

## Extra-axial Desmoplastic Medulloblastoma in Adult Cerebellopontine Angle: Case Report and Noninvasive Molecular Subgrouping Utilizing Magnetic Resonance Imaging-Based Radiomics Nomogram

### Abstract

Cerebellopontine angle (CPA) is an atypical site for adult medulloblastoma (MB) with only 12 cases reported in pure extra-axial location. None was predicted on preoperative imaging while the most common misdiagnosis was petrous meningioma. We add the 13<sup>th</sup> case to this list, attempting to reiterate the radiological features for preoperative prediction of this rare pathology on conventional magnetic resonance imaging (MRI). Molecular subtyping also is not yet reported for adult extra-axial CPA MB. We propose the routine use of MRI-based nomograms, in atypical CPA extra-axial masses, for noninvasive prediction of molecular subgroup, especially in resource-limited setups that lack the facility of genetic profiling.

**Keywords:** Adult, cerebellopontine angle, medulloblastoma, radiomics

### Introduction

Adult medulloblastomas (MBs) are relatively rare and constitute 0.4%–1.0% of adult primary brain tumors.<sup>[1]</sup> Cerebellopontine angle (CPA) is an atypical site for MB with 42 cases reported in both pediatric and adult population, intra- and extraaxial locations combined.<sup>[2]</sup> Extraaxially, the tumors have been localized in two areas: the tentorial region and the CPA.<sup>[3]</sup> In adults, only 12 cases were found in extra-axial CPA location.<sup>[2,4-13]</sup> Here, we report the 13<sup>th</sup> case of an extra-axial lesion in the CPA of a 27-year-old male, which was presumed to be meningioma on preoperative imaging but turned out to be desmoplastic MB.

As molecular subtyping is not available in resource-limited setups in low income countries, we utilized “for the first time” the MRI based nomogram as an alternative to expensive genetic profiling and propose its use in selective cases.

### Case Report

A 27-year-old male patient presented with headache, vomiting, left-sided ataxia, and left-sided mild hearing loss of 1-month

duration. The vision was normal. Fundus examination showed papilledema. He had left-sided House-Brackman Grade 1 facial paresis, left-sided mild sensorineural hearing loss, and left cerebellar signs on physical examination.

### Imaging

A computed tomography scan of the brain showed a left CPA mixed-density nonenhancing lesion (5.4 cm × 2.8 cm) with broad-based tentorial attachment and displacement of the fourth ventricle but not causing obstructive hydrocephalus. No evidence of calcification was noted. Magnetic resonance imaging (MRI) showed T1 hypo/T2 heterointense, extra-axial lesion in left CPA, which had a wide tentorial attachment and showed moderate heterogeneous enhancement with IV gadolinium. There was no meatal extension [Figure 1a-c]. Adjacent white matter edema in the left cerebellar hemisphere was noted [Figure 1d].

### Treatment

He underwent a left retromastoid craniectomy. A moderately vascular, soft suckable, grayish pink lesion was found densely adherent to petro-tentorial

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junction laterally and to the inferior surface of left hemi tentorium till hiatus medially. This attachment was heavily coagulated [Figure 2a]. The tumor-brainstem interface was well defined, but the tumor-cerebellar interface was ill-defined. All cranial nerves from 4 to 11 were

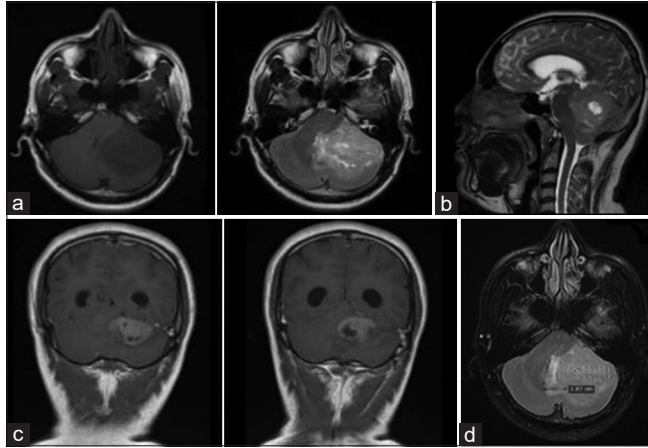


Figure 1: (a) Axial T1 showing hypointense and axial T2 showing heterointense mass in left cerebellopontine angle (b) T2 Sagittal showing central hyperintensity (c) Coronal contrast images showing heterogeneous moderate enhancement and wide tentorial attachment (d) T2 FLAIR showing adjacent cerebellar edema

preserved [Figure 2b]. Gross total excision achieved in a piecemeal fashion [Figure 2c]. The central necrotic part corresponded to T2 hyperintensity on imaging.

Histopathology showed a nodular arrangement of round-to-oval cells having hyperchromatic nuclei and scanty cytoplasm, with brisk mitotic activity suggestive of Desmoplastic MB–WHO Grade IV [Figure 3a]. Immunohistochemical staining showed patchy cytoplasmic staining of beta-catenin, wild type p53, and synaptophysin positive with background GFAP activity [Figure 3b-d]. Molecular subtyping is currently not available in our country.

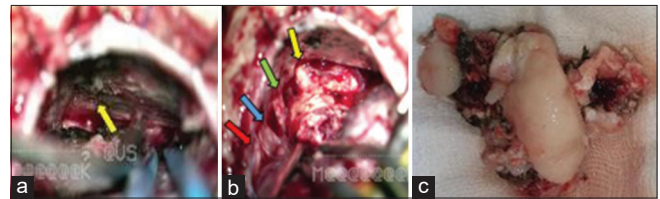


Figure 2: (a) Perioperative image showing heavy coagulation of tentorial attachment (b) Cranial nerve 5 (yellow arrow), 7, 8 (green arrow), 9, 10 (Blue arrow), and 11 (Red arrow) seen intact following tumor resection (c) tumor specimen

Table 1: Summary of Previously Reported Extra-axial Medulloblastoma in Adult Cerebellopontine Angle

Author and years	Age/sex	Contrast uptake on CT/MRI	Tent attachment/IAC extension	Histopathology	Treatment	Follow-up/recurrence/mets
Becker <i>et al.</i> , 1995 <sup>[4]</sup>	32 female	Moderate/heterogeneous	Wide/no	Not mentioned	-	-
Akay <i>et al.</i> , 2003 <sup>[5]</sup>	21 male	Moderate/heterogeneous	Wide/no	Classic	PE, CT, RT	18 months
Gil Salú <i>et al.</i> , 2004 <sup>[7]</sup>	40 male	Intense/homogeneous	Wide/no	Desmoplastic	TE, CT, RT	Leptomeningeal infiltration/died at 16 months
Fallah <i>et al.</i> , 2009 <sup>[8]</sup>	47 male	MRI not done. Homogeneous on CT	Wide/no	Classic	TE, RT	-
Furtado <i>et al.</i> , 2009 <sup>[9]</sup>	32 male	Moderate/heterogeneous	Wide/no	Classic	TE, CT, RT	-
Singh <i>et al.</i> , 2011 <sup>[10]</sup>	21 male	Nonenhancing on CT/MRI not mentioned	Wide/no	Classic	TE only	15 months/+spinal mets (IM cervical, IDEM sacral)
Spina <i>et al.</i> , 2013 <sup>[11]</sup>	22 male	Moderate/heterogeneous	Wide/no	Classic	TE, RT	-/no recurrence/M0
Spina <i>et al.</i> , 2013 <sup>[11]</sup>	26 female	Intense/homogeneous	Wide/no	Classic	TE, RT	-/no recurrence/M0
Bahrami <i>et al.</i> , 2014 <sup>[12]</sup>	23 male	Moderate/heterogeneous	Wide/no	Desmoplastic	TE, RT	12 months
Goudihalli <i>et al.</i> , 2018 <sup>[13]</sup>	50 male	Moderate/heterogeneous	No/yes	Classic	PE	Vegetative/died
Ratha <i>et al.</i> , 2019 <sup>[2]</sup>	42 female	Moderate/heterogeneous	Wide/no	Classic	TE, RT	15 months
Singh and Kumar 2020 <sup>[6]</sup>	26 male	Moderate/heterogeneous	Wide/no	Classic	NTE, CT, RT	-/-/intracranial mets at presentation
Present case, 2020	26 male	Moderate/heterogeneous	Wide/no	Desmoplastic	GTE, CT, RT	9 months

PE - Partial excision; CT - Chemotherapy; RT - Radiation therapy; TE - Total excision; GTE - Gross total excision; NTE - Near-total excision; CT - Computed tomography; MRI - Magnetic resonance imaging; IAC - Internal auditory canal; IDEM - Intradural extramedullary

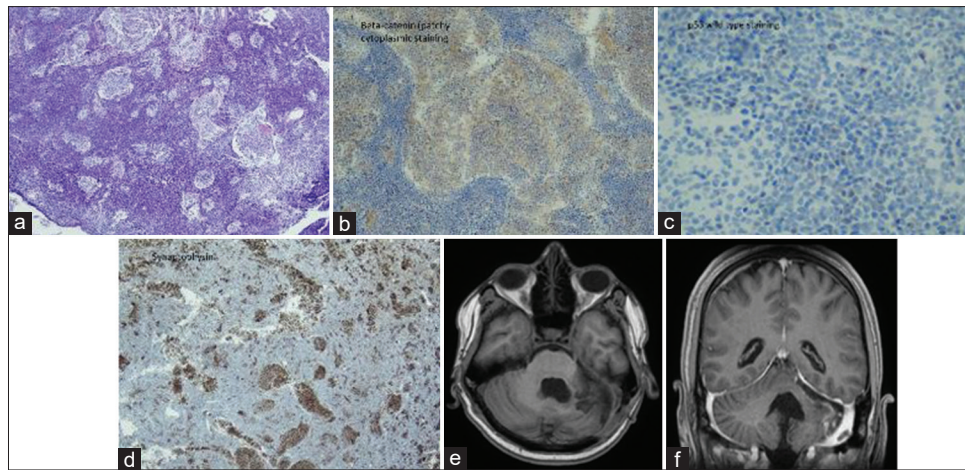


Figure 3: (a) H and E stain illustrating the peculiar nodular arrangement (b) cytoplasmic reactivity of Beta catenin (c) wild type P53 (d) Synaptophysin positive (e) Axial T1 without contrast at 9-month FU (f) Coronal Contrast at 9-month FU showing no evidence of recurrence or mets

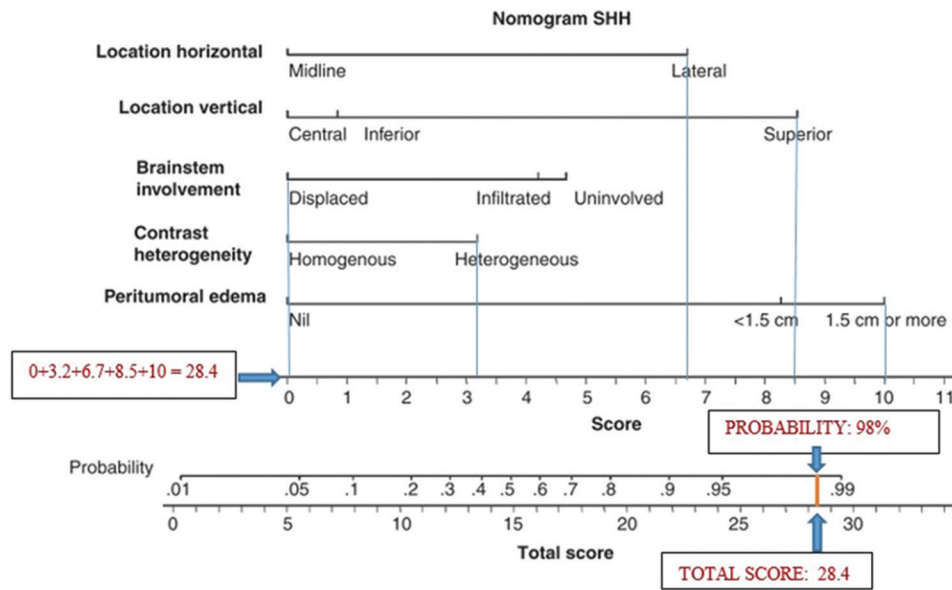


Figure 4: Nomogram for SHH used to predict the molecular subgroup (used with permission of Dasgupta et al.<sup>[21]</sup>)

Postoperatively, his headache and ataxia improved but his facial paresis transiently worsened to Grade 2 which improved to Grade 1 over 2 weeks. His craniospinal MRI with contrast was done after 4 weeks of surgery. Cerebrospinal fluid analysis from lumbar tap turned out to be negative for malignant cells. He was labelled as “standard risk” based on the size of residual <1.5 cm<sup>2</sup>, no metastasis, nonlarge cell histology, and age >3 years. The patient underwent craniospinal irradiation as well as chemotherapy with vincristine, cisplatin, and cyclophosphamide. Postadjuvant therapy, craniospinal imaging was clear for any metastasis or recurrence at 9 months [Figure 3e and f].

## Discussion

Adult MB is known to be lateral hemispheric. CPA is a rarely reported location, challenging to diagnose

both clinically and radiologically. There have been only 12 reported cases of extra-axial MB in the adult literature [Table 1].<sup>[2,4-13]</sup>

A review of all reported cases shows that CPA MB is twice more common in males in their 2<sup>nd</sup>–3<sup>rd</sup> decade, with the classic variety seen in more than half of the cases. Ten out of 12 reports so far published considered meningioma as a provisional diagnosis based on broad tentorial attachment, despite heterogeneous enhancement. Meatal extension which is considered pathognomonic for vestibular schwannoma was only seen in one case.<sup>[13]</sup>

Our preoperative diagnosis was based on a broad base extra-axial lesion, without extension into the internal auditory meatus favoring meningioma as well as disapproving schwannoma. Although the lack of dural tail and heterogeneous enhancement was not classical of

a meningioma, the short clinical course and white matter edema in the adjacent cerebellar lobe favored atypical meningioma preoperatively. Classical radiological features of adult MB are well delineated in the literature but not for atypical locations. All 12 cases reported so far were diagnosed after histopathology leaving MRI features to be focused more than ever before.

Molecular subtyping has not yet been reported for adult CPA MBs. We lack the facility in our setup but tried to speculate on the basis of location, histology, and immunohistochemistry (IHC) retrospectively. Moreover, in the era of molecular genetics, radiogenomics have provided sufficient data to define certain molecular subtypes noninvasively, although it is quite clear that no single imaging feature is pathognomonic of any particular subgroup, certain imaging characteristics are much more prevalent in one subgroup compared to others and may even be highly specific for an individual molecular subgroup.<sup>[14]</sup>

Here, we intend to emphasize the use of an integrated approach utilizing location, histology, IHC, and radiomics to predict molecular subgroup in adult cases of MB, in developing countries that lack the facility of genetic subtyping. A brief review of the correlation of molecular subgroup to location, histology, IHC, and radiomics is presented individually, which can help predict the molecular subgroup with a fair degree of accuracy when combined.

#### Location-molecular subtype correlation

Adult MBs unlike pediatric are reported to be of two molecular subtypes, instead of four, with Group 3 occurring as an exception and Group 4 restricted to midline.<sup>[15,16]</sup> Lateral location is reserved for WNT and SHH tumors, with the former mostly seen in CPA and the latter in the cerebellar hemisphere. Furthermore, superior location abutting and/or reaching the tentorium is a specific imaging feature of SHH-subgroup MB seen in 48% of patients as opposed to 6% in other groups.<sup>[14]</sup>

#### Histology-molecular subgroup correlation

There is a consensus among researchers that all desmoplastic histology in adults belongs to the SHH subgroup, but the opposite is not true: Not all SHH tumors in adults are of desmoplastic histology.<sup>[15,17,18]</sup> Moreover, another study reports that 9% of adult SHH-MBs are located in CP/CPA.<sup>[19]</sup>

#### Immunohistochemistry-molecular subgroup correlation

Beta-catenin localization to cytoplasm instead of nucleus excludes WNT.<sup>[18]</sup> In addition, some markers such as GAP 1 and YAP1 are considered pathognomonic for SHH and WNT type, respectively.<sup>[20]</sup>

#### Radiomics-molecular subgroup correlation

Nomograms based on multiparametric MRI have suggested 95% predictive accuracy for SHH subgroup,<sup>[21]</sup> best among

all other subgroups. We applied the SHH subgroup-specific nomogram to our case [Figure 4] and the probability of the tumor to be SHH type turned out to be 98%. As only two molecular subgroups can be expected in adult CPA, we propose to suggest WNT type in cases where SHH type seems less probable on the nomogram, combined with nuclear reactivity for beta-catenin.<sup>[20]</sup>

In our case, CPA location was the only factor favoring WNT type, while tentorial attachment, desmoplastic histology, and lack of nuclear reactivity of beta-catenin were favoring SHH type. Hence, we used SHH specific nomogram in retrospect to predict the molecular subgroup with fair degree of accuracy. Desmoplastic histology, p53 wild type and SHH subgroup all confer good to intermediate prognosis in this case.

## Conclusion

The use of an integrated approach, based on location, appearance, histology, and demographics not only predicts molecular subgroup but also help defining prognosis. MRI-based nomograms in selected cases can substitute expensive genetic profiling in resource-limited setups.

#### Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the legal guardian has given his consent for images and other clinical information to be reported in the journal. The guardian understands that names and initials will not be published and due efforts will be made to conceal identity, but anonymity cannot be guaranteed.

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Nil.

#### Conflicts of interest

There are no conflicts of interest.

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