Case Report

Extra-axial adult cerebellopontine angle medulloblastoma: Revisiting a rare entity

ABSTRACT

A purely extra-axial position of medulloblastoma in adults at cerebellopontine (CP) angle is extremely rare. To the best of our knowledge, only ten cases have been reported till date. The authors report a case of extra-axial medulloblastoma in a 30-year-old female located at right CP angle. It was surgically treated with a provisional diagnosis of meningioma. Histopathological diagnosis of desmoplastic/nodular medulloblastoma was made with the routine hematoxylin eosin (HE) stain and immunohistochemical markers. This case report highlights the fact that, although extremely rare, the possibility of an extra-axial CP angle mass being a medulloblastoma still needs to be considered in the differential diagnoses, even in adults.

KEY WORDS: Adult neoplasm, cerebellopontine angle, extra axial, medulloblastoma

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INTRODUCTION

Cerebellopontine (CP) angle in adults may harbor a number of tumors. The most common tumors in this location include schwannoma, meningioma, and epidermoid tumor followed by metastatic lesions. Medulloblastoma at CP angle is quite exceptional and a purely extra-axial CP angle medulloblastoma in an adult as reported in this paper is extremely rare. To the best of our knowledge, only ten cases of adult extra-axial CP angle medulloblastoma have been reported so far.[1]

The authors report a case of extra-axial medulloblastoma in a 30-year-old female located at right CP angle with a review of literature.

CASE REPORT

A 30-year-old female presented with a history of headache along with bouts of giddiness for the last 6 months. On neurological examination, ataxia was noted. Computed tomography (CT) of the brain showed an extra-axial hyperdense lesion with broad attachment toward petrous bone with effacement of the fourth ventricle, torsion of the brain stem with previous craniectomy defect [Figure 1a and b]. Magnetic resonance imaging (MRI) of the brain revealed a large extra-axial mass in the right CP angle with a broad dural base causing mass effect on the underlying cerebellum and brain stem with resultant compression and displacement of fourth ventricle causing upstream obstructive hydrocephalus. The mass showed moderate heterogeneous contrast enhancement with prominent dural enhancement [Figure 1c and d]. The 7th–8th nerve complex was intact, not infiltrated by the tumor mass. Diffusion-weighted images showed restricted diffusion suggesting dense cellularity. Based on the anatomical and radiological findings, a provisional diagnosis of meningioma was considered.

The patient underwent a retromastoid occipital craniotomy exposing an extra-axial mass adherent to the dura which was grayish white, soft, suckable, and nonvascular. The peroperative specimen sent to the histopathology laboratory was subjected to squash smear preparation, but only imprint smears could be prepared as the tissue was noncrushable. HE-stained imprint smears showed small nests and scattered pleomorphic tumor cells with markedly hyperchromatic nuclei [Figure 2a]. Based on the imprint smear findings, a diagnosis of high-grade tumor was suggested. Gross total excision was done, the latter specimen received in formalin for paraffin sections showed a cellular tumor arranged in nodules and nests separated by

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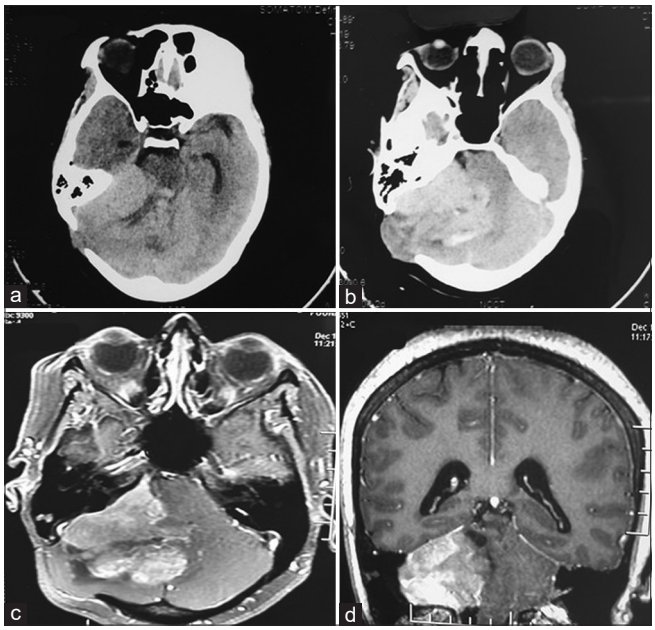

Figure 1: (a) Computed tomography scan (axial view) showing a hyperdense lesion in the right cerebellopontine angle with broad attachment toward petrous bone; (b) computed tomography scan (axial view) showing extra-axial hyperdense lesion with broad attachment toward petrous bone with effacement of the 4th ventricle, torsion of the brain stem with previous craniectomy defect; (c) T1-weighted axial magnetic resonance imaging image with contrast showing extra-axial lesion in the right cerebellopontine angle; (d) T1-weighted image coronal magnetic resonance imaging image with contrast showing a lesion involving right-sided posterior fossa dura-based mass with dural enhancement

fibrous septae. The tumor cells showed marked pleomorphism with round-to-oval or carrot-shaped hyperchromatic nuclei surrounded by scanty cytoplasm along with brisk mitosis. Desmoplastic stroma was markedly evident on HE and reticulin stain [Figure 2b and c]. Tumor cells showed diffuse immunopositivity for synaptophysin, neuron-specific enolase, and Neu N. Tumor cells also showed strong cytoplasmic as well as membranous immunopositivity for β-catenin. Tumor overall showed a high proliferative activity as determined by Ki67 proliferation index [Figure 2d-h]. In addition to these, the immunohistochemistry (IHC) panel also included GFAP and pan-cytokeratin as the perioperative report was of a high-grade tumor; however, the tumor cells were completely immunonegative for GFAP and pan-cytokeratin. This case was reported as desmoplastic/nodular medulloblastoma (World Health Organization [WHO] Grade IV). The postoperative course was uneventful, and the patient was referred for radiotherapy. The 4-month follow-up has showed sustained improvement in the patient status.

DISCUSSION

The 2007 WHO classification considered medulloblastoma as a distinct embryonal tumor, distinguishing it from other primitive neuroectodermal tumors. Later, in 2016 update of the WHO classification of tumors of the central nervous system (CNS), medulloblastomas were classified according to molecular characteristics in addition to the histopathological features. This molecular classification relates to the clustering of medulloblastomas into these groups *(Medulloblastoma, WNT-activated, Medulloblastoma, SHH-activated, TP53-mutant, Medulloblastoma, SHH-activated, TP53-wildtype, Medulloblastoma, non-WNT/non-SHH, group 3, Medulloblastoma, non-WNT/non-SHH, group 4*) on the basis of transcriptome or methylome profiling and has been introduced because of its increasing clinical utility.[2] However, a histopathological classification (medulloblastoma classic, desmoplastic/nodular medulloblastoma, medulloblastoma with extensive nodularity, and large cell/anaplastic medulloblastoma) was also retained, due to its clinical utility when molecular analysis is limited or not feasible. This updated 2016 classification has introduced an integrated approach to diagnosis, where molecular analysis is feasible, an integrated diagnosis combining both molecular group and morphological variant provides optimal prognostic and predictive information, and the accuracy is further enhanced by integrating the genetic data into this. Although due to the limited resources in our setup, based on HE and the IHC panel, this case was classified as desmoplastic/nodular medulloblastoma as per the WHO 2016 histopathological classification.

Medulloblastoma is the most common CNS embryonal tumor of childhood and is second in frequency among the pediatric brain tumors. The median patient age at diagnosis of medulloblastoma is 9 years, with peaks in incidence at 3 and 7 years of age.[3] Of all patients with medulloblastoma, 77% are aged <19 years.[4] Although about 25% of all medulloblastomas occur in adults, but <1% of adult intracranial tumors are medulloblastomas.[5] The tumor overall has a male predominance with male-to-female ratio ranging from 1.5:1 to 4:1, although our paper reports an extra-axial medulloblastoma in a female patient, contrary to the existing literature and the ten cases reported in the past.

Mostly medulloblastomas arise in the cerebellar midline at inferior vermis often compressing and projecting into the fourth ventricle. A smaller proportion of medulloblastomas usually desmoplastic/nodular variant are located in cerebellar hemispheres, generally manifesting in adolescents or young adults. However, a purely extra-axial location of medulloblastoma at CP angle other than these usual locations in an adult patient is quite exceptional as only ten cases have been reported so far in adults [Table 1].[1]

Radiologically, the typical CT appearance of medulloblastoma is that of a well-defined, hyperdense enhancing soft-tissue mass with surrounding edema arising in the cerebellar vermis, associated with obstructive hydrocephalus. MRI shows an iso- or hypointense signal on T1-weighted images, are heterogeneous on T2-weighted images, and exhibit homogeneous contrast enhancement, sometimes

Table 1: The clinical, radiological and histopathological details of the previous case reports

Case	Author	Year	Age/sex	Clinical features	Radiological diagnosis	Histopathology	Treatment	Follow up
1	Becker RL *et al*.	1995	32/female	Hearing loss, ataxia, diplopia, nausea	Meningioma/ schwannoma	Medulloblastoma	NA	NA
2	Becker RL *et al*..	1995	52/female	NA	Meningioma/ schwannoma	Medulloblastoma	NA	NA
3	Akay KM *et al*.	2003	21/male	Headache, nausea/ vomiting, ataxia	Meningioma/ schwannoma	Medulloblastoma	PE, CT	18 months
4	Salu Gil JG *et al*.	2004	40/male	Headache, vomiting, hearing difficulties	Meningioma	Desmoplastic medulloblastoma	NA	NA
5	Fallah A *et al*.	2009	47/male	Headache, nausea/ vomiting	Meningioma	Medulloblastoma	TE, RT	NA
6	Furtado SV *et al*.	2009	32/male	Headache, vomiting, gait unsteadiness, papilledema, dymetria, dysdiadokinesia, ataxia	Meningioma	Medulloblastoma-classic	TE, AT	NA
7	Singh M *et al*.	2011	22/male	Headache, vomiting, facial weakness, papilledema, ataxia	Extra axial mass	Medulloblastoma-classic	TE	Recurrence and drop metastasis after 15 months
8	Bahrami E *et al*.	2013	23/male	Deafness, nausea/ vomiting, ataxia	Extra axial mass	Desmoplastic medulloblastoma	TE, RT	1 year
9	Goudihalli SR *et al*.	2018	50/male	Facial asymmetry, hearing loss	Schwannoma	Medulloblastoma-classic	TE	Vegetative
10	Ratha V *et al*.	2019	42/female	Headache, ataxia	Meningioma/ schwannoma	Medulloblastoma-classic	TE, RT	15 months
11	Our case	2020	30/female	Headache, nausea/ vomiting	Meningioma	Desmoplastic medulloblastoma	TE	4 months

NA=Not available, PE=Partial excision, CT=Chemotherapy, AT=Adjuvant therapy, TE=Total excision, RT=Radiotherapy

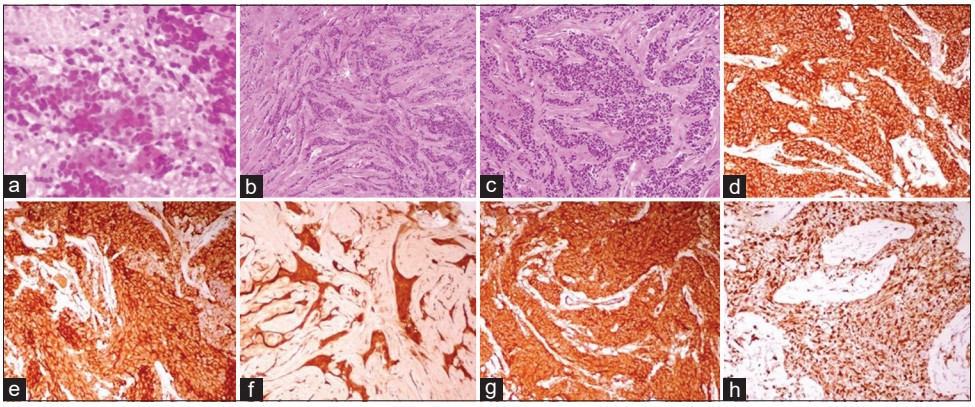

Figure 2: (a) Imprint smears showing small nests and scattered pleomorphic tumor cells against a desmoplastic stroma (HE × 400); (b and c) histopathology showing a cellular tumor exhibiting nodules and nests of densely packed hyperchromatic cells against a desmoplastic stroma (HE × 100; ×200); (d-h) tumor cells showing strong immunopositivity for synaptophysin, neuron-specific enolase, Neu N, β–catenin, and Ki67 (×400)

demonstrating a central hemorrhagic zone.[6] These radiological findings have been attributed to high tumor cellularity. Desmoplastic/nodular medulloblastomas are relatively hypointense in comparison to classical variants reflecting a greater degree of desmoplasia histologically. Moreover, in proton magnetic resonance spectroscopy, medulloblastomas characteristically show a small taurine peak detectable at short echo time, have an elevated choline peak, and a decreased N-acetyl aspartate peak.[7]

Among the histologically defined medulloblastomas, desmoplastic/nodular medulloblastoma is defined as an embryonal tumor arising in the cerebellum, characterized by nodular, reticulin free zones (so-called pale islands) and intervening densely packed, poorly differentiated cells highly proliferative cells with hyperchromatic and moderately pleomorphic nuclei that produce an intercellular network of reticulin-positive collagen fibers. Typical Homer Wright (neuroblastic) rosettes are not found in this variant. This variant accounts for 47%–57% of all cases in children aged <3 years, while in adult patients, the incidence is much less.[8,9] As per the existing literature, extra-axial medulloblastomas located at CP angle may originate either by the proliferating remnants of the external granular layers of the cerebellar hemispheres including the flocculus, or from germinal cells or their remnants present at posterior medullary velum, or by the lateral extension from the fourth ventricle through the foramen of Luschka, or there may be

direct exophytic growth from the site of origin at the surface of cerebellum or pons.[10]

When corroborating the molecular and morphological variants of medulloblastoma listed in the WHO 2016 classification, desmoplastic/nodular medulloblastomas align with the SHH-activated molecular group. Genetic studies display pathological activation of the SHH pathway, which is often caused by mutations in genes encoding member of the pathway including PTCH1, SMO, and SUFU.[11] In a recent analysis using next-generation sequencing, 85% of desmoplastic/nodular medulloblastomas carried genetic alterations in PTCH1, SUFU, SMO, SHH, GL/2, or MYCN. This study also showed a predominance of SUFU and PTCH1 mutations in young children, whereas PTCH1 and SMO mutations were more common in adults.[12]

Basically, CP angle medulloblastomas are a surgically treated disease. Concerning the management, the best therapeutic approach is surgery along with chemotherapy/radiotherapy. In most cases, desmoplastic/nodular medulloblastoma in early childhood has a better outcome with surgery and chemotherapy alone. In a meta-analysis of prognostic factors in infant medulloblastomas, progression-free or overall survival at 8 years was significantly better for desmoplastic variants than for other medulloblastomas.[13] In contrast, in a European multicenter trial involving the older children, no survival difference was found between desmoplastic/nodular medulloblastoma and classic medulloblastoma.[14] In terms of genetic classification, it has been found that SHH-activated and TP53-mutant medulloblastomas are associated with a very poor outcome. In a study conducted by Zhukova *et al*., the 5-year overall survival of patients with an SHH-activated medulloblastoma was found to be 76% for those with a TP53-wildtype tumor and 41% for those with a TP53-mutant tumor.[15]

CONCLUSION

The most common CP angle tumors in adults are schwannomas, meningiomas, and epidermoid tumors followed by metastatic lesions. Contrary to these, extra-axial medulloblastomas at CP angle are extremely rare and may present as a diagnostic challenge, especially in adults. Thus, to reach to an accurate preoperative radiological diagnosis, it needs to be considered in the differential diagnosis of extra-axial CP angle lesions, even in adults.

Declaration of patient consent

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

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Conflicts of interest

There are no conflicts of interest.

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