

Diffuse Skeletal and Bone Marrow Metastases from Adult Medulloblastoma Presenting with Severe Pancytopenia: A Case Report

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DOI: <https://doi.org/10.36347/sjmcr.2026.v14i10.035>

| Received: 19.08.2026 | Accepted: 12.10.2026 | Published: 14.10.2026

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Abstract

Case Report

Background: Medulloblastoma is a malignant embryonal tumor occurring predominantly in children. Extraneural dissemination is rare, particularly in adults, with skeletal and bone marrow metastases representing an uncommon and aggressive pattern of relapse. **Case presentation:** We report a 27-year-old man with a posterior fossa non-WNT/non-SHH medulloblastoma, CNS WHO grade 4, treated with surgical resection, carboplatin–etoposide chemotherapy, and craniospinal irradiation (36 Gy with an 18-Gy boost). Complete radiological regression was initially achieved. Five months after chemotherapy, the patient developed recurrent severe epistaxis and pancytopenia. Imaging revealed diffuse mixed osteolytic and osteosclerotic skeletal lesions associated with suspected local intracranial recurrence. Bone marrow biopsy confirmed metastatic medulloblastoma. Temozolomide was planned but could not be initiated because of persistent severe thrombocytopenia and hemorrhagic manifestations despite transfusional support. The patient died in April 2025. **Conclusion:** Diffuse skeletal and bone marrow metastases are a rare and aggressive manifestation of adult medulloblastoma. Unexplained cytopenias should raise suspicion of marrow involvement, which may reveal systemic relapse and preclude further systemic therapy.

Keywords: Medulloblastoma; Adult; Extraneural metastasis; Bone metastasis; Bone marrow metastasis; Pancytopenia.

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INTRODUCTION

Medulloblastoma is a highly malignant embryonal tumor of the central nervous system, predominantly affecting children and rarely occurring in adults. Adult medulloblastoma accounts for approximately 0.4–1% of adult central nervous system tumors and differs from its pediatric counterpart in terms of molecular distribution and clinical behavior [1,2,10,11].

Medulloblastoma typically disseminates through cerebrospinal fluid pathways, leading to leptomeningeal and spinal metastases, whereas extraneural dissemination is uncommon [1,3]. When systemic spread occurs, the skeleton is among the most frequently involved sites, while bone marrow involvement is less commonly reported [3–6]. Proposed mechanisms include hematogenous dissemination, surgical disruption of anatomical barriers, and cerebrospinal fluid diversion procedures [3,5].

We report a rare case of non-WNT/non-SHH medulloblastoma in a young adult who developed diffuse skeletal and bone marrow metastases following multimodal treatment, associated with a radiologically suspected local intracranial recurrence. Systemic relapse was revealed by severe recurrent epistaxis and pancytopenia, with bone marrow involvement subsequently confirmed histologically.

CASE PRESENTATION

A 27-year-old man with no significant medical history presented with an approximately one-year history of progressive headache, vomiting, and diplopia, consistent with intracranial hypertension. Brain imaging revealed a solid-cystic posterior fossa mass centered on the fourth ventricle, measuring 27 × 19 × 38 mm, associated with perilesional edema and upstream triventricular hydrocephalus. (Figures 1 and 2)

Citation: Elghanemy, M., Chafri, A., Belkhal, M., Igarramen, T., Laatitoui, S., Saadoun, M., Oumghar, N., Barkiche, S., Darfaoui, M., El Omrani, A., & Khouchani, M. (2026). Diffuse Skeletal and Bone Marrow Metastases from Adult Medulloblastoma Presenting with Severe Pancytopenia: A Case Report. *Sch J Med Case Rep*, 14(10), 2269-2273. <https://doi.org/10.36347/sjmcr.2026.v14i10.035>

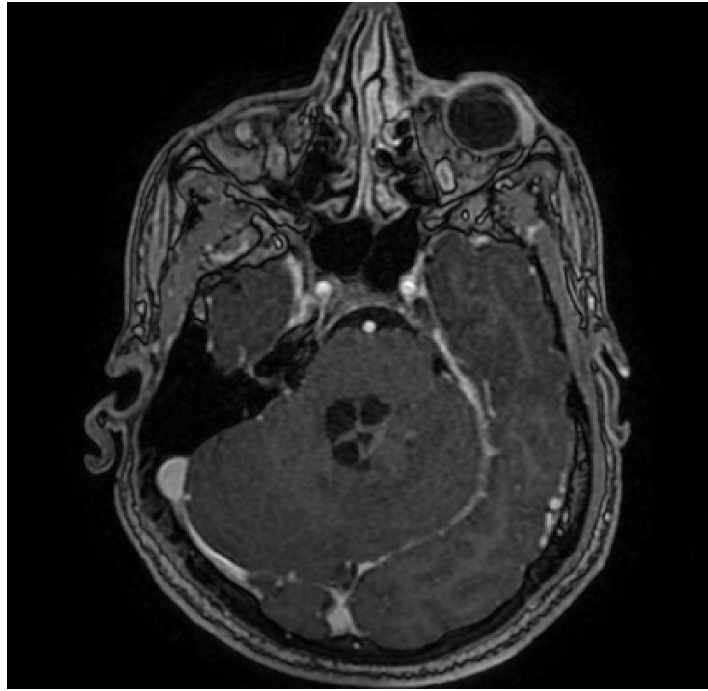


Figure 1: Preoperative axial contrast-enhanced T1-weighted brain MRI demonstrating a solid-cystic posterior fossa mass centered on the fourth ventricle



Figure 2: Preoperative axial T2-weighted brain MRI demonstrating the solid-cystic posterior fossa mass, with prominent hyperintense cystic components

On January 6, 2024, the patient underwent ventriculoperitoneal shunt placement followed by surgical resection of the posterior fossa tumor. Histopathological examination revealed a highly cellular malignant round-cell tumor composed of sheets and cords of poorly differentiated cells, with occasional rosette formation. Immunohistochemistry showed synaptophysin positivity, whereas OLIG2, β -catenin, GAB1, and p53 were negative, with a Ki-67 proliferation index of approximately 25%. The final diagnosis was a

histologically defined non-WNT/non-SHH medulloblastoma, CNS WHO grade 4.

Postoperative brain MRI performed on February 20, 2024, demonstrated a residual left-sided tumor centered on the left middle cerebellar peduncle, measuring 21×15.5 mm. Concurrent spinal MRI showed no evidence of spinal metastatic disease. Cerebrospinal fluid cytology was not performed.

Because of a delay in radiotherapy initiation, the patient received two cycles of carboplatin plus etoposide on March 18 and April 15, 2024. Craniospinal irradiation was subsequently delivered from May 6 to June 15, 2024, with 36 Gy to the craniospinal axis followed by an 18-Gy boost to the posterior fossa/tumor bed, resulting in a total dose of 54 Gy to the boosted volume. Two additional cycles of carboplatin plus etoposide were administered after radiotherapy, completing a total of four cycles, with the final cycle administered on August 1, 2024.

Follow-up medical records reported complete radiological regression of the postoperative residual tumor, and surveillance was initiated.

In January 2025, approximately five months after completion of chemotherapy, the patient developed

recurrent severe epistaxis requiring hospitalization and repeated nasal packing. Laboratory investigations revealed pancytopenia requiring repeated red blood cell and platelet transfusions. Bone marrow aspiration was diluted but demonstrated extrahematopoietic cells suspicious for metastatic involvement.

On February 4, 2025, brain MRI demonstrated a $13 \times 14 \times 22$ -mm posterior fossa lesion suspicious for local intracranial recurrence (Figure 3). Spinal MRI performed during the same assessment demonstrated multiple diffuse abnormal marrow signal changes involving the vertebral bodies, posterior vertebral arches, and sternum, consistent with diffuse secondary osseous involvement, without epidural or intramedullary extension (Figure 4).

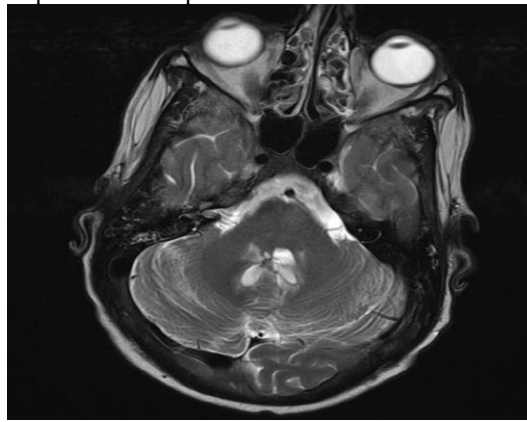


Figure 3: Axial T2-weighted brain MRI demonstrating the posterior fossa lesion suspicious for local intracranial recurrence



Figure 4: Sagittal T2-weighted whole-spine MRI showing diffuse multifocal abnormal marrow signal consistent with extensive skeletal metastatic involvement, without epidural or intramedullary extension

Thoracoabdominopelvic computed tomography performed on February 4, 2025, revealed widespread mixed osteolytic and osteosclerotic lesions involving the axial and peripheral skeleton.

Bone marrow biopsy performed on February 13, 2025, demonstrated marrow infiltration by a malignant round-cell tumor. Immunohistochemical analysis confirmed metastatic involvement by the previously diagnosed medulloblastoma.

Despite transfusional support, severe cytopenias persisted. On February 25, 2025, hemoglobin was 5.5 g/dL and the platelet count was $13 \times 10^9/L$.

Systemic salvage therapy with temozolomide was planned. However, persistent severe thrombocytopenia associated with ongoing epistaxis prevented treatment initiation. Despite repeated supportive transfusions with red blood cells and platelet concentrates, including apheresis platelet concentrates, adequate hematologic recovery could not be achieved. The patient's clinical condition progressively deteriorated, and he died in April 2025.

DISCUSSION

Extraneural metastases of medulloblastoma are uncommon, particularly in adults, as dissemination predominantly occurs through cerebrospinal fluid pathways [1,3]. When systemic dissemination occurs, however, the skeleton is the most frequently involved site. In a review of adult cases with extracranial metastases, bone involvement was reported in 77% of patients [3]. Bone marrow involvement has also been documented but remains considerably less frequently reported [4,6,8,9].

Our patient developed an early and extensive systemic relapse characterized by diffuse mixed osteolytic and osteosclerotic lesions involving the axial and peripheral skeleton, together with histologically confirmed bone marrow metastasis. Importantly, brain MRI simultaneously demonstrated a posterior fossa lesion suspicious for local intracranial recurrence. Therefore, this presentation should be considered systemic skeletal and marrow dissemination associated with suspected intracranial recurrence rather than an isolated extraneural relapse.

Several mechanisms have been proposed to explain extraneural dissemination, including hematogenous spread, surgical disruption of anatomical barriers, and dissemination associated with cerebrospinal fluid diversion procedures [3,5]. Although our patient underwent ventriculoperitoneal shunt placement, the diffuse skeletal and marrow distribution may suggest hematogenous dissemination; however, the mechanism cannot be definitively established.

A distinctive feature of our case was that systemic relapse was clinically revealed by severe recurrent epistaxis and pancytopenia rather than predominantly by skeletal symptoms. Extensive bone marrow infiltration may suppress normal hematopoiesis, resulting in anemia, thrombocytopenia, or pancytopenia and substantial transfusional requirements [4,6,8].

Spencer *et al.*, described bone marrow metastatic involvement in medulloblastoma associated with hematological abnormalities [4]. Similarly, Clifton *et al.*, reported an adult patient with recurrent medulloblastoma who developed pancytopenia associated with diffuse osseous and bone marrow metastatic disease [6]. These observations emphasize that otherwise unexplained cytopenias during medulloblastoma follow-up should raise suspicion of marrow involvement and prompt appropriate investigations, including bone marrow biopsy.

Treatment of recurrent adult medulloblastoma remains challenging, particularly in disseminated disease, and no universally established salvage regimen exists [1]. In our patient, temozolomide was planned as systemic salvage therapy. However, persistent severe thrombocytopenia with active recurrent epistaxis despite intensive transfusional support prevented treatment initiation.

The patient died approximately two months after histological confirmation of bone marrow metastasis. This case therefore illustrates an important therapeutic challenge of extensive marrow dissemination: metastatic marrow failure may not only represent a manifestation of aggressive systemic disease but may itself preclude the administration of potentially active systemic therapy.

CONCLUSION

Diffuse skeletal and bone marrow metastases represent a rare but particularly aggressive pattern of systemic dissemination in adult medulloblastoma. This case illustrates that bone marrow involvement may present primarily through hematological manifestations, including severe pancytopenia and recurrent bleeding, rather than through skeletal symptoms.

Therefore, unexplained cytopenias in patients previously treated for medulloblastoma should prompt consideration of metastatic bone marrow involvement and appropriate investigation. Early recognition is important, as profound marrow failure may indicate extensive disease while simultaneously compromising the feasibility of salvage systemic therapy and contributing to an unfavorable outcome.

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