Evaluation of Childhood Posterior Fossa Malignant Tumors: A Single-center Study

Çocukluk Çağı Arka Çukur Habis Tümörlerinin Değerlendirilmesi: Tek Merkezli Çalışma

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Abstract

patients without previous weakness. Three patients (12.5%) had mutism and one patient had dysarthria. Two patients had pneumonia during intensive care follow-up and one of these children died two months later.

Conclusion: In children with posterior fossa malignant tumors; We found that a high degree of the tumor, brainstem invasion, complete removal of the tumor, and presence of postoperative blood in the ventricle increase the risk of complications.

Keywords: Chilhood malignant tumors, complication, pediatric brain tumors, posterior fossa tumors

Introduction

Malignant central nervous system tumors are the second most common malignancies in children after leukemia and they are the most common pediatric solid organ tumors (1). The proportion of tumors located in the posterior fossa in childhood is between 54% and 70% and higher than in adults (2). Symptoms and signs of posterior fossa tumors are primarily due to increased intracranial pressure and secondary to local compression of cerebellar nuclei and brain stem. In addition, it can cause hydrocephalus by causing obstruction in the circulation pathways of cerebrospinal fluid (CSF) (3). Most of these tumors need to be treated urgently and the risk of morbidity and mortality is high (4).

In this study, the clinical and radiological findings, early surgical results, and complication rates of children that were treated for a malignant tumor located in the posterior fossa were investigated in our clinic.

Materials and Methods

This retrospective study was made with the decision of the local ethics committee numbered 2020.06.2.01.085. For the study, written and verbal consent was obtained from the families.

Between 2011 and 2020, there were 76 consecutive children treated in our clinic due to brain tumors. Of these, 35 were diagnosed as malignant posterior fossa tumors. The data of these 35 patients were analyzed by scanning from the hospital archive system. Two patients were excluded from the study because their data were insufficient. Patients at the age of 18 years and older and children with supratentorial tumors and infratentorial benign tumors were excluded from the study. For all 33 children, age, gender, symptoms, clinical signs, whether they were operated, the timing of surgery, whether external ventricular drainage (EVD) and/or ventriculoperitoneal (VP) shunt was inserted, type of tumor, grade, Ki-67 index, neurological status, early surgical complications, and results when leaving the hospital were recorded. Preoperative and postoperative magnetic resonance imagings and computed tomography were scanned. Tumor localization, whether there was a cyst or bleeding, presence of hydrocephalus, tumor removal rate (total if 100% removed; subtotal if removed 90% and above; partial if removed below 90%), and the presence of blood in the postoperative ventricles were evaluated by the same specialist doctor.

Statistical Analysis

Nominal variables were compared using the Fisher’s exact test or chi-square test, according to the number of subjects. The F test was used to evaluate the distribution characteristics of countable variables, which were compared with the Student’s t-tests. A p-value of <0.05 was considered significant.

Results

Clinical Features

The median age of 33 children was 7 years (17 months-17 years; min-max). Girl to boy ratio was 18/15. The patients were divided into 4 different groups by age: those younger than 3 years old (21.4%), those at the age range of 3-6 years (24.2%), those at the age range of 6-10 years (27.3%), and those at the age over 10 years (27.3%). The most common symptoms of admission were headache (57.6%) and gait disturbance (48.5%). Four patients were brought to the emergency service due to epileptic seizures. Papilledema, ataxia, and nystagmus were frequently observed in the examination findings of the children. Six patients had preoperative cranial nerve paralysis. Of these, 3 patients had abducens nerve, 1 patient had the oculomotor nerve, 1 patient had the facial nerve, and 1 patient had hypoglossal
nerve paralysis. All three patients had extremity weakness (Table 1).

**Pathology and Surgery**

The most common tumor was medulloblastoma (39.4%). Then, diffuse pontine glioma, ependymoma, pilocytic astrocytoma were seen, respectively. One patient had hemangioblastoma and 1 patient had Ewing sarcoma/primitive neuro-ectodermal tumors (PNET) (Table 2). The rate of World Health Organization Grade III and IV tumors among the operated tumors was 66.7%. All of the patients were operated on prone position. Tumor resection was performed in 24 patients without diffuse pontine glioma (Table 3). Total removal was achieved in half of the patients who underwent tumor resection. Three of the subtotally removed tumors (patient no: 5, 15, 22) were operated again within 24 hours and removed totally. Endoscopic third ventriculostomy (ETV) was performed in one of the patients with pontine glioma. 52% of 25 patients who underwent surgery were operated under emergency conditions. EVD was inserted into 10 (30.3%) of all patients (one with diffuse pontine glioma). Only 4 of them needed VP shunts (one of them diffuse pontine glioma).

**Complications**

The rate of development of any surgical complications in Grade III and Grade IV tumors was 13/18 and was significantly higher compared to low-grade tumors (p=0.038). The complication rate in totally removed tumors was also significantly higher than subtotally removed ones (p=0.034). There was no statistical relationship between age, gender, tumor size, timing of surgery and complication development (p=0.362, p=0.653, p=0.552, p=0.613, respectively). The most common complication was CSF fistula (16.7%). Only 1 patient with CSF fistula was operated due to dura repair. Three patients with EVD had signs of infection. *Staphylococcus epidermidis* and *Stenotrophomonas maltophilia* were grown in the CSF culture samples. All 3 patients healed with antibiotic therapy. Three patients had a postoperative hematoma at the tumor site (one of the epidural hematoma), these patients were re-operated due to hematoma evacuation. Hydrocephalus developed in two patients (8.3%) who did not receive EVD in the early postoperative period and VP shunts were inserted in these patients. Four of 6 patients with VP shunt inserted had postoperative intraventricular blood. Postoperative hemiparesis developed in two patients without previous weakness. Three patients (12.5%) had mutism and one patient had dysarthria. Two children had pneumonia during intensive care follow-up, one of whom died two months after surgery.

**Discussion**

Posterior cranial fossa has a very limited volume compared to the supratentorial area. It has a brain stem, cerebral aqueduct, 4th ventricle, outlet foramen and cerebellum. A growing posterior fossa tumor can lead to the dysfunction of the structures in this region in a short time, causing brain stem and cerebellar findings. In addition, they can cause herniation or hydrocephalus with the mass effect and edema (2). In our series, 22 patients had preoperative hydrocephalus. Thirteen of these patients were operated urgently. Three of these 13 patients were also in the herniation table. Partanen et al. (5) reported the EVD rate as 10/22 after the posterior fossa tumors they operated, and our EVD rate was similar.

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**Table 1. The rates of 33 patients’ symptoms and signs**

| Symptom                  | n  | Percentage |
|--------------------------|----|------------|
| Headache                 | 19 | 57.6       |
| Gait disturbance         | 16 | 48.5       |
| Vomiting                 | 13 | 39.4       |
| Dizziness                | 5  | 15.2       |
| Seizure                  | 4  | 12.1       |
| Diplopia                 | 2  | 6.1        |
| Weakness                 | 2  | 6.1        |

**Signs**

| Sign                      | n  | Percentage |
|---------------------------|----|------------|
| Papilledema               | 23 | 69.7       |
| Ataxia                    | 22 | 66.7       |
| Nystagmus                 | 17 | 51.5       |
| Dysmetria                 | 12 | 36.4       |
| Cranial nerve palsy       | 6  | 18.2       |
| Dysdiadochokinesia        | 6  | 18.2       |
| Paresis                   | 3  | 9.1        |
| Dysarthria                | 2  | 6.1        |

**Table 2. Distribution of tumors**

| Tumor Type                | n  | Percentage |
|---------------------------|----|------------|
| Medulloblastoma           | 13 | 39.4       |
| Diffuse pontine glioma    | 9  | 27.2       |
| Ependymoma                | 5  | 15.2       |
| Pilocytic astrocytoma     | 4  | 12.2       |
| Hemangioblastoma          | 1  | 3          |
| Ewing sarcoma/PNET        | 1  | 3          |

PNET: Primitive neuro-ectodermal tumors
Table 3. Early surgical results and complications of patients undergoing tumor resection

| No | Age (years) | Gender | Pathology | Ki-67 (%) | Preoperative hydrocephalus | Tumor removal rate | EVD | Shunt | Complications | Result (GCS) |
|----|-------------|--------|-----------|-----------|---------------------------|-------------------|-----|-------|---------------|-------------|
| 1  | 17 m        | G      | Anaplastic ependymoma | 30        | Y                         | Subtotal (95%)    | Y   | Y     | 7th nerve paralysis, hematoma | 15          |
| 2  | 17 m        | G      | Medulloblastoma      | 15        | Y                         | Subtotal (90%)    | Y   | N     | Pneumonia                  | 3 (ex)      |
| 3  | 18 m        | B      | Anaplastic ependymoma | 30        | N                         | Total             | N   | N     | None                      | 15          |
| 4  | 20 m        | B      | Pilocytic astrocytoma | 3         | N                         | Total             | N   | N     | None                      | 15          |
| 5  | 21 m        | B      | Ependymoma           | 12        | Y                         | Subtotal (90%)    | N   | Y     | CSF fistula, hydrocephalus | 15          |
| 6  | 29 m        | G      | Anaplastic ependymoma | 20        | Y                         | Partial (80%)     | Y   | N     | Infection, 6th nerve paralysis | 15          |
| 7  | 3           | G      | Ewing sarcoma/ PNET | 20        | Y                         | Partial (70%)     | Y   | N     | Epidural hematoma            | 15          |
| 8  | 5           | G      | Anaplastic ependymoma | 70        | Y                         | Total             | N   | N     | None                      | 15          |
| 9  | 5           | G      | Pilocytic astrocytoma | 4         | Y                         | Subtotal (95%)    | Y   | N     | None                      | 15          |
| 10 | 6           | G      | Medulloblastoma      | 80        | N                         | Total             | N   | N     | None                      | 15          |
| 11 | 6           | G      | Medulloblastoma      | 18        | Y                         | Subtotal (95%)    | N   | N     | CSF fistula                | 15          |
| 12 | 7           | B      | Pilocytic astrocytoma | 3         | Y                         | Partial (70%)     | N   | Y     | Mutism, hydrocephalus        | 15          |
| 13 | 7           | G      | Medulloblastoma      | 40        | Y                         | Subtotal (90%)    | N   | N     | None                      | 15          |
| 14 | 7           | B      | Medulloblastoma      | 30        | Y                         | Total             | N   | N     | Mutism, CSF fistula         | 15          |
| 15 | 8           | B      | Medulloblastoma      | 30        | Y                         | Partial (80%)     | Y   | Y     | CSF fistula, infection      | 15          |
| 16 | 8           | B      | Medulloblastoma      | 70        | Y                         | Total             | N   | N     | 6th and 7th nerve paralysis | 15          |
| 17 | 11          | G      | Medulloblastoma      | 80        | Y                         | Total             | N   | N     | None                      | 15          |
| 18 | 11          | G      | Medulloblastoma      | 9         | Y                         | Total             | N   | N     | None                      | 15          |
| 19 | 12          | G      | Medulloblastoma      | 60        | Y                         | Total             | N   | N     | 6th and 7th nerve paralysis, hemiparesis | 15          |
| 20 | 13          | B      | Pilocytic astrocytoma | 2         | N                         | Total             | N   | N     | None                      | 15          |
| 21 | 14          | B      | Medulloblastoma      | 70        | Y                         | Total             | Y   | Y     | Mutism, infection, 9th nerve paralysis | 15          |
| 22 | 15          | G      | Medulloblastoma      | 20        | Y                         | Partial (70%)     | Y   | N     | Mutism, dysarthria          | 15          |
| 23 | 15          | G      | Hemangioblastoma     | 1         | Y                         | Total             | N   | N     | None                      | 15          |
| 24 | 17          | B      | Medulloblastoma      | 80        | Y                         | Partial (80%)     | Y   | N     | Hematoma                  | 15          |

M: Months, G: Girl, B: Boy, Y: Yes, N: No, EVD: External ventricular drainage, GCS: Glasgow Coma scale, CSF: Cerebrospinal fluid, PNET: Primitive neuro-ectodermal tumour

The classic symptoms of posterior fossa tumors are irritability, lethargy, nausea, vomiting, headache, and behavioral changes with increased intracranial pressure (6). Our patients had similar symptoms and in addition, four patients had epilepsy. In a study, clinical signs were most commonly reported as ataxia, papillary stasis, dysmetria, and dysdiadiokinesia (7). In our series, 51% of patients had nystagmus and 18% had cranial nerve palsy.

Yağcı Küpeli et al. (8) reported that the median age was 8 years in childhood tumors similar to ours. In the same study, it was reported that tumors were more common in males in all age groups. Similarly, Erdinçler et al. (4) found...
the proportion of boys as 66%. However, in our series, posterior fossa tumors were more common in girls.

The most common types of tumors found in the posterior fossa are cerebellar astrocytomas, medulloblastomas, and brainstem gliomas (1). The most common tumors in our patients were medulloblastoma and diffuse brainstem glioma. Medulloblastoma rate was most common, similar to the literature. Abraham et al. (9) 51.3% and Lee et al. (10) reported it as 35.9%. However, Yaşarı Küpeli et al. (8) reported as 7.9% and Shanmugavadivel et al. (11) as 10.9% among the posterior fossa tumors, and these rates are lower than our study. In addition, one of our patients had Ewing sarcoma/PNET, which is rare in the posterior fossa, and was urgently operated due to left cerebellar hemisphere compression and hydrocephalus (Figure 1). It has been reported that ependymomas are more common in males in childhood and its rate in the posterior fossa is 5.2% (5,12). It was 15.6% in our study, but more in girls. Cerebellar astrocytomas are benign tumors of the central nervous system. It constitutes 30% of childhood posterior fossa tumors (13). In our patients, the rate of pilocytic astrocytoma was lower than in other series.

Diffuse pontine gliomas have a poor prognosis. Surgical treatment has been abandoned in the treatment of diffuse pontine gliomas. However, a stereotaxic biopsy can be performed for collecting samples from the tumor. In patients with brainstem lesions, the postoperative morbidity of stereotaxic biopsy has been reported between 0 and 20% and mortality between 0 and 3% (14). Children with diffuse pontine glioma treated in our clinic did not undergo any surgery for the tumor. Patients were followed up by pediatric oncology. One of the patients underwent EVD and then VP shunt due to acute hydrocephalus. ETV was performed on another patient.

Depending on the type of tumor, tumor localization may vary. It has been reported that tumors in the posterior fossa are mostly located in vermis localization (5). In our series, although tumors were more common in vermis origin, the rate of tumors in the fourth ventricle was higher. This was because the tumor reached a large volume and filled the fourth ventricle in a high proportion of patients. Lee et al. (10) reported the rate of tumors with extensive cerebellum and brain stem as 43.6%. This was in a quarter of our patients. Two of our patients whose tumors were totally removed had postoperative hemiparesis and these children had brainstem invasion. In another aspect, invasion into the brainstem was the most important reason for total resection of the tumor. Three of our patients were re-operated due to residual tumors. In a study with 22 patients, it was reported that 2 patients were operated twice, and 1 patient was operated three times (5). In 3 of our patients, there was postoperative bleeding in the tumor site and they were re-operated. Ur-Rehman et al. (15) gave this rate as 3.8%.

Partanen et al. (5) reported that at least one complication developed in 19 out of 22 patients. In our patients, this rate was 15/24 and most of the complications occurred in high-grade tumors. Ur-Rehman et al. (15) reported that in 79 infratentorial tumors they operated, the most common surgical complications were hydrocephalus and CSF fistula. Similarly, we saw the most common complication was CSF fistula. However, only one patient had to repair the dura mater. Bilginer et al. (13) reported CSF fistula in 6.4% of patients after 31 pilocytic astrocytoma operations.

![Figure 1. Contrasted MRIs of the patient with Ewing sarcoma/PNET tumor; a) axial, b) coronal, c) sagittal sections](image)

*MRI: Magnetic resonance imagings, PNET: Primitive neuro-ectodermal tumors*
VP shunt or ETV application has been reported at different rates due to hydrocephalus in various series. Lee et al. (10) reported the rate of patients developing postoperative permanent hydrocephalus as 61.5%. In another study, they reported this rate as 9.4% (9). In the same study, being under the age of six years and the presence of intraventricular blood were shown as risk factors for hydrocephalus. One-quarter of our operated patients had VP shunts inserted and patients who needed shunt had a high rate of intraventricular blood.

The rate of wound infection in posterior fossa surgery has been reported around 6% (15). In our series, there were no children with wound infections. Abraham et al. (9) stated that 4 of 14 patients requiring shunts had meningitis and two patients developed staphylococcus in the CSF culture. In our series, there were 3 cases showing signs of meningitis. VP shunts were inserted into two of them due to hydrocephalus. In addition, 2 patients were diagnosed with pneumonia during intensive care follow-up and a child died due to this reason in the second postoperative month. Aslantürk et al. (3) reported death rate as 20% in the early postoperative period and reported that two of them were due to surgical air embolism. We operated all patients in the prone position and did not see air embolism.

One of the complications that occur after posterior fossa tumor surgery is mutism. Cámar et al. (16) reported cerebellar mutism at a rate of 19/36. Gora et al. (17) gave this rate as 18.2% in 33 children with midline posterior fossa tumors. In the same study, they identified medulloblastoma, maximum size >45 mm tumor, superior cerebellar peduncle, and middle vermis incision as risk factors for mutism. Three patients who developed mutism from our patients had midline tumors, all of them were operated with vermicincision, and two had cerebellar peduncle involvement. Studies have shown that there may be findings accompanying mutism such as ataxia, dysarthria, and facial nerve palsy (18). One of our patients who developed mutism had difficulty swallowing, and another had dysarthria after mutism. In addition, another patient with anaplastic ependymoma had difficulty swallowing. Lee et al. (10) have stated that this complication is seen more than known. Children who were operated for 183 posterior fossa tumors were examined with videofluoroscopic swallowing study in the early period, and 39 of them had postoperative swallowing difficulty. In the same study, the most important risk factor for difficulty swallowing was shown as brain stem invasion.

The limitations of this study are its retrospective design, low number of patient group, insufficient long-term surgical follow-up, and evaluation of chemotherapy and radiotherapy treatments. Having more information about tumor biology, advances in imaging methods and microsurgical techniques, and prospective clinical studies will reduce morbidity and mortality in the future for children with posterior fossa tumors.

**Conclusion**

In our study, high-grade tumor, brainstem invasion, total tumor removal, and intraventricular blood increased the risk of complications in children. Total resection should be aimed for posterior fossa tumors, but it should be noted that the rate of morbidity increases as the resection amount increases in patients with brainstem invasion. Our goal in the treatment of these children should be to improve long-term quality of life, to maintain cognitive function and growth, to minimize complications, and to reduce the risk of secondary malignancies in the course of the disease.

**Ethics**

**Ethics Committee Approval:** Ethical approval was obtained from the University of Health Sciences Turkey, Bağcılar Training and Research Hospital Ethical Committee (decision number: 2020.06.2.01.085).

**Informed Consent:** For the study, written and verbal consent was obtained from the families.

**Peer-review:** Externally peer-reviewed.

**Authorship Contributions**

Concept: B.E., Design: B.E., Data Collection or Processing: B.E., I.G., Analysis or Interpretation: N.S.B., Writing: B.E., I.G., N.S.B.

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