

*Case Report*

Intracranial Medulloepithelioma in a Child: A Case Report

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ABSTRACT

Intracranial medulloepithelioma is an extremely rare and highly malignant fast-growing tumor that shows a propensity to spread widely throughout the central nervous system. It most commonly occurs in infants and young children. We report a rare case of 2-year-old female patient with a large mass lesion diagnosed as medulloepithelioma. Although radiological examination was characteristic for the neoplasm, it was not sufficient to make a definite diagnosis. However, when it was combined with histopathological examination, we could diagnose medulloepithelioma and differentiate it from other central nervous system tumors. We intend to provide greater understanding and knowledge of intracranial medulloepithelioma by reporting this case.

KEYWORDS: Embryonal tumor, Intracranial tumor, Medulloepithelioma

ABBREVIATIONS: **CNS:** Central nervous system, **MRI:** Magnetic resonance imaging, **GTR:** Gross total resection, **HDC:** High-dose chemotherapy, **AuPBSCT:** Autologous peripheral blood stem cell transplantation, **hTERT gene:** Human telomerase catalytic protein subunit gene, **T1WI:** T1-Weighted imaging, **T2WI:** T2-weighted imaging, **H&E:** Hematoxylin and eosin.

■ INTRODUCTION

Central nervous system (CNS) tumors are the third most common type of childhood malignancies after leukemia and lymphoma. In 2016, the World Health Organization proposed a new classification system for CNS tumors that integrated phenotype and genotype. In the new classification system, the term "primitive neuroectodermal tumor" has been removed from the diagnostic lexicon, although some rare entities have remained in use, such as medulloepithelioma (5). Intracranial medulloepitheliomas are rare embryonal tumors, with a peak incidence between 6 months and 5 years of age (7). Unlike intraorbital medulloepithelioma, which always exhibits a benign clinical course after cure with simple enucleation, intracranial medulloepithelioma exhibits a dismal prognosis, with a propensity for progression, recurrence, and dissemination; this is particularly likely in cases where

the tumor is incompletely resected (4,9). In the present study, we report the case of a 2-year-old child with a large medulloepithelioma.

■ CASE REPORT

A 2-year-old girl was admitted to our hospital with a 10-day history of drowsiness and a 2-day history of vomiting. Brain magnetic resonance imaging (MRI) revealed a large (64×63×72 mm), partly cystic, heterogeneous mass lesion in the right posterior temporal lobes and parieto-occipital lobes, which had invaded the right basal ganglia region (Figure 1A, B). Axial and coronal images obtained in enhanced MRI revealed heterogeneous enhancement of the tumor after contrast administration. The enhancement separations were obvious, with a "honeycomb" change in local areas (Figure 1C, D). Our initial MRI diagnosis was medulloblastoma.

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Emergency craniotomy was performed to resolve brain herniation. Intraoperatively, the tumor was irregular, grayish, and soft, with cystic changes and signs of hemorrhage. The tumor was well demarcated from the surrounding brain and was completely resected. A postoperative computed tomography scan of the brain confirmed complete tumor removal. Her vomiting improved in the subsequent days. The patient underwent postoperative radiotherapy. Unfortunately, she was lost to follow-up 2 months later.

Histological examination revealed that the tumor was characterized by pseudostratified columnar epithelium folded into closely packed plates, papillary structures, and tubules (Figure 2A, B). Immunohistochemical analysis showed that the tumor was positive for synaptophysin; the Ki-67 index was approximately 30% in some areas (Figure 3A, B). Further, the tumor was negative for epithelial membrane antigen and S-100 protein (Figure 4A, B).

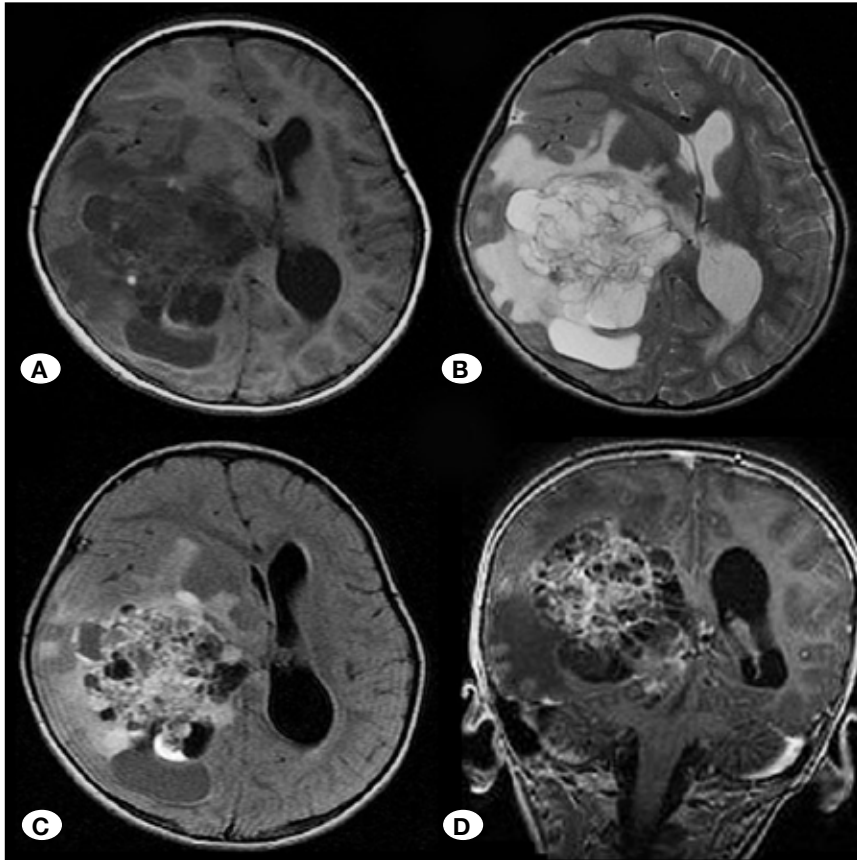


Figure 1: Brain MRI revealed a large (64×63×72 mm), partly cystic mass in the right posterior temporal lobes and parieto-occipital lobes, which had invaded the right basal ganglia region. The mass was **A)** hypointense on T1WI, and **B)** hyperintense on T2WI. **C)** Axial and **D)** coronal images obtained in enhanced MRI revealed significant heterogeneous enhancement of the mass lesion.

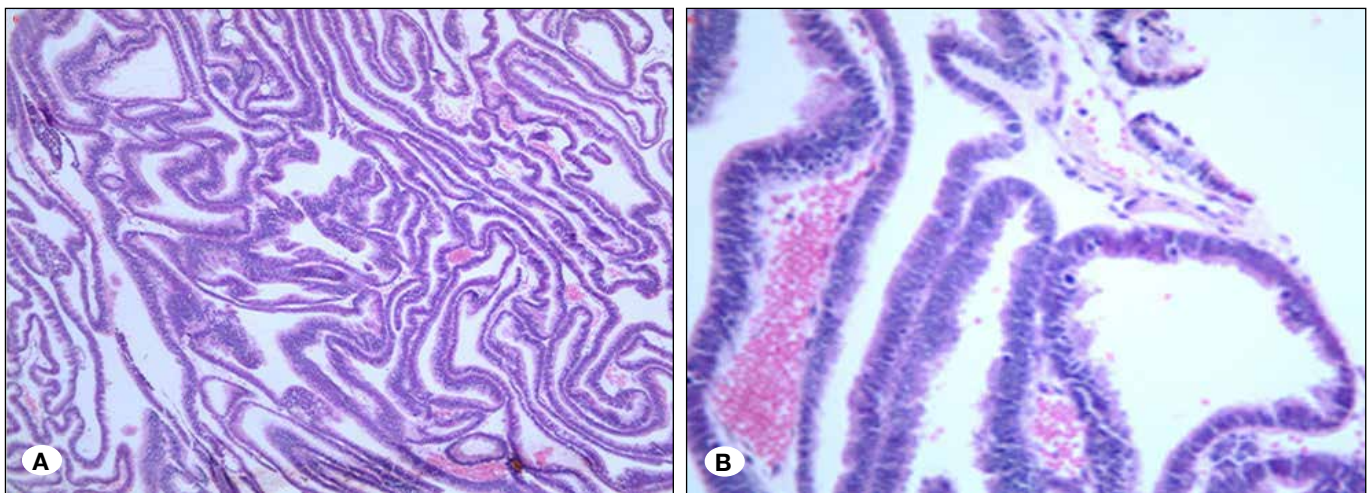


Figure 2: **A)** Histological examination showed neoplastic epithelial cells appear as papillary, tubular, or beam-like arrangement (H&E, ×10). **B)** Mitotic cells were located on the luminal surface of the pseudostratified tissue (H&E, ×40).

DISCUSSION

First described by Bailey and Cushing in 1926 (1), CNS medulloepitheliomas are extremely rare embryonal neoplasms that typically present in childhood. There have been approximately 40 cases of this entity reported in the literature (4). Notably, only two adult patients have been reported (11). Medulloepitheliomas are thought to originate from primitive pluripotency and neural tube-specific pluripotent stem cells. Therefore, medulloepitheliomas may occur anywhere along the entire neural axis. However, only five cases of peripheral medulloepitheliomas have been reported (11). The cerebrum is the most common location, accounting for nearly 30% of all cases. Medulloepitheliomas are commonly found in the periventricular location, involving (in order of frequency) the temporal, parietal, occipital, and frontal lobes (7,11). Medulloepithelioma is known for its high malignancy, and the median survival time is 5 months (10). According to the report by Hayase et al. (4), only 11 medulloepithelioma cases where patients survived for > 2 years have been reported.

Histologically, these tumors may comprise tubular, trabecular, or papillary cellular arrangements (7,9). Further, the tubular structures have both external and internal limiting membranes, as in the neural tube (7,9). These tumors may display multiple lines of differentiation, including neuronal, glial, or mesenchymal elements; this is detected with employing immunohistochemistry (2), and the tumors are typically positive for vimentin, synaptophysin, neurofilament, neuron-specific enolase, and glial fibrillary acidic protein (7). Because of the occasional mesenchymal differentiation, medulloepitheliomas may share a histogenetic overlap with teratoma. Accordingly, differential diagnoses for these patients include medulloblastoma and immature teratoma.

The imaging characteristics of medulloepitheliomas are distinct. Moftakhar et al. (7) reported one case with the tumor: the lesion was hypointense on T1-weighted imaging (T1WI), hyperintense on T2-weighted imaging (T2WI), and enhanced after contrast administration. However, according to the report by Molloy et al. (8), most medulloepitheliomas

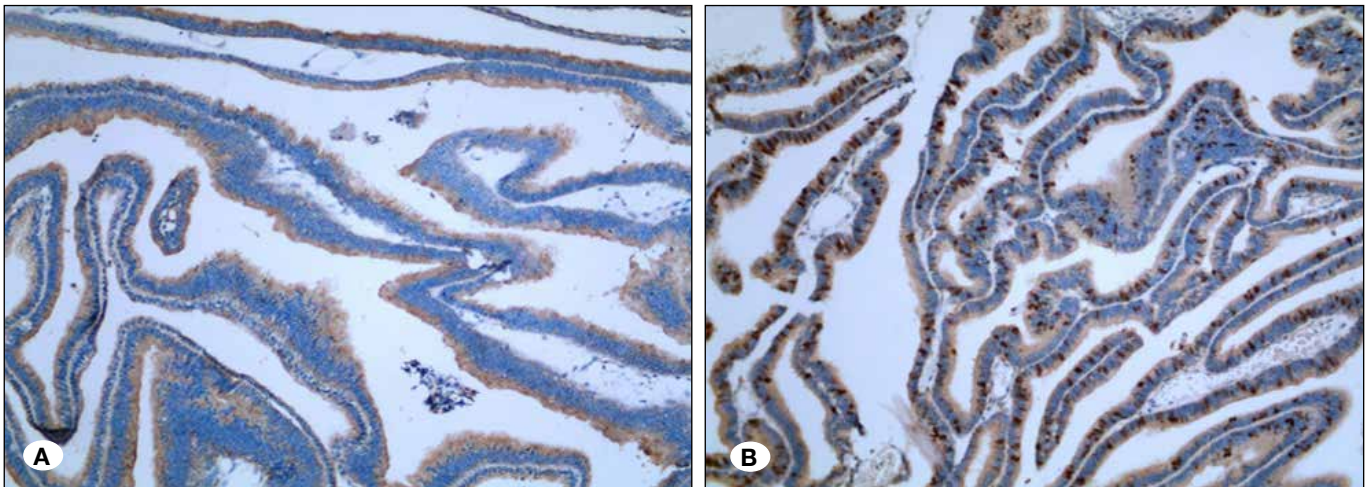


Figure 3: **A)** Immunohistochemical analysis revealed positive expression of synaptophysin (Invision, $\times 20$). **B)** Expression of Ki-67 was high, and the Ki-67 index was approximately 30% in the top left corner (Invision, $\times 20$).

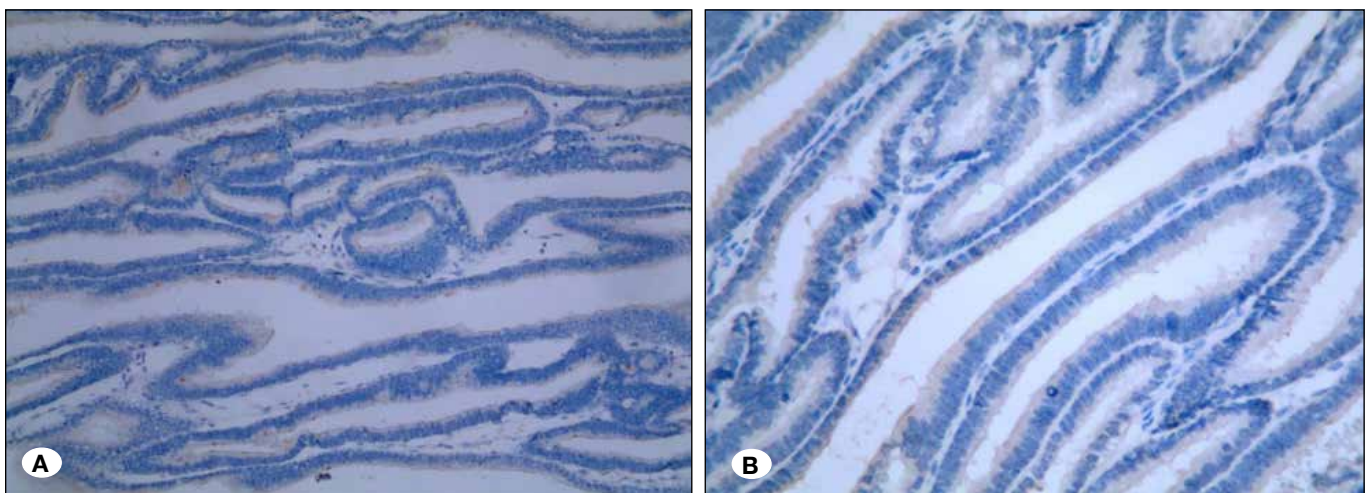


Figure 4: Immunohistochemical analysis revealed negative expression of epithelial membrane antigen **(A)** and S-100 protein **(B)** (Invision, $\times 20$).

are not enhanced on MRI. This may be due to the uniform density of early tumors, such that enhancement after contrast administration is not obvious; however, during progression and later stages, when cystic necrosis appears, destruction of the blood brain barrier or infringement upon the surrounding meninges and blood vessels may cause partial enhancement.

Treatment for medulloepitheliomas remains a challenge. Gross total resection (GTR), followed by radiotherapy and high-dose chemotherapy (HDC), is the most accepted treatment. According to a review by Matsumotu et al. (6), five long-term survivors had all undergone GTR of the tumor, followed by chemoradiotherapy. More recently, Hayase et al. (4) reported a patient who was successfully treated with HDC, followed by autologous peripheral blood stem cell transplantation (AuPB-SCT) without radiation, and suggested that radiotherapy can be replaced by HDC/AuPBSCT in infants with medulloepitheliomas after GTR. Moftakhar et al. (7) reviewed four factors predictive of a favorable outcome, including supratentorial location, GTR, absence of cerebrospinal fluid dissemination, and aggressive postoperative chemoradiotherapy. According to another literature review (9), supratentorial location was not a favorable prognostic factor; however, older age was associated with an improved prognosis.

In recent years, the role of the *human telomerase catalytic protein subunit (hTERT)* gene has been investigated in medulloepitheliomas. Fan et al. (3) demonstrated that the *hTERT* oncogene is amplified in a significant proportion of medulloepitheliomas. In addition, correlation of *hTERT* expression with survival suggests that the *hTERT* expression level is a useful molecular prognostic indicator.

■ CONCLUSION

Radiological examination is not sufficient to make a definite diagnosis for intracranial neoplasms. It should be combined with histopathological examination to diagnose medulloepithelioma and to differentiate it from other central nervous system tumors.

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■ REFERENCES

1. Bailey P, Cushing HA: Classification of the tumours of the glioma group on a histogenetic basis with correlated study of prognosis. Philadelphia: JB Lippincott, 1926:54-56
2. Chakrabarti I, Majumdar K, Giri A: Infratentorial medulloepithelioma with divergent differentiation: Possibly a predictor of poor outcome. *J Pediatr Neurosci* 7(2):142-145, 2012
3. Fan X, Wang Y, Kratz J, Brat DJ, Robitaille Y, Moghrabi A, Perlman EJ, Dang CV, Burger PC, Eberhart CG: *hTERT* gene amplification and increased mRNA expression in central nervous system embryonal tumors. *Am J Pathol* 162:1763-1769, 2003
4. Hayase T, Morimoto A, Kawahara Y, Yagi M, Kanai N, Nobusawa S, Hirato J, Gomi A: An infant with medulloepithelioma successfully treated by high-dose chemotherapy followed by autologous peripheral blood stem cell transplantation without radiotherapy. *J Pediatr Hematol Oncol* 37(6):e394-398, 2015
5. Louis DN, Perry A, Reifenberger G, von Deimling A, Figarella-Branger D, Cavenee WK, Ohgaki H, Wiestler OD, Kleihues P, Ellison DW: The 2016 World Health Organization classification of tumors of the central nervous system: A summary. *Acta Neuropathol* 131(6):803-820, 2016
6. Matsumoto M, Horiuchi K, Sato T, Oinuma M, Sakuma J, Suzuki K, Sasaki T, Kodama N, Watanabe K, Suzuki T: Cerebral medulloepithelioma with long survival. *Neurol Med Chir (Tokyo)* 47:428-433, 2007
7. Moftakhar P, Fan X, Hurvitz CH, Black KL, Danielpour M: Long-term survival in a child with a central nervous system medulloepithelioma. *J Neurosurg Pediatr* 2(5):339-345, 2008
8. Molloy PT, Yachnis AT, Rorke LB, Dattilo JJ, Needle MN, Millar WS, Goldwein JW, Sutton LN, Phillips PC: Central nervous system medulloepithelioma: A series of eight cases including two arising in the pons. *J Neurosurg* 84(3):430-436, 1996
9. Müller K, Zwiener I, Welker H, Maass E, Bongartz R, Berthold F, Pietsch T, Warmuth-Metz M, von Bueren A, Rutkowski S: Curative treatment for central nervous system medulloepithelioma despite residual disease after resection. Report of two cases treated according to the GPHO Protocol HIT 2000 and review of the literature. *Strahlenther Onkol* 187(11):757-762, 2011
10. Norris LS, Snodgrass S, Miller DC, Wisoff J, Garvin J, Rorke LB, Finlay JL: Recurrent central nervous system medulloepithelioma: Response and outcome following marrow-ablative chemotherapy with stem cell rescue. *J Pediatr Hematol Oncol* 27(5):264-266, 2005
11. Ramesh AS, Anita M, Jitender S, Somanna S: Unusual occurrence of supratentorial medulloepithelioma in a young female. *J Neurosci Rural Pract* 5(3):261-264, 2014