An official website of the United States government
Here's how you know

Risk prediction in early childhood SHH medulloblastoma treated with radiation-avoiding chemotherapy: Evidence for more than two subgroups

Svenja Tonn [1], Andrey Korshunov [2] [3] [4], Denise Obrecht [1], Martin Sill [4] [5], Michael Spohn [1] [6] [7], Katja von Hoff [8], Till Milde [4] [9] [10], Torsten Pietsch [11], Tobias Goschzik [11], Brigitte Bison [12] [13], Björn-Ole Juhnke [1], Nina Struve [14] [15], Dominik Sturm [4] [5] [10], Felix Sahm [2] [3] [4], Michael Bockmayr [1] [6] [15] [16], Carsten Friedrich [17], André O von Bueren [18] [19], Nicolas U Gerber [20], Martin Benesch [21], David T W Jones [4] [22], Marcel Kool [4] [5] [23], Annika K Wefers [15] [24], Ulrich Schüller [1] [6] [24], Stefan M Pfister [4] [5] [10], Stefan Rutkowski [1], Martin Mynarek [1] [15]

Affiliations
PMID: 36715306   DOI: 10.1093/neuonc/noad027

Abstract

Background: The prognostic impact of clinical risk factors and DNA methylation patterns in sonic hedgehog (SHH)-activated early childhood desmoplastic/nodular medulloblastoma (DMB) or medulloblastoma with extensive nodularity (MBEN) were evaluated to better identify patients at risk for relapse.

Methods: Hundred-forty-four patients with DMB (n=99) or MBEN (n=45) aged <5 years and treated with radiation-sparing approaches, including intraventricular methotrexate in 132 patients, were evaluated.

Results: Patients with DMB had less favorable 5-year progression-free survival than MBEN (5y-PFS, 71% [DMB] vs 93% [MBEN]). Patients' age >3 years was associated with more unfavorable 5y-PFS (47% [>3 years] vs 85% [<1 year] vs 84% [1-3 years]). DNA methylation profiles available (n=78) were reclassified according to the 2021 WHO classification into SHH-1 (n=39), SHH-2 (n=38), and SHH-3 (n=1). Hierarchical clustering delineated two subgroups among SHH-2: SHH-2a (n=19) and SHH-2b (n=19). Patients with SHH-2b medulloblastoma were older, predominantly displayed DMB histology, and were more often located in the cerebellar hemispheres. Chromosome 9q losses were more frequent in SHH-2b, while few chromosomal alterations were observed in SHH-2a. SHH-2b medulloblastoma carried a significantly increased relapse risk (5y-PFS: 58% [SHH-2b] vs 83% [SHH-1] vs 95% [SHH-2a]). Subclassification of SHH-2 with key clinical and cytogenetic characteristics was confirmed using two independent cohorts (total n=188). Gene mutation analysis revealed a correlation of SHH-2a with SMO mutations.

Conclusion: These data suggest further heterogeneity within early childhood SHH-DMB/MBEN: SHH-2 splits into a very low-risk group SHH-2a enriched for MBEN histology and SMO mutations, and SHH-2b comprising older DMB patients with higher risk of relapse.

Keywords: DNA methylation profiling; Medulloblastoma; Risk prediction; Sonic hedgehog-activated.

LinkOut – more resources

Full Text Sources
Silverchair Information Systems

Miscellaneous
NCI CPTAC Assay Portal