Unleashing the Mystery of a Treated Case of Medulloblastoma

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Introduction

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.

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 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...
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
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. 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.

Fig. 5  Perfusion images reveal that the lesions show hypoperfusion.
stoppage of steroid therapy; a positron emission tomogra-
phy-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 lym-
phoma. However, our case did not show any restricted
diffusion, which prevented us from diagnosing
recurrence/atypical metastasis initially (►Fig. 8).
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.

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

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. Histologically proven white matter
changes, gliosis, and inflammation presenting as new, en-
hancing lesions on MRI can be mistaken for recurrent
tumor. 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.

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

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.

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.

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).
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.\(^\text{15}\) As such, recurrent MB can present as a lesion with diffusion restriction in a patient with normal postcontrast MRI (“mismatching” pattern).\(^\text{16,17}\) 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.\(^\text{16}\) 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.\(^\text{18}\) We propose that a detailed radiopathologic review of mismatching findings in further cases such as this 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.

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Nil.

*Conflict of Interest*

None.

**References**

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