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Case Report

Pediatric Hemispheric Central Nervous System Embryonal Tumor and its Management; A Case Report

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Received: February 12, 2025; **Published:** February 24, 2025

Abstract

Embryonic tumors can occur at any age, but are more common in infants and young children. They are malignant tumors originating from fetal (embryonic) cells in the brain. They are most commonly found in the pineal region. They are believed to be spontaneous in etiology, but others have attributed the cause to incidental diagnostic X-ray exposure. Primary intracranial germ cell tumors are radiosensitive and potentially treatable when standard surgery and radiotherapy (RT) are recommended. A 1-year-old female infant was brought to our outpatient clinic by her family with complaints of sudden onset of left hemiparesis and inability to walk for the past 10 days. Magnetic resonance imaging showed a cystic-cavitated mass lesion with thick irregular walls and hemorrhagic content, approximately 98x77x82 mm in size, located in the right frontoparietal region. There was another solid component measuring 52x39 mm in size in the parafalcine area adjacent to the posterior vertex of the lesion. The patient underwent surgery and was diagnosed with WHO grade IV CNS embryonic tumor. Radiation and medical oncology clinics were consulted and treatment is still ongoing. In pediatric embryonal tumors, diagnosis of pathological subgroups with genetic studies is extremely important in order to apply appropriate treatment. More promising results are expected after treatment with developing surgical techniques and chemotherapeutic drugs.

Keywords: *Pediatric Embryonal Tumor; Management; Diagnosis; Radiotherapy*

Introduction

Intracranial germ cell tumors are malignant tumors that originate from fetal (embryonic) cells in the brain. They are rare tumors of the central nervous system (CNS). Embryonic tumors can occur at any age, but are most common in infants and young children. They constitute 2 - 3% of childhood cancers. While most are gonadal in adults, more than 50% in children originate from non-gonadal regions such as the mediastinum, retroperitoneum, and central nervous system.

They may present with different clinical findings depending on the location. Treatment is selected according to the location and histopathological subtype of the tumor. When treated appropriately, survival is over 90%, especially in germinomas. The combined use of radiotherapy and chemotherapy has also increased survival rates in non-germinoma tumors. Primary intracranial germ cell tumors (ICGCTs) are remarkably radiosensitive and potentially curable when standard surgery and radiotherapy (RT) is offered [1,2].

These are frequently found in the pineal region. They are believed to be spontaneous in etiology, although others have attributed the cause to incidental diagnostic X-ray exposure [3,4].

Studies are ongoing for treatment protocols that will reduce treatment-related side effects while not reducing the chance of survival. In the WHO 2021 classification, PNET group tumors are no longer included in the group of embryonal tumors.

Intracranial hemispheric localization of these tumors, which are frequently located in the pineal region, has not been encountered in the literature in the last 5 years. It is thought that our case will attract the attention of readers and contribute to the literature.

Histopathological types of embryonal tumours of WHO 2021 classification:

Embryonal tumors
Medulloblastoma
Medulloblastomas, molecularly defined
Medulloblastoma, WNT-activated
Medulloblastoma, SHH-activated and TP53-wildtype
Medulloblastoma, SHH-activated and TP53-mutant
Medulloblastoma, non-WNT/non-SHH
Medulloblastomas, histologically defined
Other CNS embryonal tumors
Atypical teratoid/rhabdoid tumor
Cribriform neuroepithelial tumor
Embryonal tumor with multilayered rosettes
CNS neuroblastoma, FOXR2-activated
CNS tumor with BCOR internal tandem duplication
CNS embryonal tumor

Table

Case Report

A 1-year-old baby girl was brought to our outpatient-clinic by her family with complaints of sudden onset of left hemiparesis and inability to walk in the last 10 days. The patient, who also had loss of strength in his left wrist, began to keep his fingers in constant flexion. Weakness also began in his left ankle. He began to keep his head constantly on the right side. The patient, whose motor skills had deteriorated, began to be unable to sit without support. In the examination of the patient, he was conscious, his head was in a macrocephalic appearance (head circumference: 52.5 cm and anterior fontanelle: 1.5x2 cm), myoclonus and hyperreflexia were observed in the left lower extremity, while patellar reflex could not be obtained in the right lower extremity. No papilledema was observed in the fundus examination. He had no epileptic seizures.

A contrast-enhanced brain magnetic resonance was planned for the patient and the pediatric neurology clinic was consulted. Due to developmental delay, the perioperative pediatric metabolism and nutrition clinic was also consulted.

Magnetic resonance imaging; showed a cystic-cavitary mass lesion with thick irregular walls and hemorrhagic content, measuring approximately 98x77x82 mm, located in the right frontoparietal region. There was another solid component measuring 52x39 mm in

the parafalcine area adjacent to the posterior vertex of the lesion (Figure 1A and 1B). The mass had significant compression on the brainstem, right lateral ventricle and third ventricle. This caused significant uncal herniation (15 mm), subfalcine shift (24 mm) and acute hydrocephalus in the left lateral ventricle. Cerebral cortical sulci were swollen and the mass was in contact with the superior sagittal sinus. There was significant diffusion restriction in the mass wall, therefore, atypical teratoid rhabdoid tumor and infantile type hemispheric glioma were considered in the differential diagnosis. Embryonal tumor and desmoplastic infantile ganglioglioma were considered as other possibilities.

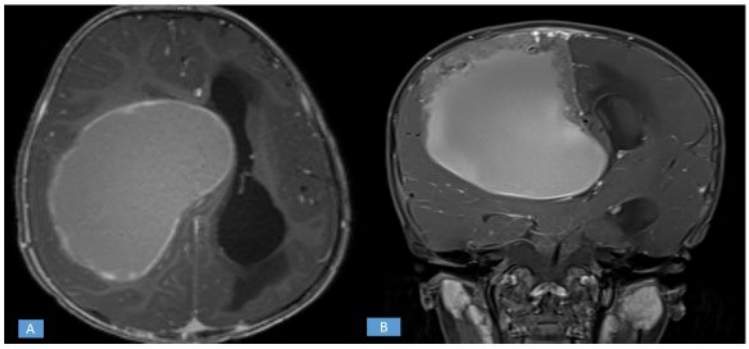

Figure 1A and 1B: *Preoperative contrast-enhanced brain MRI, axial and coronal sections show a mass lesion with a cystic area in the right hemisphere.*

Operation procedure

The patient was under general anesthesia; in supine position, the head was fixed with a nailed head. A skin incision was made and the burr-hole and craniotomy was performed. When the dura was opened, it was seen that the brain was excessively edemated. The tumor also had a cystic component. The tumor was debulked and removed as much as possible without damage to the neural tissue. Homeostasis was done and the patient was closed. The patient was taken to the postoperative pediatric intensive care unit.

Histopathological examination

A tissue sample, measuring 4 x 6 x 3 cm in its largest diameter and of a beige colour, was sent to the clinical pathology unit for examination. The immunohistochemical study was conducted in our laboratory using a fully automated Ventana Benchmark XT instrument (Arizona, USA). The tissues were fixed in buffered formaldehyde and an internal control for antibodies was employed in order to ensure the reliability of the results. The antigen was retrieved using an automated system. A total of 16 distinct immunohistochemical examinations were conducted for the purpose of differential diagnosis. Positive staining was observed for glial fibrillary acidic protein (GFAP). Positive staining was obtained with S100 and focal positive staining was obtained with *CD56*Anti-ATRX*NSE*Neurofilament*INI-1. Negative staining was observed with *Olig2*ALK*Chromogranin*Synaptophysin*IDH-1*EMA. Positive staining for CD45 was observed in lymphoid cells and negative staining in the tumor. Ki67 evaluation noted a 65 - 70% increase in proliferation. With P53, 40 - 50% proliferation was observed in focal areas. Based on the histopathological examination of the specimen by a double-blinded pathologist with at least 10 years of experience, a diagnosis of CNS Embryonal tumor, WHO grade IV, was made (Figure 2).

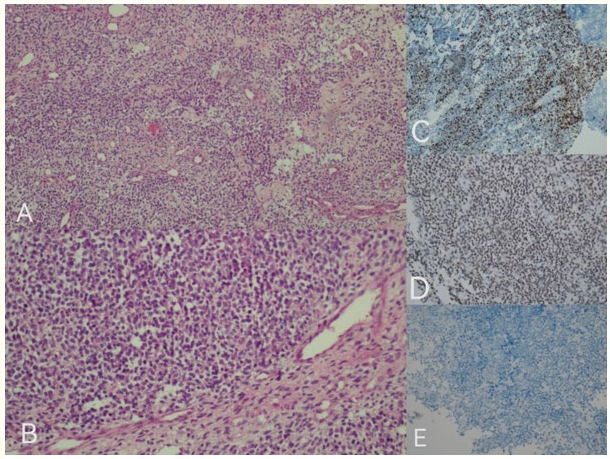

Figure 2A-2C: *A: Tumor infiltration consisting of small, round, narrow cytoplasmic cells with occasional high mitotic activity. H&E x100. B: Closer view of these cells H&E x200. C: Increased proliferation reaching 60-70% with Ki-67, Ki-67 x100.*

Progress

The patient, who underwent surgery in December 2024, was discharged with recovery. In January 2025, i.e. 1 month later, the first contrast-enhanced brain MRI check-up was performed. The patient had no neurological deficits and had never had an epileptic seizure.

In the postoperative 1st month imaging, there was a right frontal 16 mm subdural hypointense effusion*hygroma, a smeared hyperdense subdural effusion in the posterior parietal. Hydrocephalus, 7 mm left shift in the midline, thick-walled, macrocalcific components, mass*residual tumoral tissue in the right frontoparietal vertex, and postoperative changes (Figure 3A and 3B).

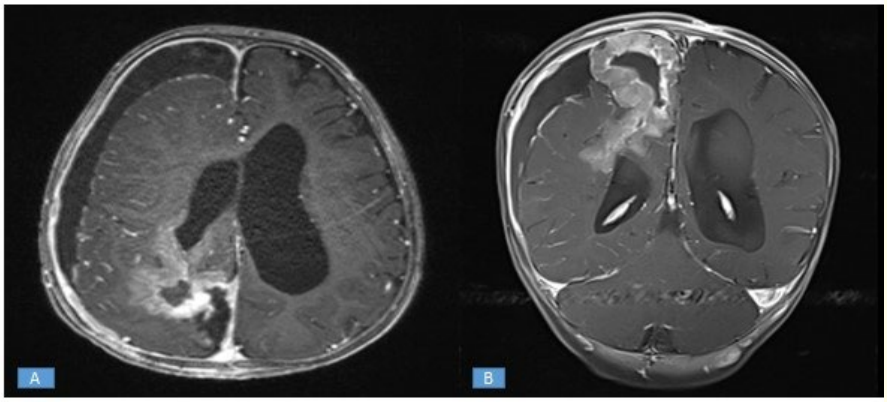

Figure 3A and 3B: *Postoperative contrast-enhanced brain MRI, axial and coronal sections, residual lesion with contrast enhancement adjacent to the posterior horn of the right lateral ventricle.*

The radiation and medical oncology clinic was consulted, and his treatment is still ongoing.

Discussion

Embryonic brain tumors are heterogeneous and highly aggressive malignancies that occur mostly in infants and young children. This group of tumors is highly cellular with rapid and vibrant mitotic activity and spreads along the neural axis. Immunohistochemical and molecular genetics data, which have been used frequently in recent years, have allowed for improved diagnostic and prognostic differentiation for these tumors [5]. Due to their aggressive potential, they are treated similarly with multimodality therapy, including maximal safe resection, chemotherapy, and age- and risk-adapted radiotherapy. These tumors include medulloblastomas (MBs), atypical rhabdoid/teratoid tumors (ATRT), pineoblastoma (PB), embryonal tumor multiple rosettes (ETMR)/C19MC-altered tumors, and newly recognized embryonal tumors with FOXR2 activation or BCOR alteration [6].

The imaging features of MBs/PNETs are fairly homogeneous throughout the CNS. MBs typically arise in the cerebellar vermis and the roof of the fourth ventricle, grow anteriorly toward the fourth ventricle, and this ventricle is displaced anteriorly. In our case, they are located in the right cerebral hemisphere and exhibit a different location than is commonly seen. They tend to invade the dorsal brainstem or extend into the medial cerebellar hemisphere and are often 3–5 cm in maximum diameter [5]. They tend to be seen in the cerebellar hemisphere or near the cerebellopontine angle cistern in older children and adolescents [7]. Cystic or large necrotic areas and hemorrhage are examples of atypical appearance. Our patient had a large cystic lesion.

According to the current World Health Organization (WHO) classification for central nervous system tumors (WHO classification 2021), the tumors discussed here primarily include "embryonal tumors with multilayered rosettes" (ETMR); the presence or absence of a specific genetic alteration on chromosome 19 (known as C19MC amplification), referred to as ETMR C19MC modified or ETMR NOS (not otherwise specified). Other tumors in this group include the very rare medulloepithelioma and other embryonal non-rhabdoid CNS tumors not further specified. Both embryonal non-rhabdoid CNS tumors and pineoblastoma are highly malignant tumors referred to as WHO grade IV tumors.

According to the German Childhood Cancer Registry, the chance of cure for children and adolescents with embryonal CNS tumors is approximately 60% (5-year survival rate). Embryonic CNS tumors are a very heterogeneous group, meaning that survival chances can vary depending on the type of tumor. The stage of the disease and the age of the patient also play a special role. Children and adolescents with metastatic disease generally have a lower expectation of cure than patients with localized disease. The prognosis is poor for patients who cannot receive radiotherapy as part of their treatment because of their young age; long-term tumor-free survival is only 20% to 30% in these patients [8].

Demonstrating SHH and WNT pathways, FOXR2 SMARC-B1, BCOR internal tandem duplication and C19MC amplification and being able to subtype is extremely important in order to achieve the "tumor-free" status. Because although current treatment methods can enable long-term tumor-free survival, subtyping and definitive diagnosis are necessary to select the appropriate treatment. Unfortunately, since we could not perform genetic analysis in our health center's pathology laboratory, subtyping for definitive and differential diagnosis could not be performed for our case.

Conclusion

The current treatment of pediatric embryonal CNS tumors is very challenging and can lead to long-term sequelae in young children. In these cases where surgery is absolutely necessary, the innovative presentation and reduced neurotoxicity of chemoradiotherapy are important gateways for future clinical studies. Diagnosis of pathological subgroups through genetic studies is extremely important. With the developing surgical techniques and chemotherapeutic drugs, more promising results are expected after treatment.

Author Contributions

ŞG and YG, ZYB contributed equally to the development and writing of the manuscript. KK, SKB contributed with operating patient. ZH and AET contributed to the histopathological examination.

Conflicts of Interest Disclosure

There aren't any conflicts of interest all of the authors.

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Financial Support and Sponsorship

No author in the study received financial support.

Presentation

The study has not been published anywhere before.

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Volume 14 Issue 3 March 2025