

Secondary High-Grade Astrocytoma after Craniospinal Irradiation for Medulloblastoma: A Case Report

Jackes Burga Salazar

burgasalazar@gmail.com

National University of San Marcos

Rolando Rojas Apaza

Hospital Nacional Edgardo Rebagliati Martins

Alan Latorre

Hospital Nacional Edgardo Rebagliati Martins

J. Lorena Vera Ubillus

National University of San Marcos

Case Report

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Abstract

Background

Craniospinal irradiation (CSI) for pediatric medulloblastoma improves survival but is associated with an increased risk of radiation-induced second primary neoplasms (SPNs), which can be difficult to distinguish from tumor recurrence.

Case presentation

We report a 14-year-old male treated with surgery, CSI, and chemotherapy for desmoplastic/nodular medulloblastoma (WHO grade IV), whose treatment course was complicated by pulmonary tuberculosis requiring temporary interruption of therapy. After six years of disease-free follow-up, he developed new neurological symptoms; imaging revealed a contralateral posterior fossa lesion, and histopathology confirmed a histologically distinct WHO grade III astrocytoma, consistent with a second primary neoplasm rather than recurrence. Despite gross total resection, the patient experienced rapid neurological deterioration and died of infectious and systemic complications.

Conclusions

This case highlights the risk of radiation-induced high-grade gliomas in pediatric medulloblastoma survivors and underscores the importance of distinguishing recurrence from a second primary neoplasm, maintaining long-term radiological surveillance, and considering strategies such as proton therapy to reduce late radiation-induced complications.

BACKGROUND

Medulloblastoma is the most common malignant brain tumor in childhood. Although multimodal treatment has improved survival, craniospinal irradiation (CSI) is associated with an increased risk of radiation-induced second primary neoplasms^{1–3}, especially in pediatric patients due to the radiosensitivity of developing tissues and their longer life expectancy^{4,5}.

Radiation-induced complications may manifest years or decades later and include central nervous system neoplasms, among the most devastating². The risk of meningiomas increases progressively over time, whereas radiation-induced gliomas exhibit a shorter latency and a distinct biological behavior.^{4,5}

In this context, we present the case of a patient with medulloblastoma treated with craniospinal irradiation (CSI) and chemotherapy, who developed a grade III astrocytoma six years later, highlighting the importance of considering secondary neoplasms in the presence of new neurological symptoms in survivors of pediatric cancer.^{3,6}

CASE PRESENTATION

A 14-year-old male with no significant past medical history and no family history of malignancy, genetic syndromes, or neurological disorders presented in June 2019 with progressive moderate-to-severe holocranial headache, exacerbated by Valsalva maneuvers and associated with dizziness and vomiting. Physical examination revealed no focal neurological deficits. An emergency computed tomography (CT) scan demonstrated obstructive hydrocephalus with panventricular dilatation secondary to a posterior fossa lesion. Due to clinical and radiological evidence of increased intracranial pressure, a ventriculoperitoneal shunt was placed. Subsequently, brain magnetic resonance imaging (MRI) was performed for further characterization of the lesion, revealing a left cerebellar mass (Fig. 1). The patient then underwent elective suboccipital craniotomy with gross total tumor resection. Histopathological examination confirmed desmoplastic/nodular medulloblastoma (WHO grade IV), with negative β -catenin, reactive p53 expression, and elevated Ki-67 in the internodular areas (Fig. 2A).

Subsequently, he received craniospinal irradiation and chemotherapy according to the Packer protocol. Treatment was temporarily interrupted because of cavitary pulmonary tuberculosis and resumed after completion of a standard six-month antituberculous regimen consisting of a two-month intensive phase with isoniazid, rifampicin, pyrazinamide, and ethambutol (HRZE), followed by a four-month continuation phase with isoniazid and rifampicin (HR). No severe treatment-related toxicities were documented. The patient subsequently completed eight cycles of chemotherapy. Between 2021 and 2022, follow-up magnetic resonance imaging showed no evidence of recurrence.

In 2025, six years after the initial diagnosis, the patient developed headache, dysarthria, hemianopsia, and oculomotor disturbances. Neurological examination showed findings consistent with posterior fossa involvement. Brain computed tomography (CT) demonstrated a new right cerebellar lesion with mass effect on the fourth ventricle (Fig. 3). Differential diagnoses included medulloblastoma recurrence, radiation necrosis, and a radiation-induced secondary neoplasm. The contralateral location of the lesion relative to the original tumor and the prolonged disease-free interval raised suspicion of a second primary tumor. The patient underwent suboccipital craniotomy with gross total tumor resection, and histopathological examination confirmed a WHO grade III astrocytoma, histologically distinct from the original medulloblastoma and consistent with a second primary neoplasm (Fig. 2B). No adjuvant radiotherapy or chemotherapy was administered following surgery, and management was focused on symptomatic and supportive care. The patient subsequently experienced progressive neurological deterioration and infectious complications, ultimately developing infectious respiratory failure and dying on October 30, 2025, at the age of 21 years.

DISCUSSION AND CONCLUSIONS

The present case illustrates one of the most critical complications in survivors of pediatric medulloblastoma: the development of a second primary neoplasm (SPN) within the central nervous system. Although current protocols of craniospinal irradiation (CSI) and chemotherapy have improved

survival, this benefit is accompanied by a risk of radiogenic stochastic effects. In this patient, the six-year latency period between the diagnosis of desmoplastic medulloblastoma and the appearance of a WHO grade III astrocytoma is consistent with the dynamics described for radiation-induced gliomas, which typically exhibit shorter latency than meningiomas.^{2,3}

Histopathological distinction was crucial: the initial tumor was a medulloblastoma (WHO grade IV), whereas the new lesion corresponded to a WHO grade III astrocytoma, confirming an SPN rather than recurrence. This finding fulfills one of the key criteria for radiation-induced neoplasms, namely the development of a histologically distinct tumor after a latency period within a previously irradiated field. This distinction is clinically relevant, as it directly impacts therapeutic decision-making and prognosis. According to Bavle et al,⁵ gliomas are among the most frequent SPNs following radiotherapy in medulloblastoma patients. The radiosensitivity of developing brain tissue promotes the accumulation of genomic damage, reflecting a dose-dependent phenomenon.^{1,4}

The clinical course was marked by interruption of treatment due to pulmonary tuberculosis. Although not directly causally related, this introduced confounding factors. Nevertheless, the development of the astrocytoma is attributable to exposure to CSI, reinforcing the need to optimize techniques such as proton therapy.¹ This report has several limitations. Molecular characterization was not available for either tumor, precluding comparative genomic analyses that could further support the distinction between the primary medulloblastoma and the secondary astrocytoma. In addition, detailed radiotherapy dosimetry was unavailable, preventing precise assessment of the radiation dose delivered to the site where the secondary neoplasm subsequently developed. Finally, although pulmonary tuberculosis may have influenced the patient's overall clinical course and treatment timeline, no evidence supports a causal relationship between this event and the development of the secondary neoplasm.

The fatal outcome underscores the aggressiveness of these neoplasms and the need for prolonged surveillance. Progression after six years of stability highlights the importance of long-term follow-up and strategies aimed at early detection of SPNs in survivors.^{3,4} This case reinforces the need for tailored surveillance strategies in long-term survivors of pediatric brain tumors.

In conclusion, this case underscores that the control of pediatric medulloblastoma entails a risk of radiation-induced second neoplasms. The occurrence of a high-grade astrocytoma after six years of stability highlights the need for lifelong radiological surveillance and histopathological confirmation in the presence of new symptoms. It also emphasizes the importance of optimizing radiotherapy techniques to reduce exposure of healthy tissue. The observed latency period is consistent with radiogenic gliomas, requiring a high index of suspicion during long-term follow-up.

Abbreviations

CSI

Craniospinal irradiation

SPN
Second primary neoplasm
WHO
World Health Organization
MRI
Magnetic resonance imaging
CT
Computed tomography
HRZE
Isoniazid, rifampicin, pyrazinamide, ethambutol
HR
Isoniazid, rifampicin.

Declarations

Ethics approval and consent to participate

This case report was reviewed by Hospital Edgardo Rebagliati Martins, ethics department reference number and was approved, in accordance with the Declaration of Helsinki.

Consent for publication

Written informed consent was obtained from the patient's legal guardian for publication of this case report and any accompanying clinical images.

Availability of data and materials

The datasets used and/or analysed during the current case report are available from the corresponding author on reasonable request.

Competing interests

The authors declare that they have no competing interests.

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Authors' contributions

JBS drafted the manuscript and acquired clinical data. RRA performed the surgical procedures, supervised patient management, and critically revised the manuscript for important intellectual content. ALT performed and interpreted the histopathological examination. LVU contributed to literature review and critical revision of the manuscript for important intellectual content.

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Authors' information

Not applicable.

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Figures

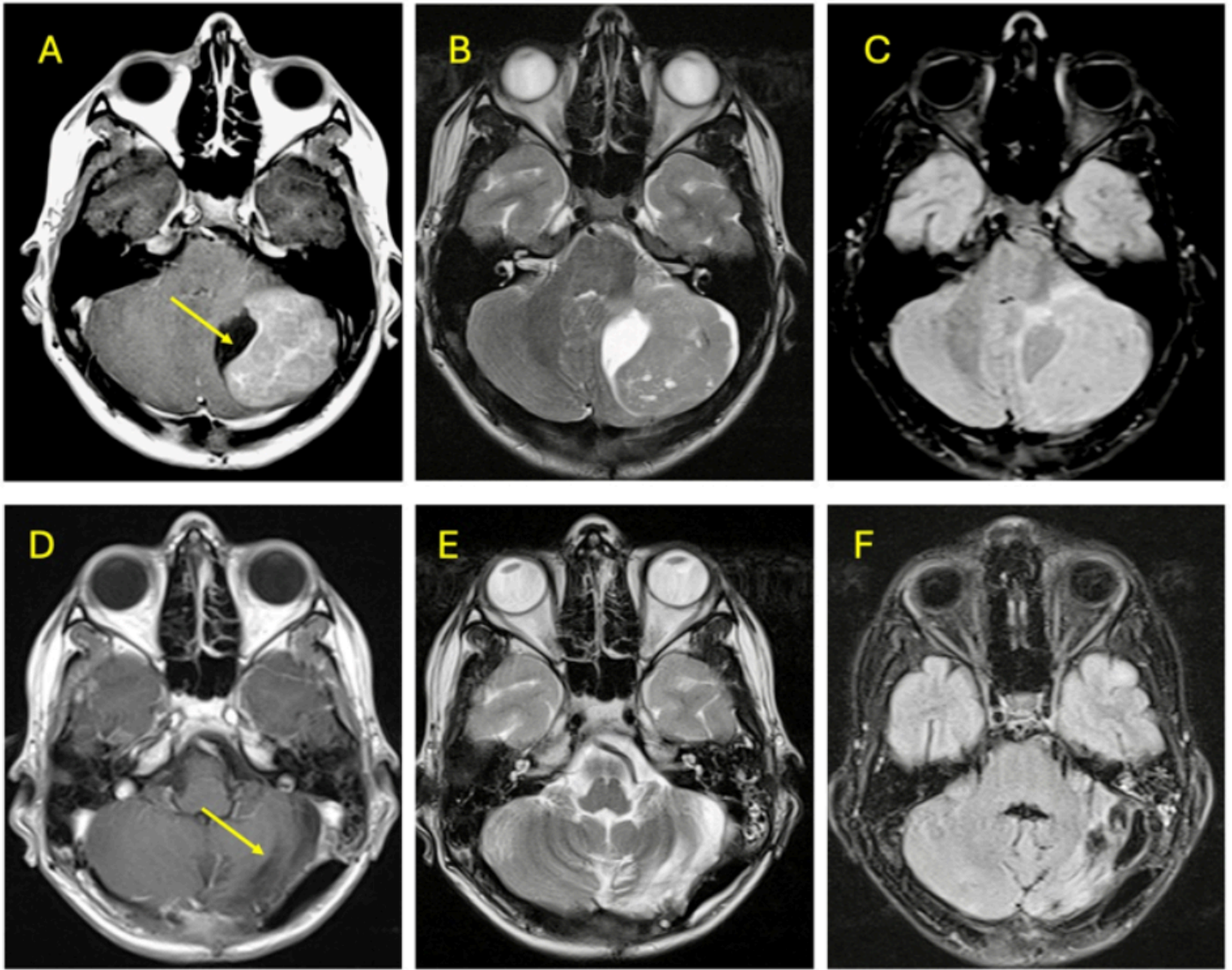


Figure 1

Brain magnetic resonance imaging (MRI) at initial diagnosis demonstrating a left cerebellar mass associated with obstructive hydrocephalus. (A–C) Preoperative MRI sequences. (D–F) Postoperative MRI showing the resection cavity after tumor resection.

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Figure 2

Fig. 2 Histopathological comparison between the primary and secondary tumors. (A) Desmoplastic/nodular medulloblastoma at initial diagnosis (H&E). (B) WHO grade III astrocytoma diagnosed six years after craniospinal irradiation (H&E).

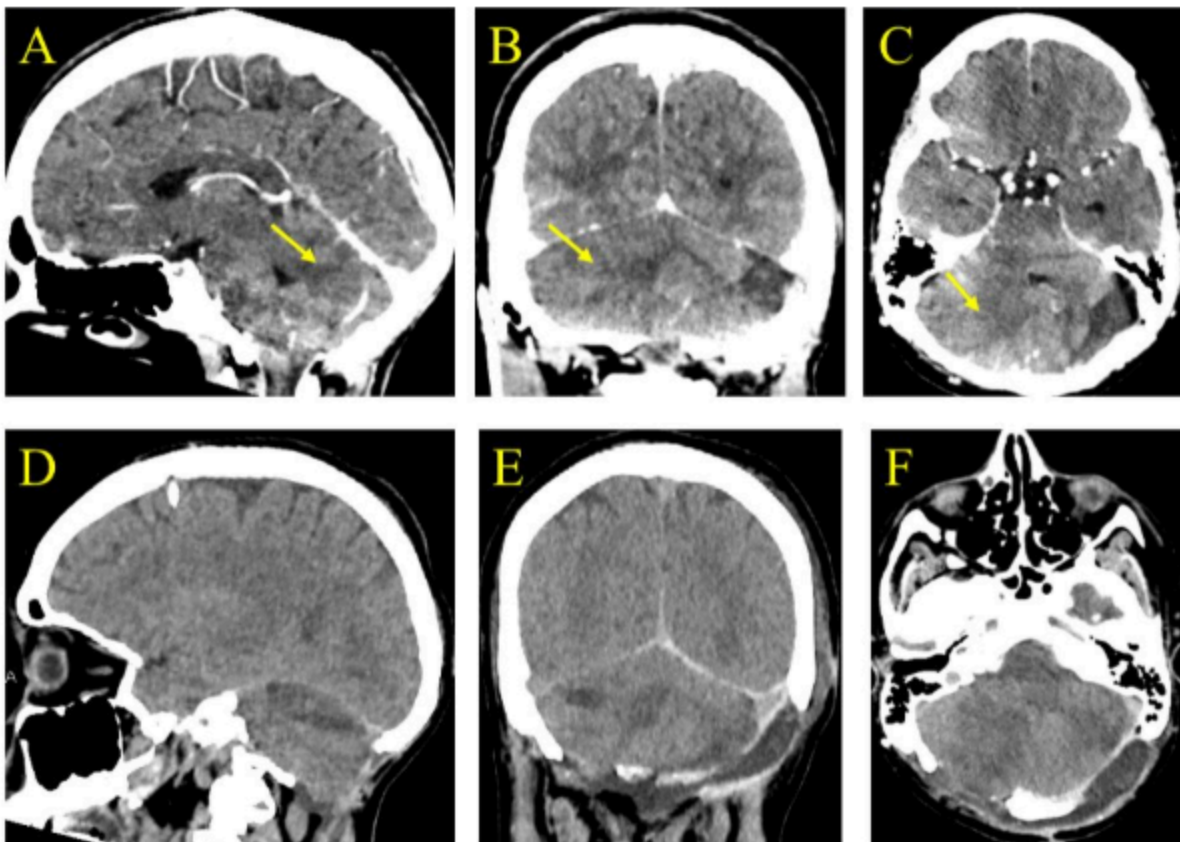


Figure 3

Brain computed tomography (CT) demonstrating a new posterior fossa lesion six years after craniospinal irradiation. (A–C) Preoperative images. (D–F) Postoperative images showing the resection

cavity.