World Journal of Advanced Research and Reviews
eISSN: 2581-9615 CODEN (USA): WJARAI
Cross Ref DOI: 10.30574/wjarr
Journal homepage: https://wjarr.com/

(CASE REPORT)

DESMOPLASTIC/NODULAR MEDULLOBLASTOMA IN A 2-YEAR-OLD CHILD WITH A FAVORABLE OUTCOME: A CASE REPORT AND LITERATURE REVIEW

Jala El-Biali [1], Andressa Balbi [2], Leander Galan [1], Corey Steinman [1], Cindy Almaraz [3], Jessica Jahoda [4] and Mohamed Aziz [5,*]

[1] American University of the Caribbean, AUC, St. Maarten.
[2] HCA Palms West Hospital, Florida, USA.
[3] Ross University School of Medicine, Barbados.
[4] Memorial Healthcare System, Pembroke Pines, FL, USA.
[5] Research Writing & Publication (RWP), LLC.
* Corresponding Author

ORCID Details
Jala El-Biali: https://orcid.org/0009-0004-8178-5483
Corey Steinman: https://orcid.org/0009-0002-5284-7337
Cindy Almaraz: https://orcid.org/0009-0007-7759-968X
Leander Galan: https://orcid.org/0009-0002-3969-9608
Mohamed Aziz: https://orcid.org/0000-0003-2397-0117
Jessica Jahoda: https://orcid.org/0009-0005-5196-3186

World Journal of Advanced Research and Reviews, 2026, 31(02), 965–971

Publication history: Received on 08 July 2026; revised on 17 August 2026; accepted on 19 August 2026

Article DOI: https://doi.org/10.30574/wjarr.2026.31.2.2156

ABSTRACT

Desmoplastic/nodular medulloblastoma (DNMB) is a histologically and molecularly distinct variant of a common pediatric embryonal brain tumor. DNMB is disproportionately represented among Sonic Hedgehog (SHH)-activated tumors in infants and very young children. When it is TP53-wildtype, a comparatively favorable prognosis is expected.

We report on a 2-year-old boy who presented with a four-week history of morning headaches, vomiting, lethargy, developmental regression, head tilt, and diplopia. Examination revealed papilledema, a setting-sun sign, and truncal ataxia; magnetic resonance imaging (MRI) demonstrated a heterogeneously enhancing vermian mass with fourth-ventricular extension and obstructive hydrocephalus. Following multidisciplinary tumor board discussion, the patient underwent suboccipital craniectomy with gross total resection. Histopathology confirmed DNMB, WHO grade 4, with immunohistochemistry (IHC) showing GAB1 and YAP1 positivity and absent nuclear beta-catenin, confirming SHH pathway activation; p53 was wildtype, and downstream testing identified Patched homolog 1 (PTCH1) pathway alterations.

Staging studies were negative for metastatic disease. Given his age, the patient received intensive, radiation-sparing chemotherapy rather than craniospinal irradiation. At 18-month follow-up, he remained in complete remission with only mild residual ataxia and age-appropriate neurocognitive function.

Keywords: Desmoplastic/nodular medulloblastoma; Sonic Hedgehog; WNT-activated, Sonic Hedgehog (SHH)-activated; SHH-activated; TP53-wildtype; Medulloblastoma molecular subgroups; Medulloblastoma four histological types

1 INTRODUCTION

Medulloblastoma is the most common malignant central nervous system tumor of childhood, arising in the cerebellum and classified as a WHO grade 4 embryonal neoplasm. [1] Among the four molecularly defined subgroups, WNT-activated, Sonic Hedgehog (SHH)-activated, and non-WNT/non-SHH (Group 3 and Group 4), the SHH-activated subgroup predominates in infants and very young children. It is disproportionately associated with the nodular/desmoplastic histologic variant. [2,3]

This clinicopathologic combination is particularly significant because, unlike classic or large-cell/anaplastic histology in the same age group, it defines a biologically favorable entity that can often be cured without the neurocognitively damaging craniospinal irradiation historically required for medulloblastoma. [4,5]

Affected children typically present with signs of posterior fossa mass effect and obstructive hydrocephalus, morning headache, vomiting, lethargy, ataxia, and, in the youngest patients, regression of previously acquired motor milestones, prompting neuroimaging that reveals a heterogeneously enhancing vermian or fourth-ventricular mass with restricted diffusion. [1] Diagnosis rests on histopathological confirmation of the characteristic biphasic nodular architecture together with IHC and molecular subgrouping, most practically GAB1 and YAP1 positivity with absent nuclear beta-catenin accumulation. [6]

Management centers on maximal safe resection followed by molecular-risk-adapted, radiation-sparing chemotherapy in very young children, an approach increasingly supported by favorable survival data specific to this histologic and molecular combination. [5,7]

We report a 2-year-old boy with SHH-activated, TP53-wildtype DNMB who achieved durable remission with preserved neurocognitive function, and we review the relevant literature.

2 CASE PRESENTATION

2.1 Clinical Presentation

A 2-year-old boy presented to the pediatric emergency department with a four-week history of progressively worsening morning headaches, intermittent vomiting, and increasing lethargy. His parents reported that he had become irritable and had started to regress in his developmental milestones, particularly in his ability to walk steadily, which he had achieved at 14 months.

Over the preceding week, he had developed a head tilt and appeared to be in discomfort. There was no history of recent trauma or infection. The family had initially attributed his symptoms to a viral illness. However, the persistence and escalation of symptoms, along with the new onset of diplopia, prompted them to seek medical attention.

2.2 Physical Examination and Diagnostic Workup

On physical examination, the child was afebrile and had a head circumference at the 95th percentile for his age. Fundoscopic examination revealed bilateral papilledema, and he exhibited a "setting-sun" sign with impaired upgaze. Neurological assessment demonstrated truncal ataxia, dysmetria on finger-to-nose testing, and a wide-based, unsteady gait. No other significant personal or family history was noted.

Brain MRI revealed a well-defined, heterogeneously enhancing mass lesion centered in the cerebellar vermis, extending into the fourth ventricle and causing obstructive hydrocephalus. The lesion demonstrated restricted diffusion on apparent diffusion coefficient (ADC) mapping, a finding characteristic of the high cellularity of medulloblastoma. Given the patient's age and tumor location, the primary differential diagnoses included medulloblastoma, anaplastic ependymoma, and atypical teratoid/rhabdoid tumor (AT/RT).

2.3 Multidisciplinary Tumor Board Discussion

The multidisciplinary tumor board discussed the case, including pediatric neuro-oncologists, neurosurgeons, neuroradiologists, and neuropathologists. The discussion centered on the patient's young age, the tumor's location, and the crucial need for molecular subtyping to guide therapy. The decision to proceed with surgical resection was unanimous, to achieve a gross total resection to alleviate the hydrocephalus and obtain definitive tissue for diagnosis. The board recognized that treatment would be heavily dependent on the molecular subgroup and metastatic status, and that a radiation-sparing strategy would be strongly preferred for this very young patient to avoid long-term neurocognitive deficits. The plan was to proceed with a suboccipital craniectomy for tumor resection, followed by postoperative MRI to assess the extent of resection and a lumbar puncture for cerebrospinal fluid (CSF) cytology to evaluate metastatic disease.

2.4 Treatment, Special Studies and Pathology

Histopathological examination of the resected tumor revealed a DNMB, which is classified as WHO grade 4. The microscopic examination showed the classic biphasic architectural pattern of DNMB, with a desmoplastic stromal background. There were well-circumscribed pale islands (nodules) and round-to-oval lighter pink areas distributed throughout the tissue. The nodules were relatively hypocellular and were composed of more uniform, mature neurocytic tumor cells, with reduced mitotic activity. In contrast, the internodular regions surrounding these islands were highly cellular, showing dark purple streams of densely packed primitive embryonal cells with hyperchromatic, pleomorphic nuclei and brisk mitotic activity. Dense intercellular collagenous and reticulin networks were prominent in the internodular areas. Homer-Wright rosettes, typical of the classic medulloblastoma variant, were rarely seen in scattered foci. (Figure 1, A, B, C)

To determine the molecular subgroup, IHC was performed. The tumor cells showed strong, diffuse positivity for GAB1 and YAP1, confirming activation of the Sonic Hedgehog (SHH) pathway. Conversely, the absence of nuclear β-catenin accumulation ruled out the WNT-activated subgroup.

Profiling for p53 showed a wildtype pattern with low expression, and the Ki-67 proliferation index was approximately 15–20% in the internodular areas. Downstream genetic evaluation confirmed underlying PTCH1 pathway alterations. Given the desmoplastic/nodular variant and a favorable p53-wildtype status, this patient's tumor aligned with a low-risk clinical profile within the SHH-activated molecular group.

2.5 Outcome and 18-Month Follow-up

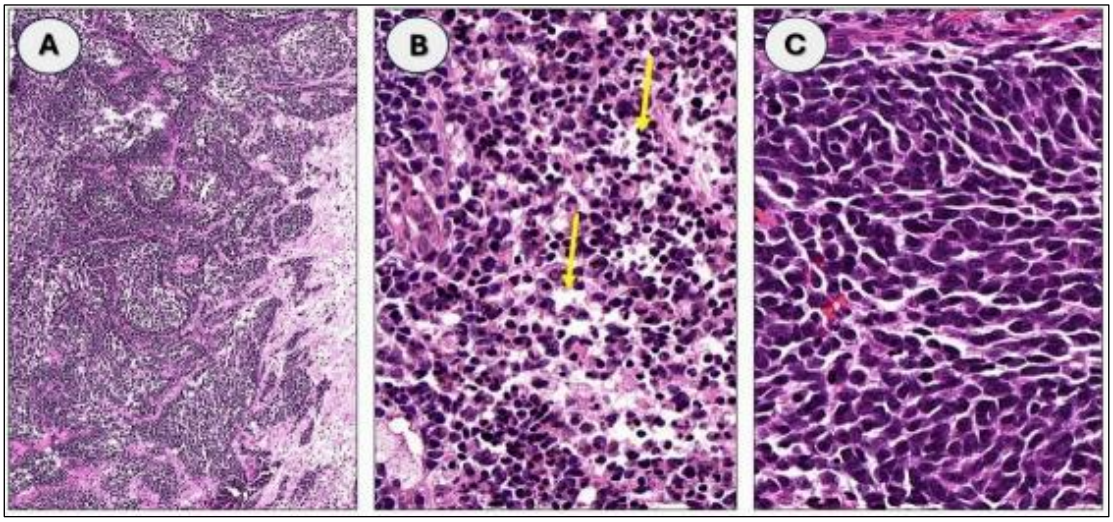

Figure 1: Microscopic features of desmoplastic/nodular histologic subtype of medulloblastoma

- 1A**:** Low-power view showing classic biphasic architectural patterns with pale islands (Nodules) and hypercellular internodular regions associated with dense intercellular collagenous and reticulin network (H&E X20)
- 1B**:** Intermediate-power view showing relatively hypocellular nodules consisting of more uniform, mature neurocytic tumor cells with reduced mitotic activity. Rare rosettes are identified (yellow arrows) (H&E X40)
- 1C**:** High-power view showing the highly cellular pale islands with dark purple streams of densely packed primitive embryonal cells featuring hyperchromatic, pleomorphic nuclei and brisk mitotic activity (H&E X60)

Following a gross total resection confirmed by postoperative MRI, staging studies including CSF cytology and spinal MRI were negative for metastatic disease, classifying the patient as average-risk. The tumor board recommended an intensive chemotherapy regimen to delay or avoid craniospinal irradiation, given the significant long-term neurocognitive risks in children under three years of age.

The patient received cycles of intensive chemotherapy (details are not available), which was complicated by episodes of myelosuppression requiring supportive care. At the 18-month follow-up, the patient was alive and in complete remission. Surveillance MRI scans showed no evidence of tumor recurrence. He continued to receive developmental support for mild residual ataxia; however, his neurocognitive function was reported to be within age-appropriate limits, a promising outcome that supported the decision for radiation-sparing therapy.

3 DISCUSSION

3.1 Background

Medulloblastoma is a WHO grade 4 embryonal tumor of the cerebellum. It remains the most common malignant central nervous system neoplasm of childhood, accounting for approximately 20-25% of pediatric CNS tumors and roughly 300-350 new diagnoses annually in the United States. [1,8]

What was once classified purely by histology is now understood to comprise four molecularly and clinically distinct entities: among children aged 0-14 years, embryonal tumors account for the large majority of medulloblastoma diagnoses, and SHH-activated, TP53-wildtype disease represents the single most common molecular subtype in this age band. [8,15] Incidence follows a bimodal age distribution, with an early childhood peak and a smaller peak in later childhood and adolescence, a pattern that corresponds to the distinct age clustering of the WNT and non-WNT/non-SHH subgroups in older children versus the characteristic enrichment of the SHH subgroup in infants and, separately, in adolescents and young adults. [4,9] Although SHH-activated tumors account for only about one-quarter of medulloblastoma overall, they constitute the majority of tumors diagnosed in infants and children younger than three to four years. [3]

Nodular/desmoplastic histology, together with its extreme variant of extensive nodularity, is disproportionately concentrated within this SHH-activated, young-age population, even though classic histology remains numerically most common across the pediatric population as a whole. [1,10] The WHO 2021 fifth edition classification of central nervous system tumors formalizes this biology by defining medulloblastoma along two parallel axes: four molecular subgroups, WNT-activated, SHH-activated and TP53-wildtype, SHH-activated and TP53-mutant, and non-WNT/non-SHH, and four histological types, classic, desmoplastic/nodular, medulloblastoma with extensive nodularity, and large cell/anaplastic, a dual framework that directly shaped the diagnostic workup and risk stratification applied in the present case. [1,11,12,13]

3.2 Pathogenesis, Pathophysiology

SHH-activated medulloblastoma arises from constitutive, ligand-independent activation of the Sonic Hedgehog signaling cascade, most often through loss-of-function mutations in the tumor-suppressor receptor PTCH1, which normally restrains the transmembrane effector Smoothened (SMO), through activating SMO mutations, or through loss-of-function alterations in suppressor of fused homolog (SUFU), a negative regulator acting downstream of SMO. Each lesion converges on unrestrained activity of the GLI family of transcription factors, driving unchecked proliferation of cerebellar granule neuron precursors, the presumed cell of origin for this subgroup. [2,14,15,16]

Germline SUFU mutations are notably enriched among children younger than three years with desmoplastic/nodular histology, providing a mechanistic link between this specific genotype and the infantile, nodular phenotype. [17]

The desmoplastic/nodular architecture itself, reticulin-free pale islands of neurocytic differentiation surrounded by reticulin-rich internodular stroma, is thought to reflect abortive neuronal differentiation imposed on SHH-driven precursor cells. This explains why this histology consistently tracks with SHH activation and with the developmental window of infancy and early childhood. [2,4,10] Within this subgroup, TP53 status further stratifies prognosis: TP53-mutant SHH tumors, often germline and associated with Li-Fraumeni syndrome, arise almost exclusively in older children, favor large-cell/anaplastic histology, and behave aggressively, whereas TP53-wildtype tumors, the category into which desmoplastic infant tumors such as the present case fall, carry a comparatively favorable biology, particularly when combined with nodular histology and complete surgical resection. [18,19]

3.3 Comparative Analysis of Our Case with Existing Literature

The presentation, histology, and immunophenotype of the present case closely mirror those reported by Goode and colleagues, whose 11-month-old patient with desmoplastic/nodular medulloblastoma likewise presented with truncal ataxia, head tilt, lethargy, and emesis, and whose tumor was confirmed SHH-activated and TP53-wildtype using an essentially identical GAB1/YAP1/beta-catenin IHC panel. [20]

Similarly, Kratz and colleagues described a 13-month-old girl with desmoplastic medulloblastoma, vomiting, ataxia, and developmental regression who, like the present patient, was treated with intensive multiagent chemotherapy, including high-dose methotrexate, and achieved complete remission without irradiation, underscoring the reproducibility of this radiation-sparing strategy across institutions. [21]

Šoukalová and colleagues reported a 21-month-old girl with desmoplastic/nodular medulloblastoma harboring a germline SUFU deletion, illustrating the hereditary predisposition that can underlie this histologic and molecular combination; however, germline testing was not pursued in the present patient, and this possibility remains unconfirmed rather than excluded. [22]

At the cohort level, the Head Start III trial demonstrated markedly superior five-year event-free and overall survival (89 percent each) for nodular/desmoplastic histology compared with classic or large-cell/anaplastic tumors, directly supporting the favorable trajectory observed in this patient. [5]

In contrast, the Children's Oncology Group ACNS1221 trial, which used a chemotherapy regimen without high-dose or intraventricular methotrexate, closed early due to unexpectedly frequent relapse in this same histologic and molecular subgroup, a divergence that highlights how outcome is highly regimen-dependent rather than guaranteed by biology alone, and that reinforces the rationale for the methotrexate-intensive protocol selected for the present patient. [23]

4 WHAT HAVE WE LEARNED FROM THIS CASE?

This case reinforces several practical issues for clinicians managing posterior fossa tumors in very young children. Subtle, evolving symptoms, morning headache, vomiting, irritability, and especially regression of previously acquired motor milestones, should prompt urgent neuroimaging rather than attribution to a viral illness, since developmental regression is a red flag that should distinguish a possible intracranial mass from self-limited illness. [1]

Histopathological typing alone is insufficient; a focused IHC panel of GAB1, YAP1, beta-catenin, and p53, feasible in most neuropathology laboratories without requiring methylation array profiling, can reliably identify the SHH-activated, TP53-wildtype, desmoplastic phenotype that defines a genuinely low-risk biological entity. [6,19]

This case, together with the comparator literature, affirms that gross total resection followed by sufficiently intensive, methotrexate-based chemotherapy can achieve durable remission while sparing very young children from craniospinal irradiation and its well-documented, age-dependent neurocognitive morbidity. [24,25]

Finally, the divergent outcomes between chemotherapy regimens of differing intensity in the comparator trials caution against treating SHH activation, desmoplastic histology, and infancy as an automatic guarantee of cure; regimen selection, particularly the inclusion of high-dose or intraventricular methotrexate, meaningfully affects survival and should be individualized through multidisciplinary tumor board discussion, as occurred in this case. [5,7,23]

4.1 Abbreviations

- Desmoplastic/nodular medulloblastoma (DNMB)
- Sonic Hedgehog (SHH)
- immunohistochemistry (IHC)
- Patched homolog 1 (PTCH1)
- Smoothened (SMO)
- Fused homolog (SUFU)

5 CONCLUSION

This case of a 2-year-old boy with SHH-activated, TP53-wildtype nodular/desmoplastic medulloblastoma who achieved gross total resection, avoided craniospinal irradiation, and remained in complete remission with age-appropriate neurocognitive function at 18 months illustrates the favorable trajectory now recognized for this specific molecular and histologic combination. By documenting the clinical presentation, diagnostic pathway, immunohistochemical and molecular workup, and radiation-sparing treatment course in detail, and by situating them alongside comparable

published cases and cooperative-group trials, this report reinforces the growing consensus that biology-driven, risk-adapted therapy can spare very young children the long-term consequences of radiotherapy without compromising survival.

We share this case to help pediatric oncology and neuropathology teams recognize this entity promptly and to add to the still-limited body of individually reported outcomes in this population.

STATEMENTS ON COMPLIANCE WITH ETHICAL STANDARDS

Acknowledgments

Special thanks to Karen Sanabria for her assistance in reviewing the final manuscript. Additionally, we appreciate the assistance of Grammarly's language editor and the Manus 1.6 program, which provided valuable writing support by identifying and correcting errors in grammar, spelling, punctuation, and writing style, ultimately enhancing the manuscript.

Disclosure of conflict of interest

All authors make the following declarations:

- Payment/services information: All authors have declared that they received no financial support from any organization for the submitted work.
- Financial relationships: All authors have declared that they have no financial relationships at present or within the previous three years with any organizations that might be interested in the submitted work.

Statement of ethical approval

This research does not include any studies involving animal or human subjects by any of the authors. This study was conducted as a retrospective review of archival pathology material collected during routine clinical care. All data were fully de-identified prior to analysis.

Statement of informed consent

Informed consent was obtained from the patient’s family for publication of this case.

Data access statement

All relevant data are included in the paper.

Author contributions

All authors contributed equally to producing this manuscript.

REFERENCES

[1] Guild A, Raulji C, Karsonovich T, et al. Medulloblastoma. StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; updated 2024. Available from: https://www.ncbi.nlm.nih.gov/books/NBK431069/

[2] Northcott PA, Robinson GW, Kratz CP, et al. Medulloblastoma. Nat Rev Dis Primers. 2019;5(1):11.

[3] Frappaz D, et al. Clinical, histological, and molecular prognostic factors in childhood medulloblastoma: where do we stand? Diagnostics (Basel). 2023;13(11):1915.

[4] DeWitt J. SHH activated. PathologyOutlines.com website. https://www.pathologyoutlines.com/topic/cnstumortumorshhactivated.html. Accessed Aug 16, 2026.

[5] Dhall G, O'Neil SH, Ji L, et al. Excellent outcome of young children with nodular desmoplastic medulloblastoma treated on "Head Start" III: a multi-institutional, prospective clinical trial. Neuro Oncol. 2020;22(12):1862-1872.

[6] Chiang J, Moreira DC, Pytel NJ, Liu YC, Blackburn PR, Shi Z, Cardenas M, Wheeler DA, Furtado LV. A CTNNB1 ‐ altered medulloblastoma shows the immunophenotypic, DNA methylation and transcriptomic profiles of SHH ‐ activated, and not WNT ‐ activated, medulloblastoma. Neuropathology and applied neurobiology. 2022 Aug;48(5):e12815.

[7] Finlay J, Mynarek M, Dhall G, et al. Chemotherapy strategies for young children newly diagnosed with desmoplastic/extensive nodular medulloblastoma up to the era of molecular profiling: a comparative outcomes analysis of prospective multi-center European and North American trials. Neuro Oncol. 2021;23(Suppl 4):iv6.

[8] Huang A M, Coppes M J, et al. Pediatric medulloblastoma: background, epidemiology, etiology. Medscape. Updated 2026. Available from: https://emedicine.medscape.com/article/987886-overview

[9] Kee Kiat Yeo, Michael SD Agus. Medulloblastoma. Merck Manual Professional Edition. Updated 2024. Available from: https://www.merckmanuals.com/professional/oncology/pediatric-cancers/medulloblastoma

[10] Min HS, Lee JY, Kim SK, Park SH. Genetic grouping of medulloblastomas by representative markers in pathologic diagnosis. Translational Oncology. 2013 Jun 1;6(3):265-72.

[11] Ryall S. Medulloblastoma, histologically defined. Atlas Genet Cytogenet Oncol Haematol. 2023. Available from: https://atlasgeneticsoncology.org/solid-tumor/209198

[12] Jackson K, Packer RJ. Recent advances in pediatric medulloblastoma. Current Neurology and Neuroscience Reports. 2023 Dec;23(12):841-8.

[13] Kool M, Korshunov A, Remke M, et al. Molecular subgroups of medulloblastoma: an international meta-analysis of transcriptome, genetic aberrations, and clinical data of WNT, SHH, Group 3, and Group 4 medulloblastomas. Acta Neuropathol. 2012;123(4):473-484.

[14] Kool M, Jones DTW, Jäger N, et al. Genome sequencing of SHH medulloblastoma predicts genotype-related response to smoothened inhibition. Cancer Cell. 2014;25(3):393-405.

[15] Eibl RH, Schneemann M. Medulloblastoma: from TP53 mutations to molecular classification and liquid biopsy. Biology. 2023 Feb 8;12(2):267.

[16] Kieran MW. Targeted treatment for sonic hedgehog-dependent medulloblastoma. Neuro-oncology. 2014 Jun 20;16(8):1037-47..

[17] Brugières L, Remenieras A, Pierron G, et al. High frequency of germline SUFU mutations in children with desmoplastic/nodular medulloblastoma younger than 3 years of age. J Clin Oncol. 2012;30(17):2087-2093.

[18] Babaoglu B, Hanalioglu S, Varan A, Oguz KK, Bilginer B, Dolgun A, Soylemezoglu F. Molecular subgrouping based on immunohistochemistry in medulloblastoma: A single-center experience. Turk Neurosurg. 2024 Jan 1;34(6):999-1008.

[19] Zhukova N, Ramaswamy V, Remke M, et al. Subgroup-specific prognostic implications of TP53 mutation in medulloblastoma. J Clin Oncol. 2013;31(23):2927-2935.

[20] Goode E, Montoya L, Graham E, et al. Diagnostic and prognostic implications of GNAS inactivation in sonic hedgehog-activated medulloblastoma: case report with comprehensive molecular profiling and review of literature. JCO Precis Oncol. 2022;6:e2100403.

[21] Kratz CP, Hoell JI, et al. Diagnostic challenges in a child with early-onset desmoplastic medulloblastoma and homozygous variants in MSH2 and MSH6. Eur J Hum Genet. 2018;26(3):440-444.

[22] Šoukalová J, Vejmělková K, Cermanová T, et al. Identification of a family with SUFU germline deletion based on a case of desmoplastic medulloblastoma in an infant. Klin Onkol. 2016;29(Suppl 1):83-88.

[23] Lafay-Cousin L, Bouffet E, Strother D, et al. Phase II study of nonmetastatic desmoplastic medulloblastoma in children younger than 4 years of age: a report of the Children's Oncology Group (ACNS1221). J Clin Oncol. 2020;38(3):223-231.

[24] Merchant TE, et al. Impact of craniospinal dose, boost volume, and neurologic complications on intellectual outcomes in patients with medulloblastoma. J Clin Oncol. 2014;32(17):1760-1768.

[25] Palmer SL, et al. Patterns of intellectual development among survivors of pediatric medulloblastoma: a longitudinal analysis. J Clin Oncol. 2001;19(8):2302-2308.