Clinical Case Report

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Infantile medulloepithelioma in the lateral ventricle and cerebellopontine angle

Two case reports

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Abstract

Rationale: Intracranial medulloepitheliomas are extremely rare and highly malignant. Intraventricular medulloepitheliomas are even rarely reported, and little is known about the clinical features.

Patient concerns: In this article, we report two cases of intracranial medulloepitheliomas. In the first patient, a one-month old boy, the tumor was located in in right lateral ventricle, which was the first report of such location of this disease; in the second patient, an eleven-month old girl, the tumor was in right cerebellopontine angle.

Diagnoses: Both patients were diagnosed as medulloepithelioma by pathologists.

Interventions: Both patients underwent craniotomy to resect the lesion totally.

Outcomes: The boy underwent chemotherapy after operation and was alive 3 months after operation. The girl died 6 months after operation, despite aggressive adjuvant chemotherapy.

Lessons: Surgical resection is safe and effective to prolong patient survival. However, despite aggressive adjuvant therapy, prognosis of medulloepithelioma remains poor, and further study is needed to improve treatment of this rare disease.

Abbreviations: ABMT = autologous bone marrow transplantation, CPP = choroid plexus papilloma, CT = computed tomography, ETMR = embryonal tumors with multilayered rosettes, GFAP = glial fibrillary acidic protein, MRI = magnetic resonance imaging, NSE = neuronal specific enolase, PAS = Periodic Acid-Schiff stain.

Keywords: craniotomy, embryonal tumors with multilayered rosettes, medulloepithelioma, prognosis

1. Introduction

Medulloepithelioma is a rare malignant tumor in childhood that arises from primitive neuroectodermal epithelium lining the neural tube.[1] It is the most common congenital tumor in ciliary body, but medulloepithelioma in central nervous system is rarely reported.[2,3] In this article, we report 2 cases of infantile medulloepithelioma. The first one is a 1-month-old boy with tumor in the lateral ventricle, and the second one is an 11-month-old girl with tumor in the right cerebellopontine angle.

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2. Case description

2.1. Patient 1

The 1-month-old boy was admitted to our department because a routine ultrasonography 3 days before his birth had revealed an intracranial mass. Before his admission, the baby showed no sign of intracranial hypertension, such as bulging fontanel, irritation, failure to thrive, or seizure. A magnetic resonance imaging (MRI) study showed a giant, lobulated mass in the occipital horn of the right lateral ventricle, but there was no sign of hydrocephalus. After gadolinium injection, the tumor showed marked enhancement, especially in the peripheral section (see Fig. 1). Because of its location, initial diagnosis of choroid plexus papilloma was suspected.

The patient underwent craniotomy to resect the tumor under intubated anesthesia. Surgical corridor was through parietal cortex. The tumor was pink, mixed with greyish parts. Its texture was rigid, tenacious with ample blood perfusion. The tumor was resected in a piecemeal fashion under high magnification. Care was taken to prevent excessive blood loss, but still around 100 cc red blood cells and 80 cc fresh frozen plasma was transfused. After operation, the boy was transferred to pediatric intensive care unit, and the next day, he was extubated. His postoperative course was unremarkable. Our pathology review board confirmed the diagnosis of medulloepithelioma. The tumor formed primitive neural tube like structure, lined by ill-differentiated primitive epithelial tumor cells. His specimen showed positive stain for Nestin, negative for Lin28A, and Ki-67 index was 10% to 20% (see Fig. 2). Chemotherapy using cyclophosphamide, vincristine, followed by carboplatin and

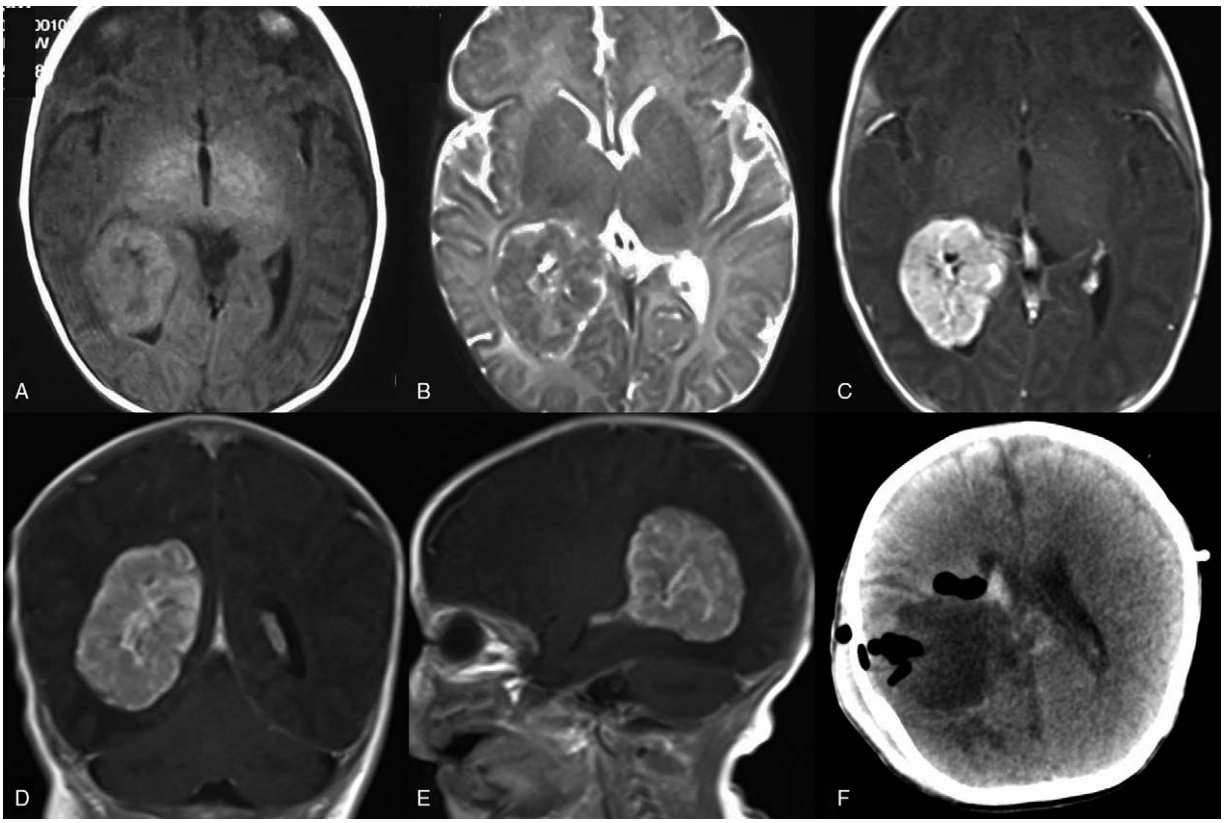

Figure 1. Images for patient 1. (A) Preoperative T1-weighted magnetic resonance imaging (MRI) showing the mass in the right lateral ventricle. (B) Preoperative T2-weighted MRI showing cerebrospinal fluid surrounding the tumor. (C) Postcontrast T1-weighted MRI showing heterogeneous enhancement of the tumor. (D) Coronal section of the tumor. (E) Sagittal section of the tumor. (F) Postoperative computed tomography (CT) of the patient showing complete resection of lesion. CT = computed tomography, MRI = magnetic resonance imaging.

etoposide was administered. Three months after operation, the patient was able to thrive with no sign of recurrence.

2.2. Patient 2

The 11-month-old girl was admitted to our department because of recurrent seizure for 3 days and vomiting for 2 days. Three days prior to her admission, the girl had repeated generalized tonic-clonic seizures, and she was not fully alert between seizure attacks. Two days before admission, her situation deteriorated, and vomited several times. She was then referred to our department, and her preliminary computed tomography (CT) scan showed marked hydrocephalus and a mass in the right cerebellopontine angle. An extraventricular drainage was performed under emergency to relieve hydrocephalus, and she was fully alert after the procedure. On physical examination, the patient showed decreased hearing in her right ear. Her MRI showed a giant mass with cystic change located in the right cerebellopontine angle. The tumor showed marked enhancement in solid part and in the rim of cyst in postcontrast MR imaging (see Fig. 3). Because of significant compression of brainstem and hydrocephalus, a craniotomy was scheduled.

The patient underwent operation via retrosigmoid approach. The tumor occupied the right cerebellopontine angle, and circumscribed acoustic nerve and facial nerve. It was solid with cystic changes, and its solid part was like fish flesh with hemorrhage, and was soft in texture. Tumor was grossly totally removed under microscope, and great care was taken to avoid damage to cranial nerves. No transfusion was needed. Her postoperative recovery was fine. Her extraventricular drainage was withdrawn the second day after operation, and she was discharged about 4 days after operation. Postoperative pathology confirmed diagnosis of medulloepithelioma. The specimen was positive for Nestin stain, but negative for Lin28A or cytokeratin 7, and its Ki-67 index was 20% to 30%. The patient died 6 months after operation, despite aggressive adjuvant chemotherapy. Study and report of both patients was reviewed and approved by Ethnic Committee of West China Hospital, and consent was obtained from both patients' guardians.

3. Discussion

Medulloepitheliomas are rare, highly malignant embryonal tumors, accounting for only 1% of all primary central nervous system tumors.[4] Its peak incidence is at 6 months and 5 years of age, and has no gender difference.[5] The tumor was reported to occur in the cerebral hemisphere, brainstem, cerebellum or peripheral nerves, with nearly 30% of medulloepitheliomas located in cerebrum.[5] Its most common location in cerebrum is paraventricular region, followed by temporal, parietal, occipital and frontal lobes. This is the first report regarding supratentorial medulloepithelioma in lateral ventricle, and adds to differential

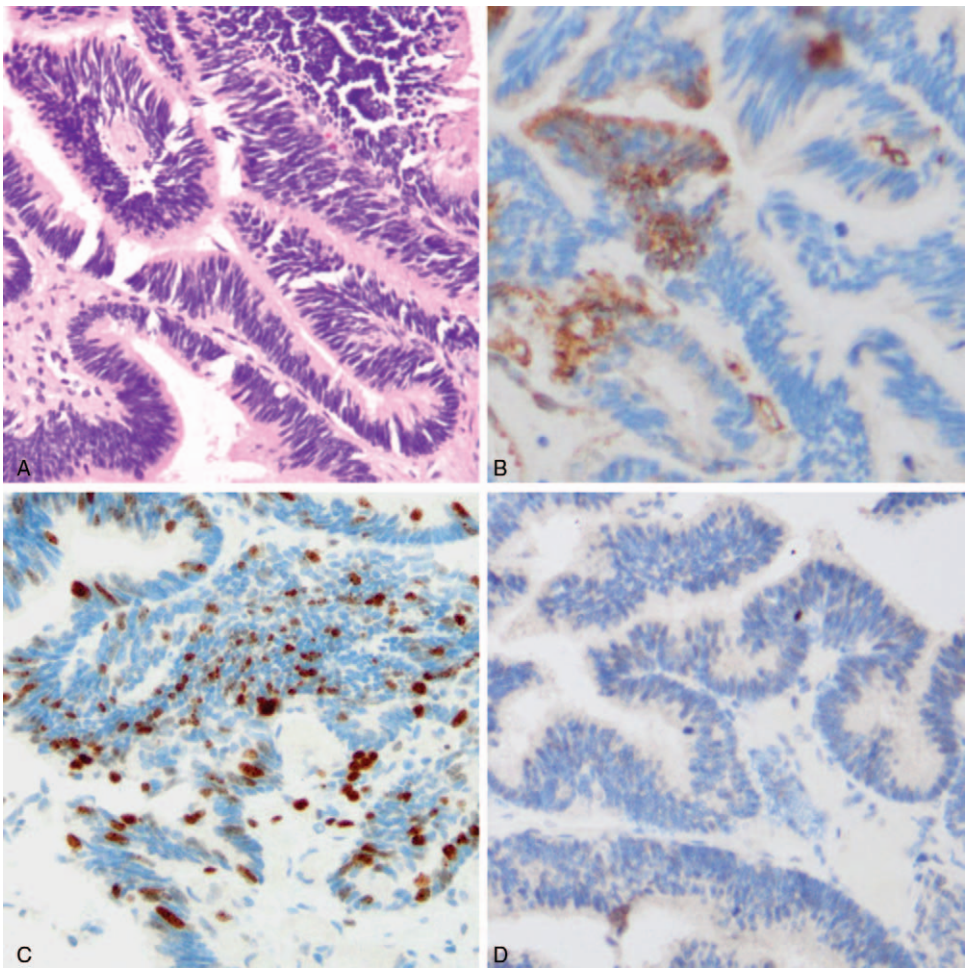

Figure 2. Micrograph of tumor in patient 1 (X200). (A) Hematoxylin-eosin stain showing pseudostratified laminated epithelium similar to primitive neural tube. (B) Patched positive stain for Nestin. (C) Ki-67 stain showing active mitosis. (D) Negative stain for Lin28A.

diagnosis of tumor in this place. Prognosis for medulloepithelioma is very poor, with median survival of 5 months despite aggressive therapy.[6] However, medulloepithelioma can also occur intraorbitally, and in contrast to central nervous system medulloepitheliomas, excellent long term prognosis can be achieved with enucleation procedure alone. The survival difference of the 2 entities seems to be associated with divergent cytogenetic and epigenetic features, suggesting that they are distinct nosologic entities.[2]

Microscopically, medulloepithelioma consists of pseudostratified primitive-like epithelium, which forms laminated structures, similar to primitive neural tube. The stratified epithelium rests on a continuous, periodic acid-Schiff stain (PAS)-positive basement membrane, which may also coat the luminal surface. The tumor cells are large, polygonal cells with scant cytoplasm and hyperchromatic nucleoli.[4,7] Mitotic figures are frequent. These tumor cells may differentiate along astroglial, neuronal, or ependymal lines, and co-existence of different lines can be detected by immunohistochemistry. The astroglial and ependymal lines are positive for glial fibrillary acidic protein (GFAP) staining, and neuronal lines are positive for synaptophysin or neuronal specific enolase (NSE).[4] Currently, medulloepitheliomas are classified as a distinct group from embryonal tumors with multilayered rossettes (ETMR), and majority of medulloepitheliomas do not carry alterations of C19MC microRNA cluster.[8] Also, Lin28A, once considered a diagnostic marker to ETMR, is now found also expressed in gliomas, germ cell tumors and terotomas.[1] Lin28A is also associated with prognosis. It was reported that patients without Lin28A expression in the tumor had higher probability of progression free survival.[9] Nevertheless, a diagnostic marker for medulloepithelioma remains to be defined,[1] and diagnosis of medulloepithelioma largely relies on microscopic morphology observation.

Radiological appearance of medulloepitheliomas is not specific. On CT scans, it appears as well circumscribed, iso- or hypodense neoplasm.[1] Molloy et al[6] described typical MR imaging for these tumors, which were iso-or hypotense in T1-weighted imaging, hypertense in T2-weighted imaging, and not enhanced with gadolinium. However, recent reports showed that over 95% of medulloepitheliomas displayed postcontrast enhancement, particularly the solid parts, reflecting more aggressive nature with higher recurrence possibilities.[1,4,5,10,11] In the present cases, both tumors showed marked heterogeneous enhancement, and one tumor was found before birth, while the other invaded cranial nerves. These features suggest that the tumors progress rapidly and are prone to recurrence.

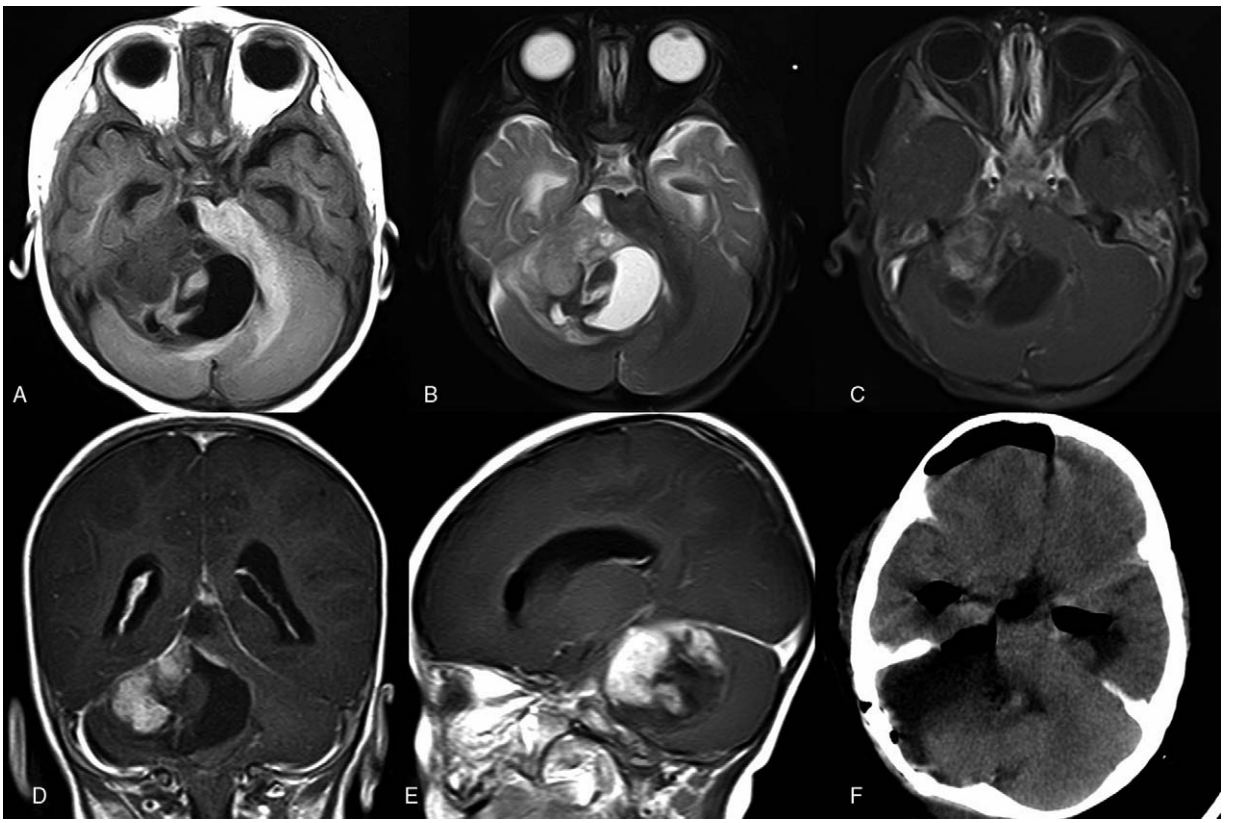

Figure 3. Images for patient 2. (A) Preoperative T1-weighted magnetic resonance imaging (MRI) showing the mass in the right cerebellopontine angle. (B) Preoperative T2-weighted MRI showing cystic changes of the tumor. (C) Postcontrast T1-weighted MRI showing heterogeneous enhancement in solid part of the tumor. (D) Coronal section of the tumor. (E) sagittal section of the tumor. (F) Postoperative computed tomography (CT) of the patient showing complete resection of lesion and relief of supratentorial pressure. CT = computed tomography.

The specific lesion location in present cases adds to differential diagnosis of other tumors frequently seen in such places. Intraventricular tumor with similar MR features to our first patient often suggests choroid plexus papilloma (CPP). Choroid plexus papilloma has been described as lobulated, mulberry-like mass in ventricular systems with iso-or slight hypo-intensity in T1 weighted imaging, and heterogeneous iso-intensity in T2 weighted imaging. After gadolinium injection, CPP shows marked homogenous or heterogeneous enhancement.[12] Such features are indistinguishable from radiological findings in our first patient. The only possible method for accurate diagnosis is by pathology. Choroid plexus papilloma is characterized by well-differentiated columnar epithelial cells and inner stroma rich in capillaries, and almost universal positive staining for GFAP and CK7.[13] On the other hand, medulloblastoma is frequently seen in cerebellopontine angle. Cystic changes in medulloblastoma are rare, and under microscope, it appears as round, hyperchromatic, ill-differentiated small cell with large nucleus. Wnt and Sonic hedgehog signaling pathway is activated in type 1 and 2 medulloblastomas, respectively.

Medulloepithelioma is fatal, and most children die within one year after diagnosis.[4,5,7,11] The optimal treatment includes complete resection, followed by adjuvant radio- and chemotherapy. Surgical resection is critical to relieve intracranial hypertension and offers best chance for adjuvant treatment. Tumor cell infiltration to brain tissue indicates poor survival prognosis, but extended resection up to 1 cm in surrounding brain, or including infiltrated tissue, is reported to improve patient outcome.[11] Thus, intraoperative frozen section is essential to determine degree of infiltration and extent of resection. According to Bouhoula et al,[14] optimal radiotherapy plan included 35 Gy in 21 day fraction, followed by boost dose of 20 Gy in 12 fractions to posterior fossa, primary tumor bed, or postoperative residual tumor. However, radiotherapy can cause significant cognitive and developmental impairment to young children, and children under the age of 3 years are generally considered not suitable for radiotherapy. Aggressive chemotherapy and autologous bone marrow transplantation (ABMT) seems to be a promising strategy. Kusakabe et al[1] reported up to 10 months' event free survival after partial resection of an intracranial medulloepithelioma, followed by high dose chemotherapy and ABMT. In earlier literature, Norris et al[15] reported complete radiographic response in 3 patients using similar strategy, and one of the patients survived more than 5 years after treatment. Characteristics for long term survival (≥3 years) include supratentorial location, no neuroaxis dissemination, postoperative radio- and chemotherapy, while age and sex is irrelevant.[5]

Author contributions

Conceptualization: Qiang Li, Yan Ju.
Data curation: Qiang Li, Ni Chen.
Writing – original draft: Qiang Li.
Writing – review & editing: Qiang Li, Ni Chen, Yan Ju.

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