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Surgical Management of Brain Tumors in Infants Under One Year of Age

Duygu BAYKAL[1], Metin DEMIRKAYA[2], Marzieh Karimi KHEZRI[3], Mehtap ERTEKIN[4], Aytul TEMUROGLU[4], Candan DEMIROZ ABAKAY[5], Sahsine TOLUNAY[6], Betul SEVINIR[4], Mevlut Ozgur TASKAPILIOGLU[3]

[1]Bursa State Hospital, Bursa, Turkey
[2]Biruni University School of Medicine, Department of Pediatrics, Istanbul, Turkey
[3]Bursa Uludag University School of Medicine, Department of Neurosurgery, Bursa, Turkey
[4]Bursa Uludag University School of Medicine, Department of Pediatrics, Division of Pediatric Oncology, Bursa, Turkey
[5]Bursa Uludag University School of Medicine, Department of Radiation Oncology, Bursa, Turkey
[6]Bursa Uludag University School of Medicine, Department of Surgical Pathology, Bursa, Turkey

Corresponding author: M. Ozgur TASKAPILIOGLU ✉ ozgurt@uludag.edu.tr

ABSTRACT

AIM: To comprehensively analyze clinical presentation, diagnosis, and management approaches of brain tumors in infants under one year of age.

MATERIAL and METHODS: We conducted a retrospective analysis of clinical data retrieved from medical records of infants who underwent surgical treatment for intracranial mass lesions at our institution from January 2006 to December 2016. The data encompassed parameters such as age at diagnosis, symptoms, tumor location, histology, surgical procedures, adjuvant treatment, and survival outcomes. Cases involving dermoid, epidermoid cysts, and other skull-based lesions were excluded from the analysis.

RESULTS: Our analysis identified twenty-three cases of brain tumors diagnosed within the first year of life, comprising 14 boys and 9 girls. The median age at diagnosis was 8.2 months, and the most common presenting symptoms were nausea and vomiting, as well as head circumference abnormalities. Successful gross total resection was achieved in 75.8% of patients, with choroid plexus papilloma being the most frequently encountered histopathological diagnosis. Eight patients received adjuvant chemotherapy, while one patient underwent salvage radiotherapy.

CONCLUSION: The treatment of brain tumors in infants during their first year of life presents significant challenges. The affected patients exhibit diverse tumor pathologies occurring at various locations within the brain. Further research is warranted to establish optimal treatment options for this specific population.

KEYWORDS: Brain neoplasms, Infant, Surgery

INTRODUCTION

In children, intracranial masses rank among the most common types of tumors following lymphoid-hematopoietic malignancies. However, congenital tumors involving the central nervous system are relatively rare (5). The incidence of brain tumors in infants varies between 1.1 and 3.5 cases per 100,000 live births, contributing to 0.04% to 0.18% of deaths among children under one year of age (2,9).

While progress has been made in the diagnosis of infantile brain tumors, the prognosis has not seen the same level of

Duygu BAYKAL : 0000-0003-3185-3172
Metin DEMIRKAYA : 0000-0003-2880-0117
Marzieh Karimi KHEZRI : 0000-0002-6397-0966
Mehtap ERTEKIN : 0000-0003-1622-890X
Aytul TEMUROGLU : 0000-0002-8943-6585
Candan DEMIROZ ABAKAY : 0000-0001-5380-5898
Sahsine TOLUNAY : 0000-0002-9038-0515
Betul SEVINIR : 0000-0002-3232-7652
Mevlüt Özgür TASKAPILIOGLU : 0000-0001-5472-9065

improvement. Brain tumors occurring in infancy and early childhood differ from those that develop in later stages of childhood or in adults, both in terms of their location, biological behavior, clinical presentation, treatment strategies, and prognosis.

The treatment of brain tumors during infancy requires specialized organization and approach. Surgical removal of intracranial mass lesions remains the primary treatment modality for these patients, as it minimizes the side effects associated with radiotherapy in infants. Chemotherapy can serve as a temporary measure until delayed radiation therapy can be initiated. Additionally, chemotherapy may be considered as part of the adjuvant therapy for these cases. Given the lack of a specific treatment algorithm, established tumor pathology patterns, and outcome predictions for brain tumors in infants, it is evident that further examination, research, and studies are imperative in this population.

The aim of this study was to retrospectively review the experience of a single institution in managing brain tumors in infants under one year of age. The analysis focused on evaluating demographic data, presenting symptoms, histopathological diagnoses, treatment strategies, and prognosis.

MATERIAL and METHODS

This study received ethical approval from the ethical committee of Bursa Uludag University (2018-17/17).

The medical records of patients with brain tumors who were under one year of age and primarily underwent surgical treatment between 2006 and 2016 at Bursa Uludag University School of Medicine were retrospectively analyzed.

Patient data, including demographic information, presenting symptoms, and treatment details, were summarized. The extent of tumor resection was classified based on early postoperative imaging, utilizing either magnetic resonance imaging (MRI) within one day or, if not feasible due to the patient's condition, early computed tomography. The resection categories included gross total resection (complete removal of the tumor without any residual disease), subtotal resection (removal of 50% to 99% of the tumor), and biopsy (removal of less than 50% of the tumor). The normality distribution of age was assessed using the Shapiro-Wilk test, and age was reported as median values with the range (minimum: maximum). Survival times were analyzed using the Kaplan-Meier method, and the log-rank test was employed to compare survival times across different groups.

For statistical analysis, the SPSS software (IBM Corp. Released 2012. IBM SPSS Statistics for Windows, Version 21.0. Armonk, NY: IBM Corp.) was utilized, and a p-value of less than 0.05 was considered statistically significant. The survival time was determined based on the date of the first neurosurgical intervention. Neurological outcomes were obtained from the charts of neurosurgery and/or neuro-oncology clinics.

RESULTS

Between the years 2000 and 2016, a total of twenty-three patients under the age of one underwent surgery for the diagnosis of intracranial mass lesions. Of these patients, fourteen were male (60.9%), while nine were female (39.1%) (Table I). The age range varied from 1 month to 12 months, with a median age of 8.2±3.24 months at the time of surgery. Only one patient was operated before reaching one month of age. The most common presenting symptoms were nausea and vomiting (30.4%), attributed to hydrocephalus. Additionally, one patient was identified to have a growth disorder, and another was detected during prenatal ultrasound monitoring.

In seven patients, the tumors were located either entirely or partially within the ventricular system. The neurosurgical team treated all patients, with surgical resection being the primary choice of treatment. Other treatments such as chemotherapy and radiotherapy were not taken into account in our study. Postoperatively, all patients were closely monitored in the

Table I: Demographic Characteristics of Patients (n=23)

Characteristic	**Value**
Age (months) (median) (range)	8 (1-12)
Gender	**n (%)**
Female	9 (39.1)
Male	14 (60.9)
Symptoms	**n (%)**
Nausea/vomiting	7 (30.40)
Increased head circumference	6 (26.10)
Imbalance	2 (8.70)
Vomiting	2 (8.70)
Developmental delay/vomiting	1 (4.35)
Exopthalmos	1 (4.35)
Left hemiparesis	1 (4.35)
Nausea/vomiting/anisocoria	1 (4.35)
Seizure	1 (4.35)
7th cranial nerve palsy/nausea/vomiting	1 (4.35)
Pathology	**n (%)**
Choroid plexus carcinoma	5 (21.74)
AT/RT	4 (17.4)
PNET	3 (13.01)
Atypic choroid plexus papilloma	2 (8.70)
Ependymoma	2 (8.70)
Anaplastic ependymoma	1 (4.35)
Astrocytoma	1 (4.35)
Infantile desmoplastic ganglioglioma	1 (4.35)
Infantile ganglioglioma	1 (4.35)
Infantile hemangiopericytoma	1 (4.35)
Medulloepithelioma	1 (4.35)
Pilocytic astrocytoma	1 (4.35)

AT/RT: *Atypical teratoid/rhabdoid tumor;* ***PNET:*** *Primitive neuroectodermal tumors. Data were reported as median (minimum: maximum) and n (%).*

intensive care unit. Fortunately, there were no intraoperative deaths reported. Sixty patients underwent total surgical resection, while seven patients had subtotal resection.

According to our study results, a wide range of pathological findings were observed. Among the patients, choroid plexus papilloma was reported in five cases, while atypical teratoid/rhabdoid tumor (AT/RT) was found in four cases. Additionally, there were single occurrences of pilocytic astrocytoma, anaplastic ependymoma, astrocytoma, desmoplastic infantile ganglioglioma, infantile ganglioglioma, infantile desmoplastic ganglioglioma, infantile hemangiopericytoma, and medulloepithelioma (Figure 1).

The analysis revealed no significant difference in overall survival time based on gender and adjuvant therapy ($p>0.05$). However, the total resection group exhibited longer survival time compared to the subtotal resection group ($p=0.029$) (Table II) (Figure 2).

DISCUSSION

The clinical characteristics, diagnosis, and treatment approaches for brain tumors in infants pose significant challenges. The mean age at diagnosis varies between 3.5 months and 7.2 months, as reported in several studies (1,4,11,15). In a series of 21 patients, Chung et al. reported a male-to-female ratio of 1.1:1, while other studies did not find a gender difference (4). In an epidemiological study by Yu et al., it was noted that males were more affected than females (23). Our findings align with the existing literature, showing a slight male predominance.

Clinical manifestations of brain tumors in infants differ from those observed in adults within the same age group. Infants are unable to express their symptoms, often leading to delayed diagnosis (5). The symptoms can be nonspecific, resulting from the expansion of the infant's skull and increased intracranial pressure (17). Typically, patients exhibit excessive crying. Increased head circumference, vomiting, and headaches

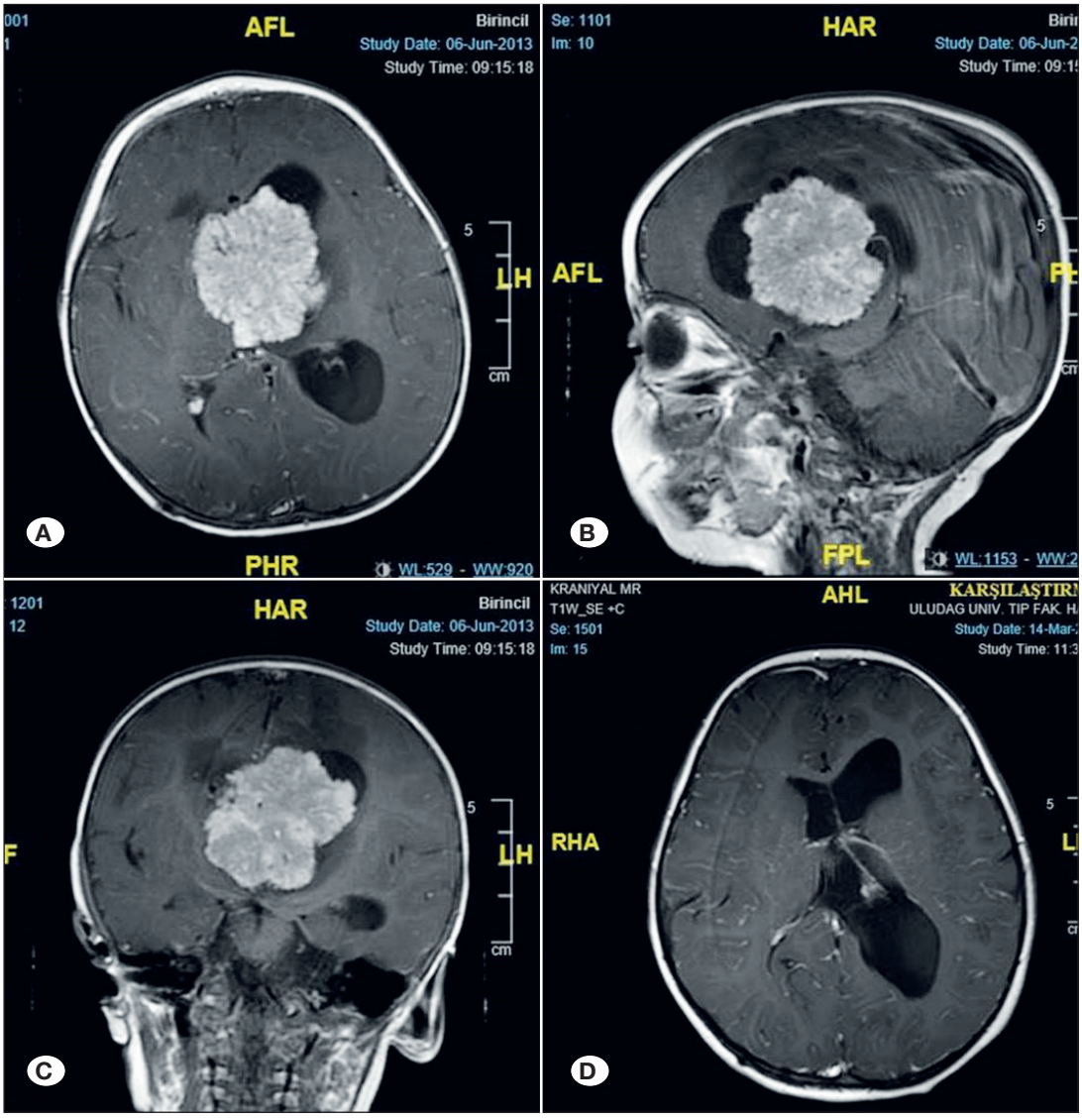

Figure 1: Preoperative contrast-enhanced MR images (**A:** axial, **B:** sagittal, **C:** coronal) of a 12-month-old boy (patient number 8); Postoperative contrast-enhanced axial MR image **(D)**. The pathology was identified as choroid plexus papilloma.

Table II: Comparison of Overall Survival Across Groups

Characteristic	Number of patients at risk (%)[x]	Number of Recurrence (%)[y]	OS (month/day)	p-value
Gender				
Female	9 (39.1)	4 (44.4)	78.95 ± 27.15	0.249
Male	14 (60.9)	9 (64.3)	45.64 ± 11.70	
Extent of Resection				
Subtotal	7 (30.4)	5 (71.4)	12.83 ± 5.06	**0.029**
Total	16 (69.6)	8 (50.0)	75.89 ± 16.78	
Adjuvant Therapy				
+	8 (34.8)	4 (50.0)	28.50 ± 5.50	0.955
-	15 (65.2)	9 (60.0)	63.33 ± 17.40	

[x]: n=23, presented as the number and proportion within the population. [y]: Presented as the number and proportion within the number of patients at risk. Overall survival (OS) was expressed as the mean ± standard error.

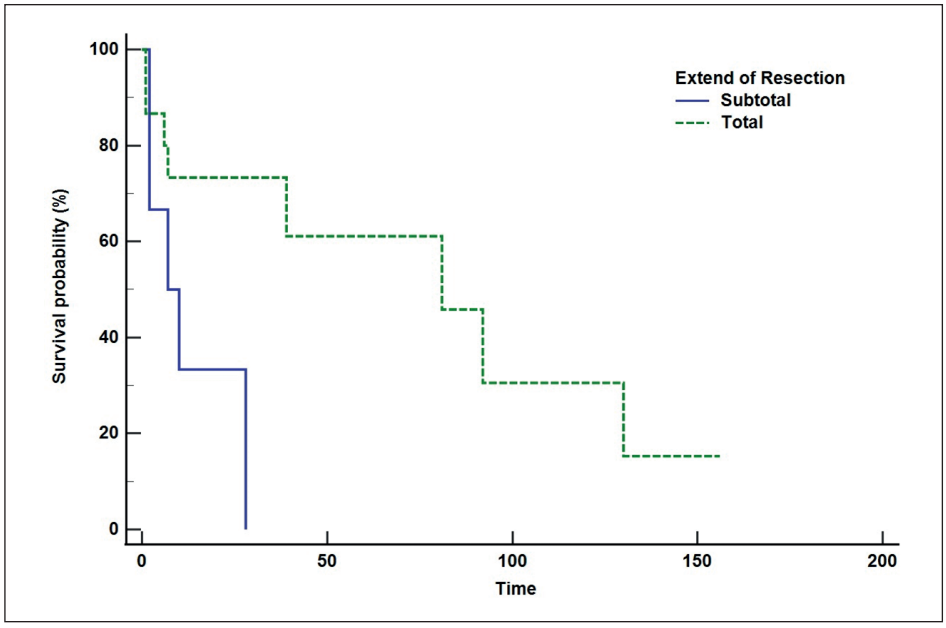

Figure 2: Kaplan Meier analysis. Total resection group exhibited longer survival time compared to the subtotal resection group (p=0.029).

are common presenting symptoms associated with elevated intracranial pressure or obstructive hydrocephalus (9). Other nonspecific clinical symptoms include developmental delay, irritability, and drowsiness (14). Torticollis, observed in approximately two-thirds of cases of infratentorial lesions, serves as a sign of the tumor's location (16). Tumors in the supratentorial space can grow to a larger size compared to those in the infratentorial compartment due to the limited space of the posterior fossa (11).

According to a cooperative study by the International Society of Pediatric Neurosurgery, 41% of the 886 patients included presented with intracranial hypertension, while 12% exhibited seizure activity (17). In our series, similar to the literature, nausea and vomiting were the primary symptoms observed.

Ultrasound is a valuable diagnostic tool for detecting intracranial tumors in infants, but magnetic resonance imaging (MRI) is considered the gold standard for precisely localizing the tumor and providing preliminary information about its possible diagnosis.

Brain tumor histologies vary significantly in this age group. The most common tumor types are teratomas, followed by choroid plexus tumors and astrocytomas (13). The most frequently encountered type of tumor during the neonatal period has been reported as germ cell tumors are (1). In older infants, astrocytomas predominate, with the majority of tumors being low-grade (2,23). Yu et al. emphasized that astrocytoma was the most prevalent tumor type among children aged two and below (23). In the series by Chung et al., medulloblastomas

accounted for 14% of cases, while Di Rocco et al. reported a rate of 23.5% (4,5).

Oi et al., in a series of 262 cases, reported teratoma and primitive neuroectodermal tumors (PNET) as the most frequent histopathological diagnoses, with a 5-year survival rate of 26% (19). Di Rocco et al. reported the most common histologic diagnosis as astrocytoma (31%), followed by medulloblastoma (13%), choroid plexus papillomas (12%), ependymoma (12%), PNETs (7%), and teratomas (6%) (5).

In a large series, the distribution of tumors in this age group was reported as follows: astrocytoma (30.5%), medulloblastoma (12.2%), ependymoma (11.1%), and choroid plexus tumors (11%). However, in our series, most of the reported astrocytomas (80%) were not graded, which differs from the common literature and aligns with the findings of Lang et al. (13) Of note, no teratoma patients were included in our series, which may be attributed to our small patient sample or our selection of patients from a surgical database.

According to the literature, the supratentorial region is the most common location of tumors (1,2,5,8), which contrasts with the higher occurrence of infratentorial tumors in older children (18). In their series, Jaing et al. mentioned a predominance of glial origin and supratentorial location (11). However, several studies have reported conflicting results. Yu et al. demonstrated a higher incidence (56.3%) of infratentorial tumors in children aged two and under, suggesting that geographical factors may contribute to this difference (23). In our series, most of the tumors were located supratentorially, aligning with the findings in the literature.

The extent of resection has a strong correlation with better outcomes (11). Di Rocco et al. reported a gross total resection rate of 44% in their study (5). Similarly, Jaing et al. found a gross total resection rate of 50% (11). Munjal et al. highlighted that supratentorial and low-grade tumors were more amenable to gross total resection compared to infratentorial and high-grade tumors (18).

McGirt et al. emphasized that achieving a greater extent of resection is associated with improved survival. However, the majority of tumors in the specified age group are situated in midline or eloquent areas of the brain, posing a challenge for surgical intervention (16). Fortunately, most of the tumors in our study were successfully resected totally.

Due to the immaturity of the central nervous system and the vulnerability of patients to treatment-induced neurotoxicity during the first two years of life, radiotherapy and chemotherapy can have potentially harmful effects. Consequently, surgery becomes the preferred choice of treatment (7,21). In our series, only one patient with anaplastic ependymoma received radiotherapy. The radiation was administered approximately two years after the surgery.

Yu et al. reported a tumor recurrence rate of 10% in their study, primarily observed in tumors located in vital centers (23). However, in our series, no recurrences were detected during the follow-up period.

Advancements in medicine have led to improved outcomes for infants under the age of one diagnosed with brain tumors (12). Based on existing studies, the 5-year survival rate for infants diagnosed with brain tumors ranges from 26% to 70%, with variations depending on the specific histology of the tumor (22). This underscores the significant variability in prognosis among different types of tumors in this particular population. According to a study, surgical intervention resulted in an average postoperative survival time of 67.6 months, whereas those treated conservatively had an average survival time of 25.3 months (23). In a survey conducted by Di Rocco et al. involving 886 patients, the authors reported a 53% survival rate with a 40% mortality rate (6). It is worth noting that the favorable survival data in our series may be influenced by the higher incidence of plexus tumors. Specifically, our series only included four cases of AT/RT, three PNETs, and no cases of medulloblastoma.

The prognosis is generally poorer for infants and younger children diagnosed with brain tumors compared to older children (3). At the time of diagnosis, over 30% of cases exhibit microscopic leptomeningeal dissemination (20). Although craniospinal irradiation is highly effective as part of the treatment for children above the age of three, it is not preferable for infants due to the potential association with neuropsychological and neuroendocrine sequelae (20).

This study has some limitations, including its retrospective design, limited information on patient history, and small sample size. Additionally, functional and cognitive outcomes were not evaluated in this study.

CONCLUSION

Surgical resection emerges as a direct and effective approach to the management of infant brain tumors. It plays a crucial role in achieving optimal outcomes for these patients. Regardless of the tumor's histology, complete resection yields a more favorable prognosis. Further research is warranted to elucidate optimal treatment strategies for this particular age group.

AUTHORSHIP CONTRIBUTION

Study conception and design: MOT
Data collection: DB, MKK
Analysis and interpretation of results: MD, ME, AT
Draft manuscript preparation: DB, CDA
Critical revision of the article: CDA, ST, BS, MOT
All authors (DB, MD, MKK, ME, AT, CDA, ST, BS, MOT) reviewed the results and approved the final version of the manuscript.

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