, or showed dissemination. Biopsy was the first surgery in 80% of patients, yielding high diagnostic accuracy with minimal complications. Hydrocephalus developed in 77.1% of patients, and 17.1% experienced non-surgical brain swelling and/or intratumoural haemorrhage. Median overall survival was 16.0 months (95% CI 7.75-24.25), and median progression-free survival was 5.0 months (95% CI 2.76-7.24). Location and molecular subtype were linked to better OS in exploratory multivariate analyses, although these results should be interpreted with caution given the limited sample size and number of survival events.

Conclusions: Literature on paediatric DMGs arising outside the pons remains limited. Biopsy appears to be a safe and effective diagnostic strategy, although resection may be beneficial in selected unilateral thalamic tumours. Observed differences in survival according to tumour location and molecular subtype should be regarded as hypothesis-generating and require validation in larger cohorts.

Keywords: Complications; Diffuse midline glioma; Molecular subtypes; Outcome; Surgery; Targeted therapies.