Case Reports Childs Nerv Syst. 2025 Dec 21;41(1):429. doi: 10.1007/s00381-025-07084-w.

Significant clinical and radiologic response to targeted therapy in pediatric cervicomedullary low-grade gliomas harboring the BRAFV600E mutation

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PMID: 41423525 DOI: 10.1007/s00381-025-07084-w

Abstract

Purpose: Children with unresectable cervicomedullary tumors (CMTs) demonstrate poor progression-free survival when treated with conventional chemotherapy and radiotherapy. The BRAFV600E mutation, commonly identified in low-grade gliomas, represents a therapeutic target for mutation-specific kinase inhibitors. This study aims to emphasize the potential role of BRAF inhibitors as upfront targeted therapy in selected tumors where surgical resection is not feasible.

Methods: A retrospective analysis was conducted on four pediatric patients with unresectable cervicomedullary low-grade gliomas harboring the BRAFV600E mutation. All patients were treated with the BRAF inhibitor dabrafenib, either as first-line or second-line therapy.

Results: Dabrafenib was administered as first-line therapy in two patients and as second-line therapy in two others. All patients experienced rapid tumor regression with significant and durable clinical and radiologic responses. Three patients tolerated long-term therapy (up to 9 years) without significant toxicity. One patient discontinued treatment after 1 year due to a serious adverse event, which resolved upon withdrawal of therapy.

Conclusion: Dabrafenib demonstrated clinical and radiographic efficacy and was generally well tolerated in pediatric patients with unresectable BRAFV600E-mutant CMTs. These findings suggest that upfront BRAF inhibition may serve as a viable therapeutic alternative to conventional chemotherapy, radiotherapy, or attempted resection in selected cases. Further prospective studies are warranted to define the optimal timing, duration, and long-term safety of targeted therapy in this population.

Keywords: BRAFV600E; Central nervous system; Cervicomedullary tumor; Dabrafenib; Pediatric low-grade glioma.