Case Report

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Unusual Metastasis to Supra Tentorial Brain from Posterior Fossa Medulloblastoma: A Rare Case

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Abstract

Medulloblastoma is a malignant invasive embryonal tumor of the cerebellum. It accounts for approximately 15% to 20% of all central nervous system tumors in children. It is the most common brain tumor in children, but it is rare in adults.1 Medulloblastoma is an aggressive tumor (WHO Grade IV) and recurrences are common even after adequate treatment. Most of the recurrences occur within two years of initial treatment. The most common location is in the posterior fossa, followed by spinal, supratentorial, and uncommonly, systemic metastases. We present a case of a 13-year-old male who was operated for Medulloblastoma and received craniospinal irradiation two years back and presented to our institute with complaints of vomiting and headache for 15 days. MRI revealed a mass in the frontal-basifrontal region. Post-excision histopathology was suggestive of supratentorial metastasis. This case is rare because supra-tentorial metastases of medulloblastoma are very uncommon.

Keywords: Medulloblastoma; Metastasis; Supra tentorial.

Key Messages: A Very Unusal case of Supratentorial metastasis from Medulloblastoma.

Introduction

Medulloblastoma is an aggressive malignant invasive embryonal tumor of the cerebellum with an inherent tendency to metastasize through CSF pathways. Surgical gross total resection followed by craniospinal irradiation and chemotherapy are the modalities of treatment. Recurrences are common even after adequate treatment.[3] Most of the recurrences occur within two years and most commonly in the posterior fossa, although there are also reports of supra-tentorial and systemic metastases. Reports on supra tentorial metastases are relatively uncommon.[2] We present here, a case of a 13 year old male treated for medulloblastoma who presented with metastases in the frontal lobe, a very rare site.

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Case History

A 13 year old boy presented to our institute with the complaints of headache and vomiting of 15 days duration in May 2021. He was previously diagnosed two years ago with medulloblastoma Grade IV along with spinal metastasis for which he underwent total excision of posterior fossa tumor and laminectomy with decompression of intra dural spinal metastasis. Histopathological and immuno-histochemical examination showed medulloblastoma (WHO Grade IV), molecular subtype non-WNT (Wingless-related integration site signaling pathway)/non-SHH (sonic hedgehog signaling pathway). He was then treated with

craniospinal irradiation. Patient was asymptomatic for two years when he presented with the CNS symptoms.

Diagnostic Imaging

Magnetic Resonance Imaging (MRI) Brain was performed which showed large ill defined solid cystic soft tissue mass lesion in left frontal basifrontal region measuring approximately 5.6 x 5.4 x 4cm, which appeared as hypodense on T1-Weighted images and hyperintense on T2-Weighted/FLAIR (Fluid attenuated inversion recovery) images shows moderate inhomogeneous enhancement on postcontrast images (Fig. 1).

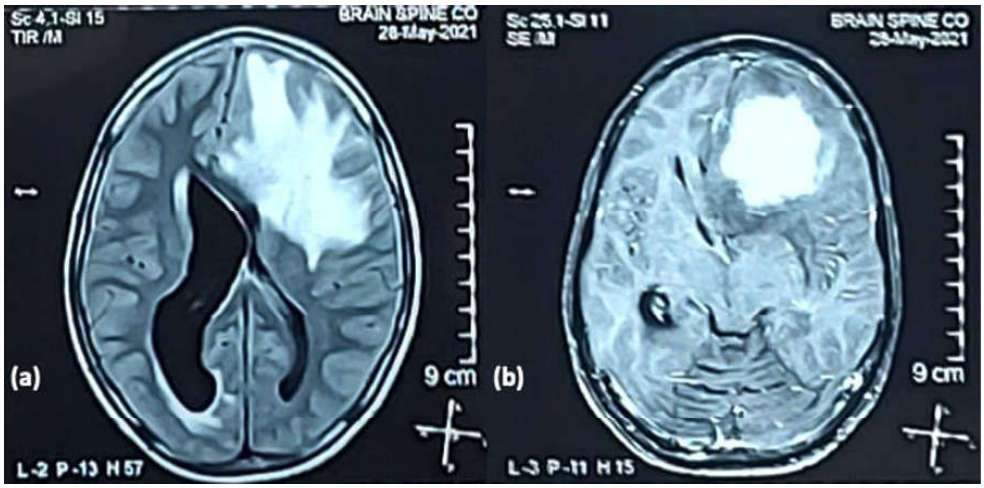

Fig. 1: T1 weighted MRI showing hypointense solid soft mass lesion in Frontal Basifrontal lobe.

Lesion was causing moderate perilesional edema with moderate mass effect as evident by compression/displacement of frontal horn of left lateral ventricle, subfalcine herniation and dilatation of right lateral ventricle with midline shift.

Pathological and Molecular Findings

The patient underwent left frontal craniotomy with total excision of tumor. The histopathological examination revealed a tumor composed of round cells with high nucleocytoplasmic (N:C) ratio, hyperchromatic nuclei, scanty cytoplasm forming diffuse sheets, lobules separated by fibrovascular bands on background of fibrillary material. Rosette formation was seen at places. Stroma showed myxoid change at focal areas. Tumor was infiltrating glial tissue. These findings were suggestive of Medulloblastoma. (Fig. 2).

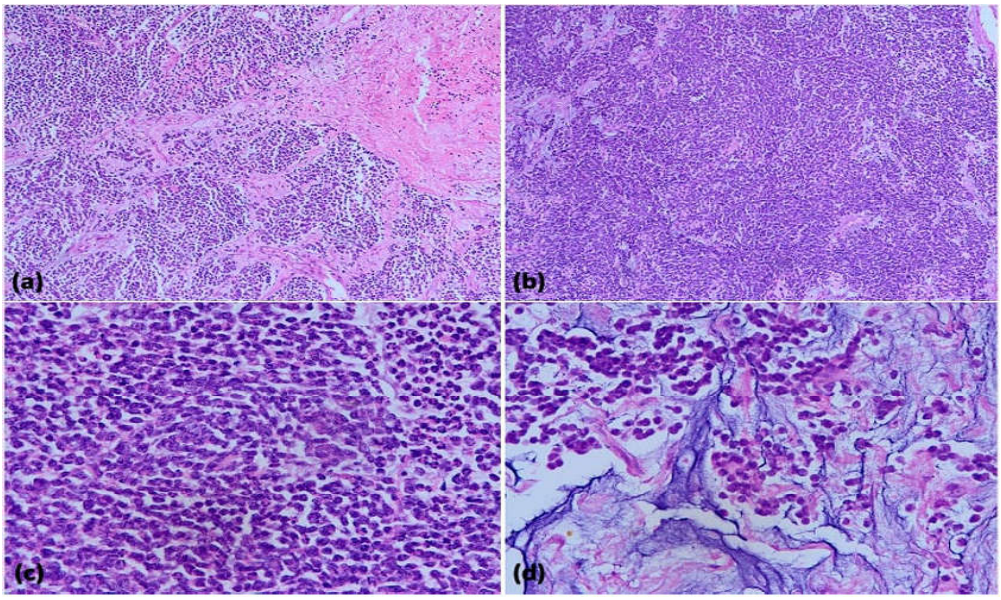

Fig. 2: Histological confirmation of metastasis of Medulloblastoma (10x (a, b) and 40x (c, d), Haematoxylin and eosin stain, HE)

The immunohistochemical (IHC) examination showed that the tumor cells were positive for synaptophysin, and negative for p53 (TP53 tumor suppressor gene), GFAP (Glial fibrillary acidic protein), GAB-1 (GRB2 Associated Binding Protein 1), B-catenin; Ki-67 (Marker Of Proliferation Ki-67) was 40-45%; INI-1 (Integrase interactor-1) retained. The post-operative histopathological report was suggestive of Classical Medulloblastoma WHO Grade IV. The molecular subtype was non-WNT/ non-SHH. This histopathological and molecular subtype was similar to the primary lesion two years ago. Patient was then treated with irradiation to postoperative tumor bed.

Discussion

Medulloblastoma is a highly malignant and aggressive tumor of the central nervous system arising from the cerebellar vermis in the roof of the fourth ventricle. Medulloblastoma is a relatively rare brain tumor and accounts for less than 2% of all primary brain tumors. It constitutes approximately 18% of all pediatric brain tumors.[4] The highest incidence rate is seen among 1–9 year old children. The incidence declines as the age advances.[5]

Patients with medulloblastoma present with the clinical signs and symptoms of raised intracranial pressure due to cerebrospinal fluid (CSF) flow obstruction or cerebellar dysfunction. Most common presenting complaints are headache, nausea, vomiting, and blurred vision.

According to the WHO guidelines, medulloblastoma is classified into four molecularly defined groups: WNT-activated, SHH-activated and tumor suppressor protein p53(TP53)-mutant, SHH-activated and TP53-wildtype, and non-WNT/ non-SHH (i.e., group 3 and group 4).[6] Each of these molecular subgroups of Medulloblastoma have unique characteristics. (Table -1).

Table 1: Features of medulloblastoma subgroups.

Subtype	Molecular characteristics	Mutations	Age group
WNT activated	WNT pathway activation	CTNNB1 DDX3X Chromatin-remodeling genes TP53	Least common of subgroups Found in children and adults, not infants
SHH activated and TP53 wild-type	SHH pathway activation	PTCH1 SMO SUFU TERT promoter Chromatin-remodeling genes	Infants, children and adults
SHH activated and TP53 wild-type	SHH pathway activation	TP53	5-18 years old
Group 3	Elevated expression of MYC GABRA5 over-expression	SMARCA4 Chromatin-remodeling genes Genes of TGF-pathways	Infants and children, not adults More common in boys than in girls
Group 4	Lmx1A expression	Chromatin-remodeling genes	More common in children than in adults Least common in infants

Chang's classification is used to categorize Medulloblastoma patients into average and high risk.7 (Table -2).

Table 2: Medulloblastoma–Risk Stratification.

Standard (Average) Risk (66%)	High risk (34%)
> 3 years old	< 3 years old
<1.5 cm2 residual disease after resection	Subtotal resection, >1.5 cm2 residual disease after resection
M0 by craniospinal MRI and CSF	M+, leptomeningeal seeding, and location outside of the posterior fossa

Surgical resection of tumor, in case of surgically resectable tumors, is the initial step in all cases, average as well as high risk. For average-risk disease, patients usually receive craniospinal radiotherapy (23.4Gy followed by conformal tumor bed boost to 54–56Gy in 30 fractions over six weeks), with or without chemotherapy with vincristine. After the radiation, children older than three years with non disseminated medulloblastoma can be given chemotherapy. For poor risk disease, craniospinal radiotherapy is given at a higher dose (36–39.6Gy followed by posterior fossa boost to 54–56Gy in 30 fractions over six weeks) and chemotherapy (commonly used agents include cisplatin, cyclophosphamide, and vincristine). In infants younger than three years, treatment with radiation is deferred until three years of age. High-dose chemotherapy along with stem cell rescue regimens can be used to delay the time or avoid completely the administration of craniospinal irradiation to avoid neurologic side effects like neurocognitive and endocrine deficits.[8,9]

Although primary treatment of medulloblastoma is now successful in most of the patients, with timely surgery followed by radiation, its secondary manifestations still have a poor prognosis.[3] Even after optimal treatment there are reports of recurrence. The most common location of metastases in case of Medulloblastoma is in the posterior fossa, followed by spinal, supratentorial, and uncommonly, systemic metastases.[2]

In our case, the patient was on regular follow up post primary disease with regular MRI Brain scans and was found to have recurrence in frontal lobe two years later for which he underwent surgical excision followed by irradiation to the tumor bed. Post treatment, the patient had no significant CNS abnormalities on clinical examination. The patient will be further followed up on a regular basis.

Conclusion

Medulloblastoma is a highly aggressive tumor with high likelihood of local recurrences and recurrence in the supratentorial area is uncommon but it is still a possibility. Thus regular follow up of these children, with detailed history, physical examination and regular scans of neuraxis, is mandatory till adulthood to detect early recurrences and metastatic disease.[2]

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