Article published online: 2022-07-31

Unleashing the Mystery of a Treated Case of Medulloblastoma

Renuka M. Ashtekar[1] Sridhar Epari[2] Prakash M. Shetty[3] Arpita A. Sahu[1]

[1] Department of Radiology, Tata Memorial Centre and Homi Bhabha National Institute, Mumbai, Maharashtra, India
[2] Department of Pathology, Tata Memorial Centre and Homi Bhabha National Institute, Mumbai, Maharashtra, India
[3] Department of Neurosurgery, Tata Memorial Centre and Homi Bhabha National Institute, Mumbai, Maharashtra, India

Address for correspondence Arpita Sahu, MD, B-308, Aradhana CHS, Spring Mill Compound, Dadar East, Mumbai 400014, Maharashtra, India (e-mail: drarpitasahu@gmail.com).

Indian J Radiol Imaging 2022;32:416–421.

Abstract

Medulloblastoma (MB) is the most common malignant brain tumor in children. Despite advancement in treatment modalities, recurrence remains common, even among those treated with a combination of neurosurgery, craniospinal irradiation, and chemotherapy. The diagnosis of recurrence is usually not difficult in these cases. However, it may pose a challenge in cases with unusual clinical presentation and imaging. Imaging findings on magnetic resonance imaging, with application of perfusion, in conjunction with positron emission tomography-computed tomography can help in clinching the diagnosis in such cases. MB subgroups show consistent patterns even in cases of recurrence, and sonic hedgehog group MB may present as local recurrence showing enhancement with no diffusion restriction, as demonstrated in this case.

Keywords

- recurrent medulloblastoma
- radiation-induced demyelination
- radiation-induced glioma
- MR perfusion

Introduction

Medulloblastoma (MB) is a small-cell embryonal brain cancer located in the posterior fossa and the most common malignant brain tumor in children.[1] We present a case of treated MB that was a diagnostic challenge, given the history of treatment and atypical imaging findings at the time of presentation. It serves as a valuable learning experience and highlights the role of imaging, particularly magnetic resonance imaging (MRI) along with application of perfusion, in reaching the right diagnosis.

Case Report

A 13-year-old male child, known case of nonmetastatic MB (sonic hedgehog [SHH]-subtype with N-Myc overexpression), presented with complaints of diplopia, ataxia, and severe headaches. He was diagnosed 4 years earlier and was operated for the same. He subsequently received craniospinal radiation therapy and chemotherapy (radiation therapy planning figure demonstrating dose received [►**Fig. 1**]), and was followed up with routine MRIs that showed no residual disease or spinal metastasis (►**Fig. 2**). Baseline MRI was not available for review.

The presenting MRI (done outside) showed T2/fluid-attenuated inversion recovery hyperintensities in the pons, medulla, and left cerebellar peduncle that were reported as diffuse intrinsic pontine glioma (DIPG) versus a radiation-induced high grade glioma (►**Fig. 3**). On reviewing these films in our department, as the lesions in the pons showed intense homogeneous enhancement with low MR perfusion values

published online
July 31, 2022

DOI https://doi.org/10.1055/s-0042-1753466.
ISSN 0971-3026.

Thieme Medical and Scientific Publishers Pvt. Ltd., A-12, 2nd Floor, Sector 2, Noida-201301 UP, India

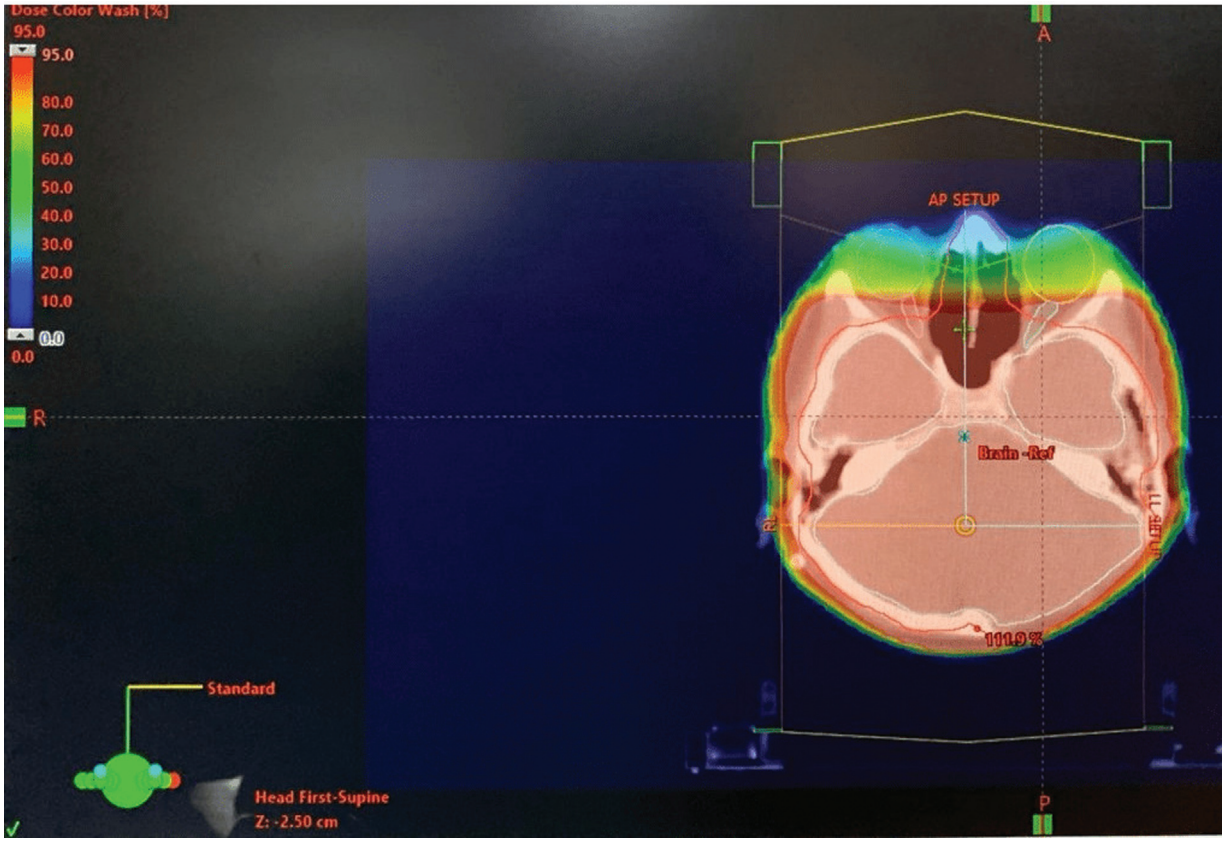

Fig. 1 Craniospinal irradiation therapy planning image demonstrating color map showing dose distribution of 95% of 11.6 Gy.

provisional diagnoses of lymphoma versus secondary demyelination following radiation (in view of significant latency period, disease free interval of 4 years) was considered.[2]

Meanwhile, the patient was started on pulse methylprednisolone. However, after initial improvement, patient deteriorated, likely due to rapid tapering of steroid therapy, and presented to casualty after 2 weeks with right-sided hemiparesis, increase in diplopia, and new onset dysarthria and dysphagia. Repeat MRI and cerebrospinal fluid (CSF) studies were ordered. CSF revealed no malignant cells. MRI revealed

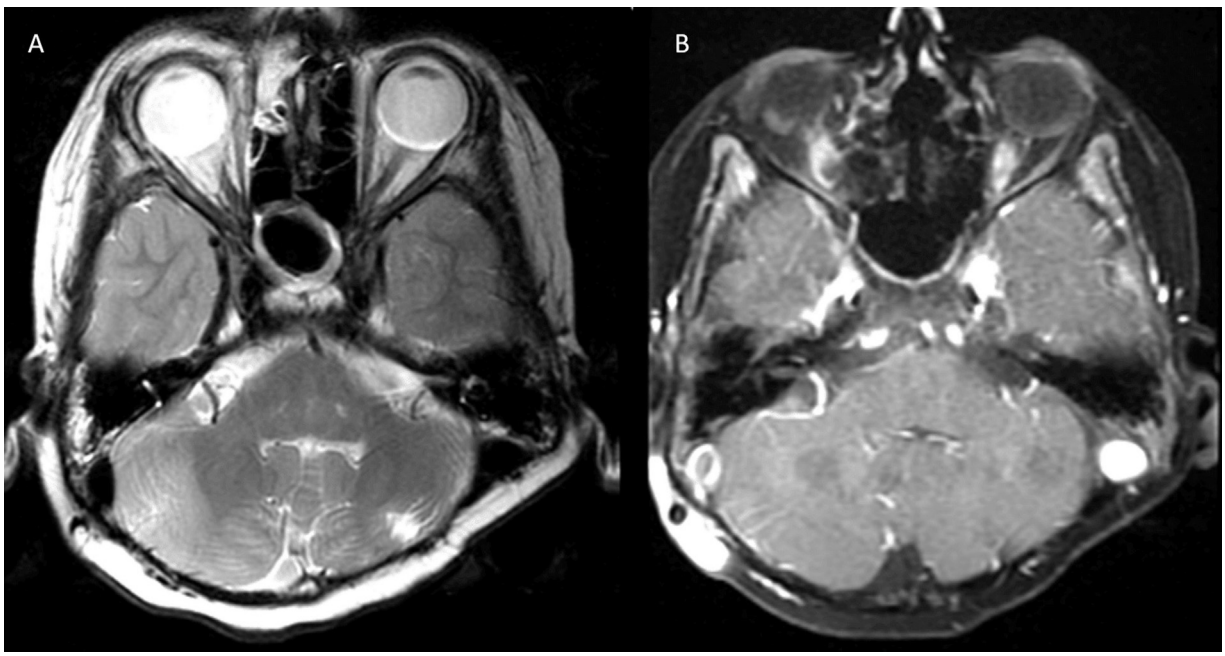

Fig. 2 Axial T2-weighted (**A**) and postcontrast images (**B**) demonstrating no evidence of residual disease postadjuvant craniospinal radiation therapy and chemotherapy.

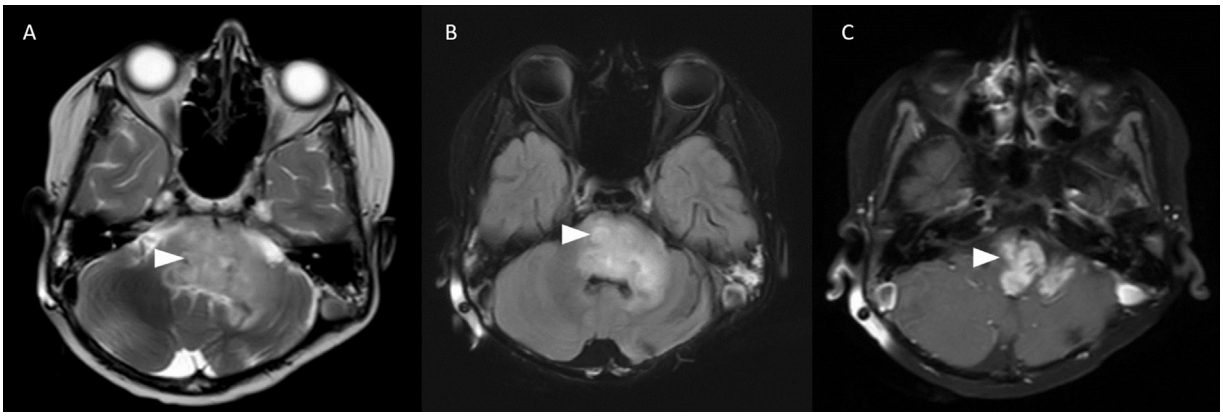

Fig. 3 Axial T2-weighted (**A**), T2/FLAIR (fluid-attenuated inversion recovery) (**B**), and postcontrast images (**C**) reveal T2/FLAIR hyperintensities with corresponding postcontrast enhancement in pons, medulla, and left cerebellar peduncle (*arrowheads*).

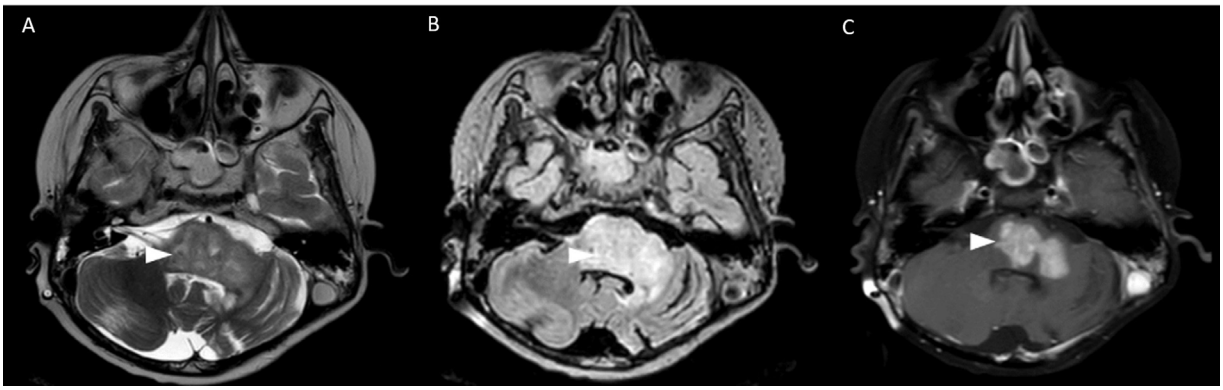

Fig. 4 Axial T2-weighted (**A**), T2-fluid-attenuated inversion recovery (**B**), and postcontrast images (**C**) showing altered signal intensity (*arrowheads*) involving inferior colliculus, pons, and left cerebellar peduncle with mild decrease in edema but persistent postcontrast enhancement.

mild reduction in edema (portion in the superior part of ventral pons, right middle cerebellar peduncle, and lower part of midbrain), likely secondary to steroid therapy. However, the intensely enhancing component in the pons remained stable with low perfusion score and no significant spectroscopy findings (►**Figs. 4** and **5**).

Demyelination usually regresses following steroid therapy and as lymphoma can show a rebound increases following

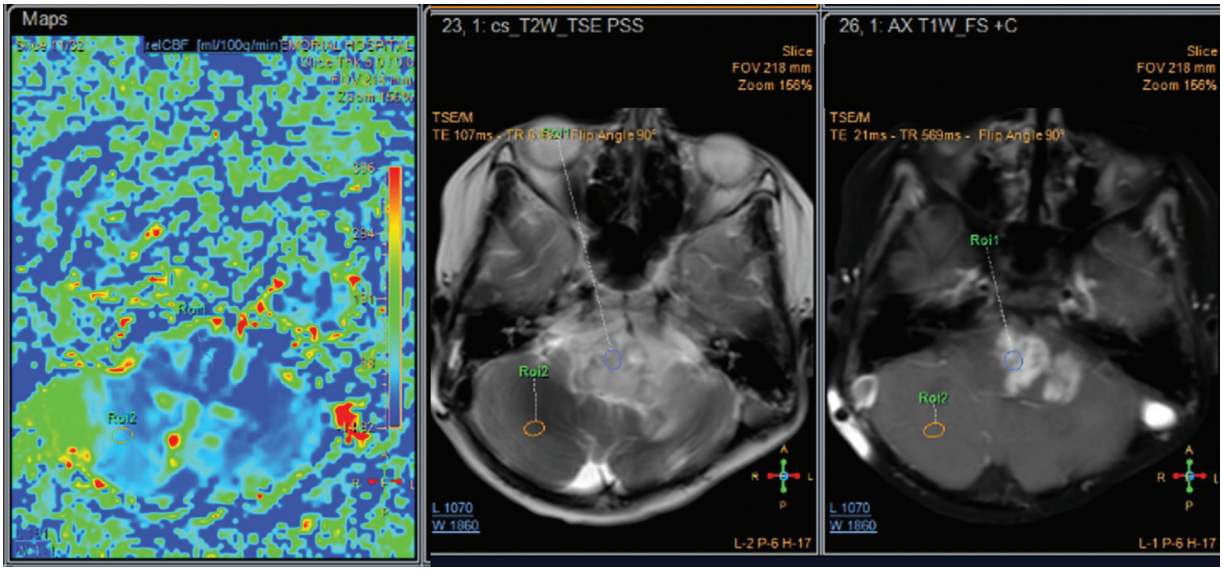

Fig. 5 Perfusion images reveal that the lesions show hypoperfusion.

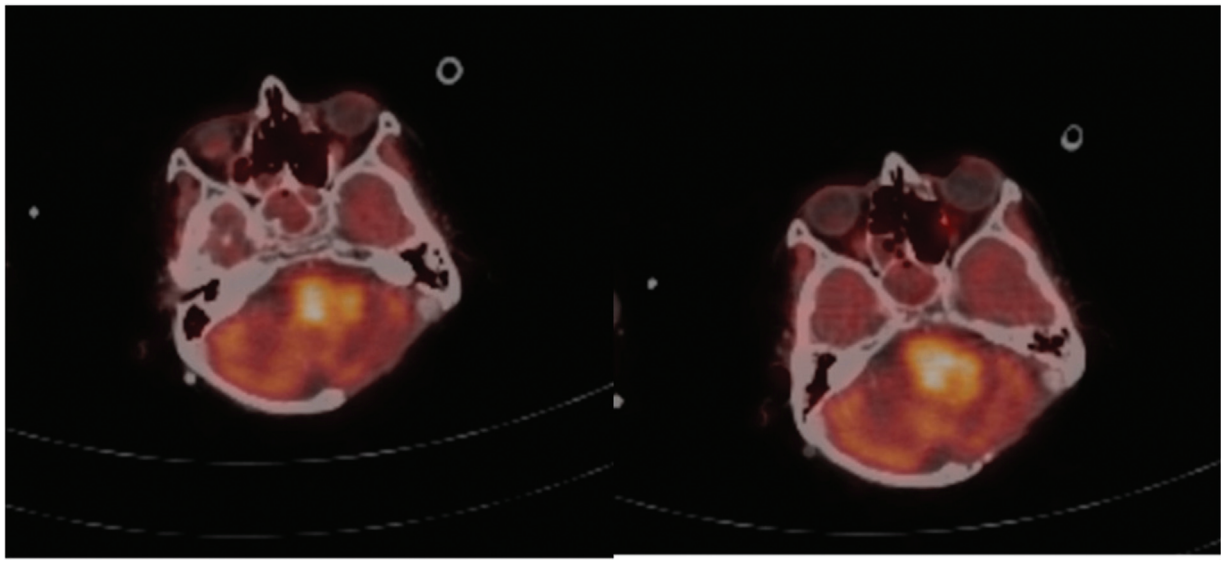

Fig. 6 Fluorodeoxyglucose-positron emission tomography images reveal avidly enhancing soft tissue lesion noted in medulla extending into left cerebellum and superiorly involving pons (standardized uptake value-max 14.6).

stoppage of steroid therapy; a positron emission tomography-computed tomography (PET-CT) was advised. PET-CT revealed the lesion to have a standardized uptake value (SUV)-max of 14 with heterogenous (fluorodeoxyglucose) FDG-PET avidity (►**Fig. 6**). This, with the finding of T2 hyperintensity went against the diagnosis of lymphoma. However, the lesion was hyperattenuating on plain CT scans (►**Fig. 7**).

The presence of persistent intense contrast enhancement on MRI and hyperattenuation on plain CT suggested the possibility of recurrence/atypical metastasis (in the absence of baseline scan location of primary disease was uncertain). This was further strengthened when PET-CT ruled out lymphoma. However, our case did not show any restricted diffusion, which prevented us from diagnosing recurrence/atypical metastasis initially (►**Fig. 8**).

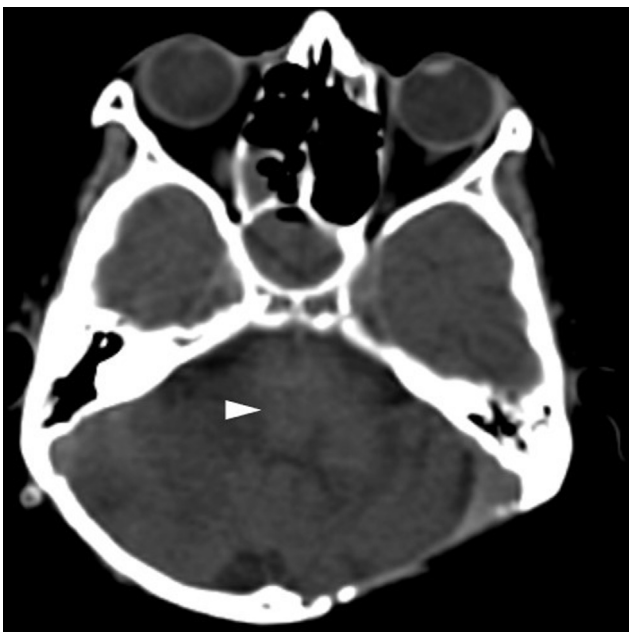

Fig. 7 Axial noncontrast computed tomography image showing a hyperattenuating mass in the pons and left cerebellar peduncle (*arrowhead*).

The case was discussed in a multidisciplinary meeting. Decision to biopsy the lesion was taken to guide further treatment. The left cerebellar lesion was biopsied under intraoperative ultrasound guidance that revealed recurrent MB (►**Fig. 9**). It was decided to proceed with palliative chemotherapy (COMBAT regimen).

Discussion

MB is a small-cell embryonal brain cancer arising in the posterior fossa. MB represents 9.2% of pediatric brain tumors in children aged between 0 and 14 years, with a higher incidence in children between 3 and 4 years of age and between 8 and 10 years of age.[3]

The CT appearance of MB is a hyperattenuated, well-defined cerebellar mass with homogeneous enhancement and surrounding vasogenic edema. The tumor is radiosensitive and a combination of surgery and radiation therapy is most commonly used.[4]

However, radiation therapy is not without substantial side effects. Subacute effects are typically transitory that affect the white matter, whereas late effects affect the periventricular region.[5,6] Histologically proven white matter changes, gliosis, and inflammation presenting as new, enhancing lesions on MRI can be mistaken for recurrent tumor.[6,7] As seen in this case, the significant latency period combined with the imaging findings favored the possibility of delayed effects of radiation. However, the location of the lesions was atypical.[6]

Radiation-induced secondary gliomas and lymphomas can occur after a latency period of 5 to 10 years.[8] Radiation-associated DIPGs may present as a poorly prognostic distinct molecular subgroup of H3 wild-type DIPG.[9] Our case showed lesions in areas typical for DIPG in the background of

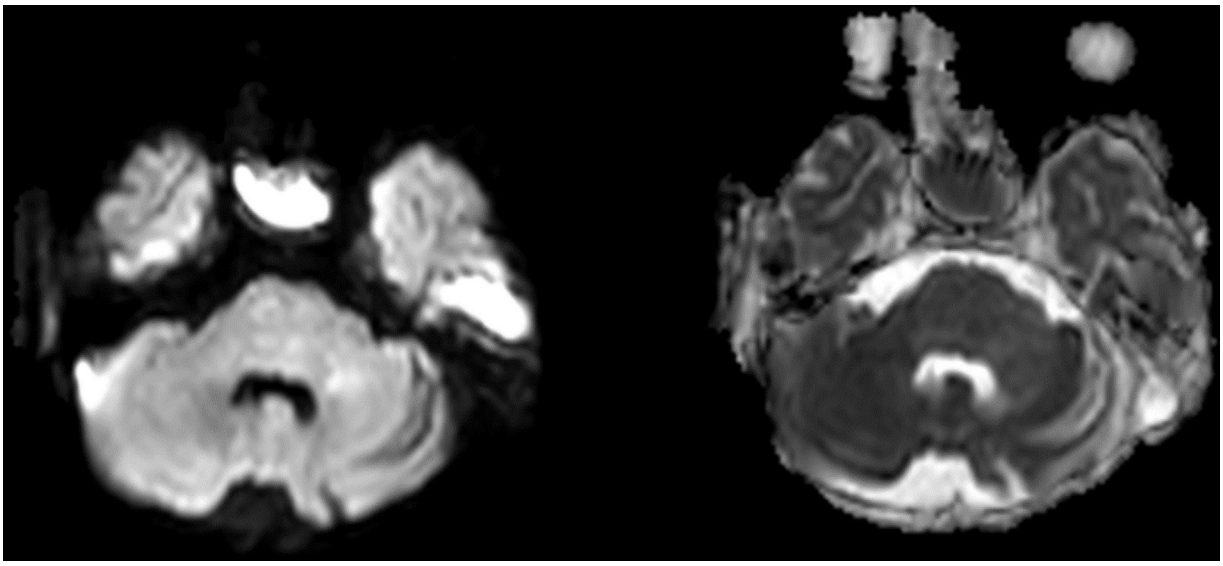

Fig. 8 Axial diffusion-weighted images showing no diffusion restriction within the areas of altered signal intensity seen in ►**Fig. 2**.

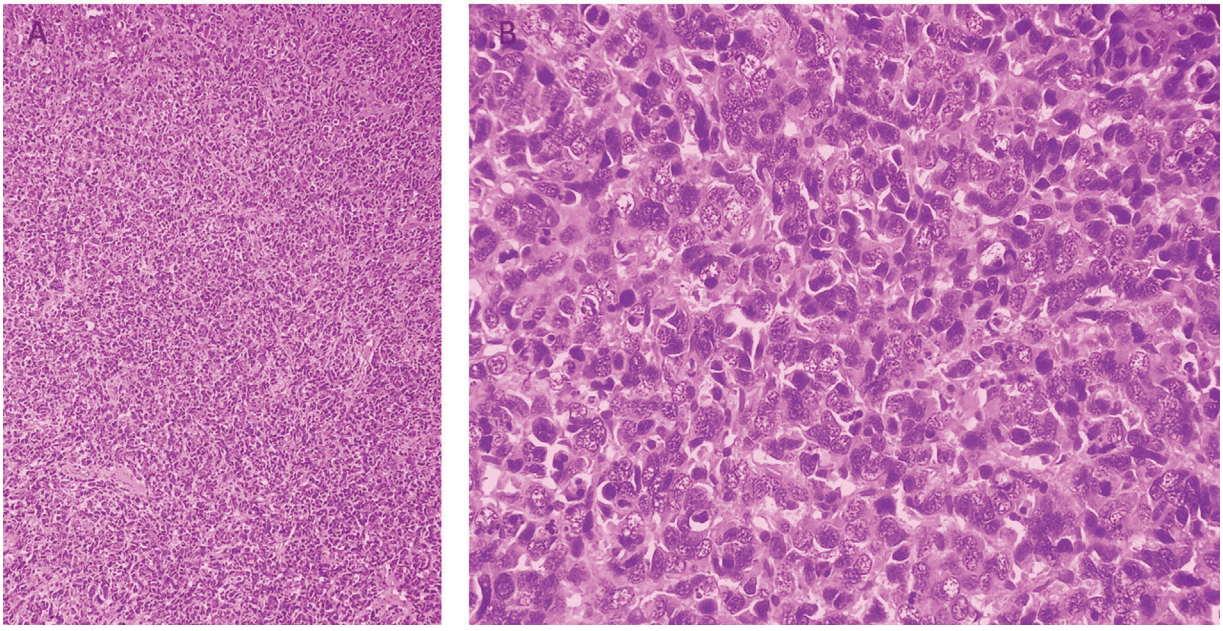

Fig. 9 Photomicrographs showing a cellular tumor of primitive embryonal cell morphology (**A**) with marked anaplasia seen in the form of cellular wrapping (**B**).

irradiation; however, presence of intense homogeneous postcontrast enhancement involving almost the entire lesion and hypoperfusion went against the diagnosis of DIPG.

Central nervous system lymphomas often enhance homogeneously but sometimes may show no enhancement or only a thin rim of enhancement in immunocompromised patients.[10] They may show a rebound increase or worsening after cessation of steroid therapy. Moreover, areas of restricted diffusion were observed in lymphomas in 90% cases on pretreatment scans with variable diffusion restriction on posttreatment scans.[11] Homogenous FDG-PET avidity and SUV value greater than 15 are in favor of lymphoma and values lesser than this cutoff along with a heterogenous FDG avidity are more in favor of other brain tumors like metastasis or glioblastoma.[12]

Recurrence of MB is unfortunately very common and usually manifests as leptomeningeal enhancement or focal parenchymal nodular enhancement within the brain. Recurrent disease develops most frequently in the posterior fossa followed by the subfrontal region.[13]

Significant differences exist across subgroups with respect to the anatomical and temporal patterns of recurrence; specifically SHH tumors mostly recur in the local tumor bed and group 3 and 4 tumors recur almost exclusively with metastases. Also, MB does not change subgroup at recurrence.[14]

Diffusion-weighted imaging is more sensitive (100% sensitivity) than contrast enhancement (76% sensitivity) for the detection of recurrent MB, particularly in leptomeningeal nonenhancing disease and distal nonenhancing focal disease.[15] As such, recurrent MB can present as a lesion with diffusion restriction in a patient with normal postcontrast MRI ("mismatching" pattern).[16,17] However, our case did not demonstrate any areas of diffusion restriction contrary to existing literature. Only one prior study had four patients with leptomeningeal disease showing contrast enhancement without restricted diffusion.[17] Such a "reverse mismatching" pattern has not been previously described in SHH subgroup. One case series reviewed 10 cases of MB of which two demonstrated no significant restricted diffusion. Pathologic review revealed that both of these nonrestricting cases displayed a lack of reticulin deposition by light microscopy.[18] We propose that a detailed radiopathologic review of mismatching findings in further cases such as these is needed to corroborate these atypical MRI features.

This case demonstrates that good clinicoradiological correlation can guide in establishing the diagnosis of recurrence at unusual sites with unusual presentation. Further, SHH group MB may present as local recurrence showing enhancement with no diffusion restriction.

Key Messages

Magnetic resonance imaging, and its applications such as perfusion, in conjunction with other imaging findings, can help differentiate recurrent medulloblastoma from other differentials such as radiation-induced demyelination or radiation induced secondary central nervous system neoplasms in posttreatment cases.

Presentation at a Meeting
Nil.

Source(s) of Support
Nil.

Conflict of Interest
None.

References

1 Staedtke V, Dzaye O, Holdhoff M. Actionable molecular biomarkers in primary brain tumors. Trends Cancer 2016;2(07):338–349
2 Kessler AT, Bhatt AA. Brain tumour post-treatment imaging and treatment-related complications. Insights Imaging 2018;9(06):1057–1075
3 Millard NE, De Braganca KC. Medulloblastoma. J Child Neurol 2016;31(12):1341–1353
4 Zimmerman RA, Bilaniuk LT, Pahlajani H. Spectrum of medulloblastomas demonstrated by computed tomography. Radiology 1978;126(01):137–141
5 Schultheiss TE, Kun LE, Ang KK, Stephens LC. Radiation response of the central nervous system. Int J Radiat Oncol Biol Phys 1995;31 (05):1093–1112
6 Russo C, Fischbein N, Grant E, Prados MD. Late radiation injury following hyperfractionated craniospinal radiotherapy for primitive neuroectodermal tumor. Int J Radiat Oncol Biol Phys 1999;44(01):85–90
7 Moghrabi A, Friedman HS, McLendon R, et al. Arteriovenous malformation mimicking recurrent medulloblastoma. Med Pediatr Oncol 1994;22(02):140–143
8 Lee JW, Wernicke AG. Risk and survival outcomes of radiation-induced CNS tumors. J Neurooncol 2016;129(01):15–22
9 Gits HC, Anderson M, Stallard S, et al. Medulloblastoma therapy generates risk of a poorly-prognostic H3 wild-type subgroup of diffuse intrinsic pontine glioma: a report from the International DIPG Registry. Acta Neuropathol Commun 2018;6(01):67
10 Bühring U, Herrlinger U, Krings T, Thiex R, Weller M, Küker W. MRI features of primary central nervous system lymphomas at presentation. Neurology 2001;57(03):393–396
11 Zacharia TT, Law M, Naidich TP, Leeds NE. Central nervous system lymphoma characterization by diffusion-weighted imaging and MR spectroscopy. J Neuroimaging 2008;18(04):411–417
12 Kawai N, Miyake K, Yamamoto Y, Nishiyama Y, Tamiya T. 18F-FDG PET in the diagnosis and treatment of primary central nervous system lymphoma. BioMed Res Int 2013;2013:247152
13 Meyers SP, Wildenhain S, Chess MA, Tarr RW. Postoperative evaluation for intracranial recurrence of medulloblastoma: MR findings with gadopentetate dimeglumine. AJNR Am J Neuroradiol 1994;15(08):1425–1434
14 Ramaswamy V, Remke M, Bouffet E, et al. Recurrence patterns across medulloblastoma subgroups: an integrated clinical and molecular analysis. Lancet Oncol 2013;14(12):1200–1207
15 Aboian MS, Kline CN, Li Y, et al. Early detection of recurrent medulloblastoma: the critical role of diffusion-weighted imaging. Neurooncol Pract 2018;5(04):234–240
16 Schubert MI, Wilke M, Müller-Weihrich S, Auer DP. Diffusion-weighted magnetic resonance imaging of treatment-associated changes in recurrent and residual medulloblastoma: preliminary observations in three children. Acta Radiol 2006;47(10): 1100–1104
17 Mata-Mbemba D, Zapotocky M, Laughlin S, Taylor MD, Ramaswamy V, Raybaud C. MRI characteristics of primary tumors and metastatic lesions in molecular subgroups of pediatric medulloblastoma: a single-center study. AJNR Am J Neuroradiol 2018;39 (05):949–955
18 Pillai S, Singhal A, Byrne AT, Dunham C, Cochrane DD, Steinbok P. Diffusion-weighted imaging and pathological correlation in pediatric medulloblastomas-"They are not always restricted!". Childs Nerv Syst 2011;27(09):1407–1411

