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ORIGINAL ARTICLE

Characteristics of childhood glial tumors, management approaches and life expectancy of the patients

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Summary

Purpose: *To evaluate the clinical characteristics, management approaches and life expectancy in pediatric patients with neuroepithelial glial tumors except ependymal tumors.*

Methods: *Between January 2003 and August 2008, 48 patients (30 boys, 18 girls; mean age: 10.9±4.6 years) who were diagnosed with neuroepithelial glial tumors except ependymal tumors and underwent curative radiotherapy (RT) for inoperable, postoperative adjuvant or palliative for residual/recurrent disease at Dr. Abdurahman Yurtsalan Ankara Oncology Education and Research Hospital, Radiation Oncology Clinic, were retrospectively analyzed. Progression-free survival (PFS) and overall survival (OS) were evaluated in relation to sex, previous surgical procedure, pathological diagnosis, low/high grade and the histopathological grade of disease.*

Results: *The mean follow-up was 28.8±4.8 months. The mean and median PFS were 36.2 months and 20 months, respectively, while mean and median OS were 40.3 months and 23 months, respectively. One-year PFS and OS were 65.8% and 71%, respectively, whereas 3-year PFS and OS were 36.3% and 42.3%, respectively. Univariate Cox regression model and Log-Rank test revealed no statistical significance. Prolonged PFS and OS were observed in boys compared to girls, those who underwent total/gross total resection compared to subtotal resection, those with low-grade tumors compared to high-grade tumors, and those with histopathological grade I disease compared to grade IV disease (p>0.05). The PFS and OS times were shortened in patients who developed side effects at any time following surgery and RT, compared to those without any side effects (p>0.05).*

Conclusion: *Low-grade disease and total/gross total resection prolong PFS and OS in patients with childhood glial tumors.*

Key words: *childhood, glial tumor, life expectancy, radiation therapy*

Introduction

Central nervous system (CNS) tumors are the third most common form of malignancies in childhood in Turkey, accounting for 20% of all childhood malignancies [1]. The majority of these tumors originate from neuroepithelial cells or primitive forms of these cells [2] and they often involve the posterior fossa [3]. These tumors are commonly seen at the age of 0-4 years (4.6/100,000) [4]. The underlying etiology is still unknown [5].

Over the last 30 years, significant improvements have been made in the diagnosis and management of childhood CNS tumors. Improved imaging techniques and pathological diagnosis have contributed to better understanding of various tumor types. In addition, improved surgical techniques and perioperative care have increased the success rate of surgical resection of brain tumors. A deeper understanding of the possible advantages of adjuvant RT and chemotherapy (Cx) have resulted in reasonable outcomes with multidisciplinary management modalities [6-9]. RT and Cx have a critical role in curative and adjuvant therapies in pediatric patients with CNS tumors. Im-

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proved RT techniques promise prolonged survival with a favorable side effect profile [10,11].

In this study, we aimed to evaluate the clinical characteristics, management approaches and life expectancy in pediatric patients with neuroepithelial glial tumors except ependymal tumors.

Methods

Clinical characteristics of the patients

Between January 2003 and August 2008, 48 patients (30 boys, 18 girls; mean age: 10.9±4.6 years) who were diagnosed with neuroepithelial glial tumors except ependymal tumors and underwent curative RT for inoperable cases, postoperative adjuvant RT or palliative RT for residual/recurrent disease at Dr. Abdurahman Yurtsalan Ankara Oncology Education and Research Hospital, Radiation Oncology Clinic were retrospectively analyzed.

Treatment

Surgery, chemotherapy and/or RT were performed in relation to age, performance status and comorbid diseases.

Surgery

All patients underwent cranial CT or MRI before surgery. Total (N=16 patients) and subtotal (N=14 patients) tumor resection or biopsy (N=2 patients) were performed. Postoperatively, staging was performed based on histopathological results using the AJCC 2002 staging system.

Radiation therapy technique

Forty-six (95.8%) of the patients underwent conventional RT, while two (4.2%) patients received conformal RT. Conventional simulator was used for conventional RT, whereas computed tomography (CT) was used for conformal RT. 6-MV and 15-MV photon energies were selected. One patient underwent conformal RT with 2-field technique, while one patient received RT with 5-field technique. Thirty-three patients received conventional RT with 2-field technique, one with 2-field technique, one from lateral side with source-skin distance (SSD) technique, 8 from left with 2-field technique, and one from two anterolateral vertical sides with minimized exposure with two-phase RT. One patient received craniospinal RT due to spinal metastatic disease, while one patient received two-phase RT in the thoracic spinal region due to spinal astrocytoma. A total of 44 (91.6%) patients excluding those who died during RT or those with missing RT doses, received a dose of 50-60 Gy.

Physical examination, full blood count and serum biochemistry assessments were performed every week during RT. Treatment responses of the patients were evaluated. Treatment was discontinued temporarily in case of acute hematological toxicity and re-initiated when toxicity subsided.

All patients underwent CT and/or MRI after RT. Repeat operation or second-line chemotherapy were performed to patients with disease progression and good performance status.

Treatment response was assessed according to WHO criteria. Briefly, complete response was defined as disappearance of disease, while partial response as regression by 50% or more in measurable lesions. Stable disease was defined as regression by less than 25% or no change in the size of lesions, for at least 4 weeks while progression as growth by more than 25% in measurable tumor areas or appearance of new lesions. Overall survival was defined as the time from chemotherapy and/or RT randomization to the last follow-up visit or death, while PFS was defined as the time from randomization to the progression.

Follow-up

Follow-up visits were every 3 months for the 1st year, every 4 months for the 2nd year every 6 months for the 3rd-5th years, and once a year thereafter. Physical examination, complete blood count and serum biochemistry assessments were performed at each visit. CT and/or MRI were repeated every 6 months to assess the involved area on a regular basis or if the attending doctor thought this was necessary.

Statistics

Statistical analysis was performed using the SPSS software (Statistical Package for the Social Sciences, SPSS Inc., Chicago, IL) for Windows, v11.5. Descriptive statistics were carried out, including mean±standard deviation (SD) for age, and median (range) for the follow-up period. Categorical variables were expressed in sample size and percent. Log-rank test and Kaplan-Meier survival analysis were performed to examine the possible effects of categorical variables on PFS and OS. Univariate and multivariate Cox regression analyses were used to assess the impact of age on PFS and OS. Relative risk and 95% confidence interval (CI) were also calculated. A p-value of <0.05 was considered statistically significant.

Results

The distribution of the patients based on age at diagnosis is shown in Figure 1.

Baseline demographic, clinical and pathological characteristics of the patients are summarized in Table 1. Of the patients, 16 were diagnosed with glial tumors which were inoperable due to the location of the tumors based on clinical symptoms and radiographic results. Of the remaining

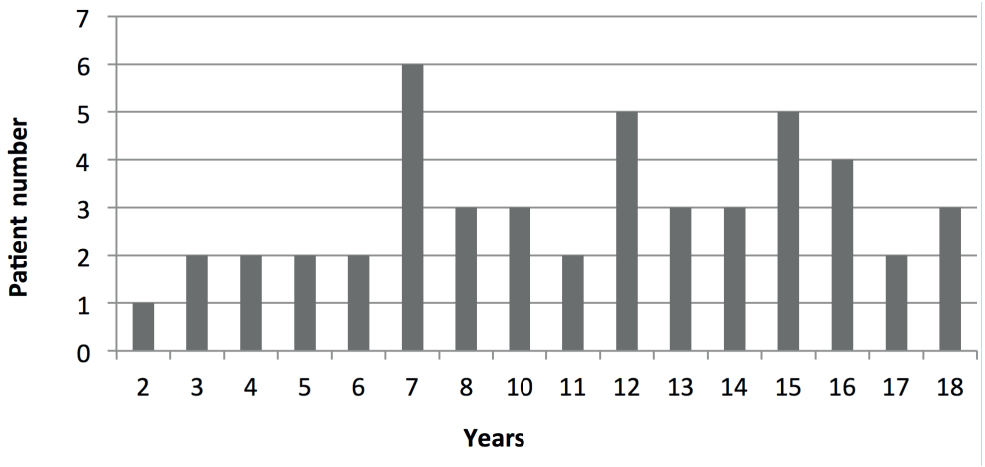

Figure 1. Distribution of patients based on age at diagnosis.

patients, 30 were diagnosed after surgical resection and 2 with tumor biopsy. Astrocytoma was present in 27 (56.3%) patients, oligodendroglioma in 4 (8.3%), glioma in 16 (33.3%), and astroblastoma in one (2.1%) patient. Nineteen (39.6%) patients had low-grade and 13 (27.1%) high-grade glial tumors.

Table 1. Baseline demographic, clinical and pathological characteristics (N=48)

Characteristics	*N (%)*
Age, years, mean±SD (range)	10.9±4.6 (2-18)
Gender	
Male	30 (62.5)
Female	18 (37.5)
Operation	
Unresectable (clinic/radiographic)	16 (33.3)
TR/GTR	16 (33.3)
STR	14 (29.2)
Biopsy	2 (4.2)
Diagnosis	
Astrocytoma	27 (56.3)
Glioma	16 (33.3)
Oligodendroglioma	4 (8.3)
Astroblastoma	1 (2.1)
Grade	
Unknown (Unresectable)	16 (33.3)
I	8 (16.7)
II	11 (22.9)
III	3 (6.3)
IV	10 (20.8)
Histopathol. grade	
Unknown (Unresectable)	16 (33.3)
Low	19 (39.6)
High	13 (27.1)

GTR: gross total resection, STR: subtotal resection, TR: total resection

The time to RT initiation after diagnosis varied widely. The mean time was 71.8±5.6 days, while the median time was 37.5 days (range 2-710). The mean and median RT doses were 51.1 and 54 Gy, respectively. Four patients died during RT. Three of them had positive glial tumors, while one had grade IV cerebral astrocytoma (glioblastoma multiforme, GBM) (Table 2).

Ten patients who were out of contact following RT due to irregular visits or missing telephone/address information were excluded from the statistical analysis of side effect and survival. Based on the post-treatment assessment, 24 (63.2%) patients had progression, 8 (21.1%) had complete remission, 2 (5.3%) had partial response and 2 (5.3%) had stable disease (Table 3).

Twenty-two patients developed several side effects. Eleven patients had neuropsychological sequelae (the most common), while 7 patients had performance loss at school/work (common). The patients with performance loss at school/work were also those with neuropsychological sequelae (Table 4).

The mean and median PFS were 36.2 and 20 months, respectively, while the mean and median OS were 40.3 and 23 months, respectively (Figures 2 and 3). One-year PFS and OS were 65.8 and 71%, respectively, whereas 3-year PFS and OS were 36.3 and 42.3%, respectively.

Male patients had better survival rates compared to female patients but without statistical significance. One- and 3-year PFS rates for males were 69.6% and 41.2%, and for females 60% and 28% (p=0.373). One- and 3-year OS rates were 78.3% and 60% and 60.0% and 26.2% for male and

Table 2. Distribution of patients based on the dose of radiation therapy

RT dose (cGy)	*Patients*		*Clarifications*
	%	*N*	
540	1	2.1	Four patients died during RT
720	1	2.1	
1260	1	2.1	
1620	1	2.1	
5000	4	8.3	Grade 1 astrocytoma in 1 patient, grade 2 astrocytoma in 2 patients, oligo-dendroglioma in 1 patient
5060	1	2.1	
5400	25	52.1	
5540	1	2.1	
5580	2	4.2	
5600	3	6.3	
5700	1	2.1	
5760	1	2.1	
5940	2	4.2	
6000	4	8.3	Grade 4 astrocytoma in 3 patients, grade 2 astrocytoma in 1 patient
Total	48	100	

Table 3. Follow-up results

Treatment outcomes	*Patients*	
	N	%
Side effects (after treatment)		
No	23	60.5
Yes	15	39.5
Response		
Complete response	8	21.1
Partial response	2	5.3
Stable disease	4	10.5
Progression	24	63.2
Disease-free survival, months; mean (range)	18 (1-82)	
Overall survival, months; mean (range)	21 (2-82)	
Death	22	57.9

Table 4. Post-treatment side effects

Side effects	*Patients*	
	N	%
Neuropsychological sequelae	11	29
IQ impairment	1	2.6
Endocrinological disorders	1	2.6
Hearing loss	1	2.6
Musculoskeletal disorders	1	2.6
Performance loss at school/work	7	18.4

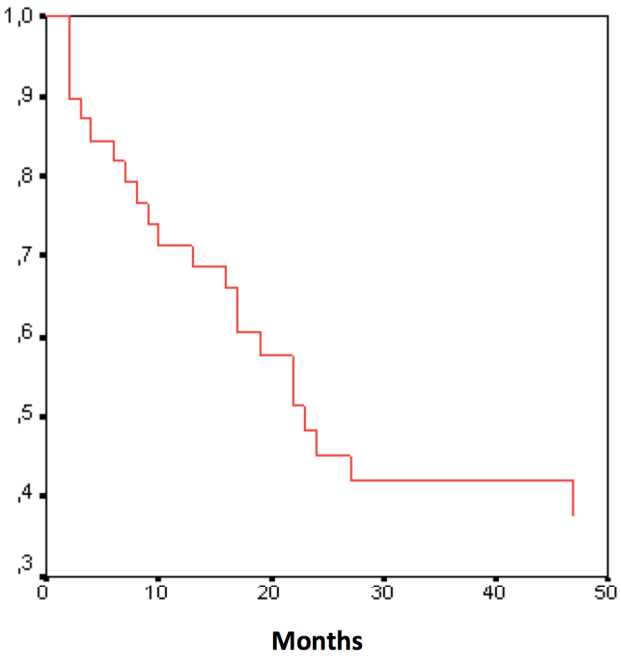

Figure 2. Progression-free survival for all patients.

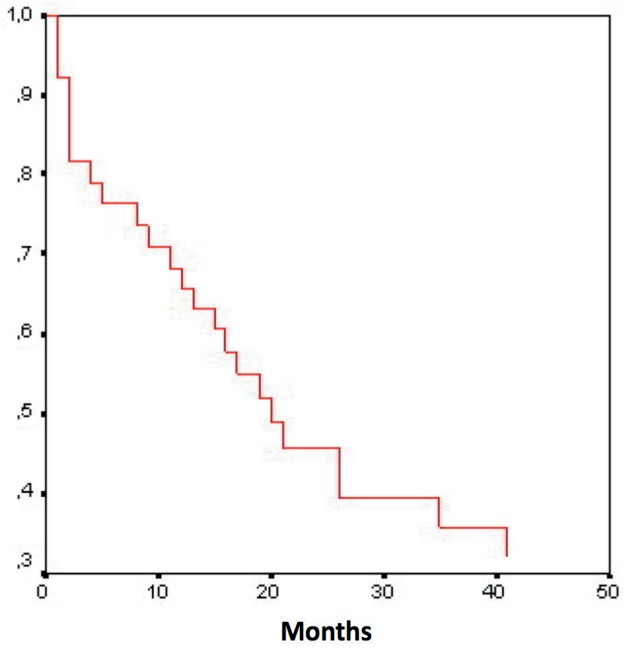

Figure 3. Overall survival for all patients.

Table 5. The effect of age on disease free and overall survival

Variables	*Age (years±SD)*
Progression free survival	
No	11.3±4.5
Yes	10.6±4.83
p-value	0.585
Relative risk (95 % CI)	0.976 (0.896-1.064)
Overall survival	
No	11.7±4.4
Yes	10.2±4.8
p-value	0.319
Relative risk (95 % CI)	0.956 (0.875-1.045)

female patients, respectively. There was no statistically significant difference in PFS and OS rates in relation to the surgical procedure performed. One-year PFS rates were 46.1, 66.7 and 83.3% in patients who were inoperable, in the subtotal resection (STR) group, and total/gross total group (TR/GTR) group, respectively (p=0.868). Although survival rates varied in relation to the histopathological degree of disease (low/high-grade), no statistically significant difference was observed. One- and 3-year PFS rates were 78.6 and 42.9% in patients with low-grade tumors, and 72.7 and 27.3% in patients with high-grade tumors, respectively (p=0.790). Similarly, one- and 3-year OS rates were 92.9 and 50% in patients with low-grade tumors, and 72.7 and 36.7% in patients with high-grade tumors, respectively (p=0.641).

Despite the difference in the mean survival

Table 6. Progression free survival in relation to different factors

Factors	*Number*	*Outcome (%)*				*95% confidence interval*	*Log Rank*	*p-value*
		Mean	*1 year*	*3 year*	*5 year*			
Gender							0.79	0.373
Male	23	39.13	69.57	41.21	35.33	39.78 (25.95-53.61)		
Female	15	33.33	60.00	28.00	28.00	29.72 (12.25-47.19)		
Operation							0.72	0.868
Unresectable	13	46.15	46.15	46.15	46.15	39.62 (18.26-60.97)		
Total GTR	12	41.67	83.33	41.67	41.67	42.67 (24.09-61.24)		
STR	12	25.00	66.67	25.00	25.00	31.75 (14.86-48.64)		
Biopsy	1	0.00	100.00	100.00	0.00	-		
Diagnosis							0.22	0.974
Astrocytoma	21	33.33	71.43	37.50	32.14	37.39 (23.78-51.01)		
Glioma	13	46.15	46.15	46.15	46.15	39.62 (18.26-60.97)		
Oligodendroglioma	3	33.33	100.00	33.33	33.33	30.67 (6.39-54.94)		
Astroblastoma	1	0.00	100.00	0.00	0.00	-		
Grade							2.84	0.585
Unknown	13	46.15	46.15	46.15	46.15	39.62 (18.26-60.97)		
I	5	60.00	80.00	60.00	60.00	57.40 (31.06-83.74)		
II	9	22.22	77.78	33.33	22.22	32.11 (14.15-50.07)		
III	3	0.00	66.67	0.00	0.00	16.00 (1.03-30.97)		
IV	8	37.50	75.00	37.50	-	24.88 (13.30-36.45)		
Low/high grade							0.47	0.790
Unknown	13	46.15	46.15	46.15	46.15	39.62 (18.26-60.97)		
Low	14	35.71	78.57	42.86	42.86	41.14 (24.96-57.33)		
High	11	27.27	77.73	27.27	-	22.45 (13.11-31.80)		
Side effects							2.90	0.088
No	23	47.83	69.57	50.17	43.90	43.79 (28.86-58.72)		
Yes	15	20.00	60.00	16.00	16.00	24.55 (10.78-38.32)		
Total	38	36.84	65.79	36.31	32.68	36.17 (25.15-47.20)	-	-

Table 7. Overall survival in relation to different factors

Factors	*Number*	*Outcome (%)*				*95% confidence interval*	*Log Rank*	*p-value*
		Mean	*1 year*	*3 year*	*5 year*			
Gender							1.48	0.224
Male	23	47.83	78.26	51.24	42.70	45.41 (31.17-59.66)		
Female	15	33.33	60.00	26.25	26.25	30.13 (13.41-46.85)		
Operation							1.14	0.767
Unresectable	13	46.15	46.15	46.15	46.15	40.38 (19.42-61.35)		
Total GTR	12	50.00	91.67	50.00	50.00	48.50 (29.90-67.10)		
STR	12	33.33	75.00	33.33	33.33	37.50 (19.70-55.30)		
Biopsy	1	0.00	100.00	100.00	0.00	-		
Diagnosis							1.42	0.701
Astrocytoma	21	38.10	80.95	42.86	35.71	41.14 (27.49-54.79)		
Glioma	13	46.15	46.15	46.15	46.15	40.38 (19.42-61.35)		
Oligodendroglioma	3	33.33	100.00	33.33	33.33	32.33 (9.38-55.29)		
Astroblastoma	1	100.00	100.00	100.00	-	-		
Grade							3.31	0.507
Unknown	13	46.15	46.15	46.15	46.15	40.38 (19.42-61.35)		
I	5	80.00	80.00	80.00	80.00	66.80 (41.91-91.69)		
II	9	22.22	100.00	33.33	22.22	34.78 (17.50-52.05)		
III	3	33.33	66.67	33.33	-	21.67 (4.47-38.86)		
IV	8	37.50	75.00	37.50	-	26.75 (16.09-37.41)		
Low/high grade							0.89	0.641
Unknown	13	46.15	46.15	46.15	46.15	40.38 (19.42-61.35)		
Low	14	42.86	92.86	50.00	42.86	46.21 (29.87-62.56)		
High	11	36.36	72.73	36.36	-	25.82 (16.39-35.25)		
Side effects							1.86	0.172
No	23	52.17	69.57	54.94	45.78	46.49 (31.47-61.51)		
Yes	15	26.67	73.33	23.33	23.33	30.11 (15.02-45.20)		
Total	38	42.11	71.05	42.32	37.62	40.31 (29.12-51.50)	-	-

rates among patients with grade I astrocytoma (pilocytic astrocytoma) and grade IV astrocytoma (GBM), this didn't reach statistical significance (p=0.701). One- and 3-year PFS rates for patients with grade I astrocytoma were 80% and 60%, respectively, while 1- and 3-year PFS rates for patients with grade IV astrocytoma were 62.5% and 37.5%, respectively. In addition, 1-year OS rates were 80 and 75% for patients with grade I and grade IV astrocytoma, respectively (p=0.507). Following RT, the patients were divided into two groups and assessed in terms of side effects of treatment. Despite different survival rates, no statistically significant difference was noted (p=0.088) (Tables 6 and 7).

Discussion

Unlike adult glial tumors, childhood glial tumors have different characteristics in terms of both localization and biological behavior [1,2]. The incidence of brain tumors, which are mostly congenital, is very low in children under the age of 2 years [4]. Most of the brain tumors are often localized supratentorially at the age of 2-3 years and infratentorially at the age of 3-11 years [1,5]. Surgery, Cx and RT may be used alone or in combination for the management of these tumors according to the stage of disease and clinical prognosis [7,9,12].

Childhood brain tumors are most commonly seen at the age of 4-8 years [1,5,13]. In our study, the age at diagnosis was most often 7, followed by 12 and 15 years. The male/female ratio was 1.88. We also observed that a higher number of girls had childhood brain tumors, which was consistent with the literature [8].

Although survival rates varied among patients who were inoperable or underwent surgery, this variation was without statistical significance in our study. However, the extent of surgical resection is of utmost importance for the prognosis of childhood glial tumors according to the relevant literature [14-16]. In a case series involving 71 patients with low-grade glial tumors of cerebral hemisphere, Pollack et al [8] reported that the type of resection was highly associated with improved PFS and OS rates. In addition, very high PFS and OS rates were reported in patients with low-grade glial tumors following gross total resection (GTR) without any adjuvant therapy. Survival rates were also higher in patients with high-grade glial tumors who underwent GTR. On the other hand, disease progression was observed and adjuvant therapies were required for patients with low-grade glial tumors who underwent STR. Prognosis was very poor in inoperable patients, particularly with diffuse brainstem glioma [14-16].

Low-grade gliomas account for 60% of all childhood supratentorial tumors [8,17]. More than half are low-grade astrocytomas [8,12,17]. In addition, brainstem gliomas account for nearly 25% of all glial tumors of the posterior fossa in children [12,13,18]. Despite the developments in surgical techniques, application of surgery is still controversial in the management of these tumors [6,12]. It is recommended that biopsy followed by RT or RT alone should be used in the management of diffuse and invasive tumors [19-21]. Similarly, we also avoided to schedule patients with diffuse brainstem gliomas for surgery, as assessed by imaging techniques before surgery and recommended RT for these patients. Furthermore, we also operated patients with supratentorial glial tumors using STR,TR/GRT. This allowed to have histopathological diagnosis, thereby increasing the efficacy of adjuvant therapy.

Brainstem gliomas account for 15-20% of all CNS tumors and 30% of all glial tumors of the posterior fossa [4]. In our study, 16 patients (33%) who underwent RT had a brainstem glioma. We also observed that there was a relationship between histopathological diagnosis and PFS and OS rates. It is established that an appropriate treatment of choice may result in better PFS and OS rates in patients with childhood low-grade glial tumors [7,15,22]. In addition, review of literature shows that an appropriate surgical modality and adjuvant RT or Cx may provide higher survival rates in patients with high-grade glial tumors [9,11,23]. However, survival rates are still poor in patients with diffuse brainstem gliomas and inoperable cases [17]. Although we achieved higher PFS and OS rates in patients with low-grade glial tumors compared to those with high-grade glial tumors, this did not reach statistical significance. This may be explained by the patient population with residual/recurrent disease following STR, despite having low-grade glial tumors.

In our study, the number of patients with histopathological diagnosis of low-grade astrocytic tumors was higher. Although grade I astrocytoma is typically more common rather than grade II in children, the ratio of grade I to grade II disease was 1:15. This may be explained by the lower requirement for RT in patients with grade I astrocytoma compared with those with grade II astrocytoma. In addition, all patients with grade I astrocytoma received RT due to residual/recurrent disease.

Conventional external beam RT is typically initiated 2-4 weeks following surgery. In other words, the time to RT initiation from the diagnosis is usually between 15-30 days [11,21]. This is critical for scar healing. In our study, the time to RT initiation from the diagnosis varied widely (range 2-710 days). One of the reasons was that the primary treatment of choice was RT in patients who were diagnosed with glioma clinically and radiographically and underwent early treatment. The patients who received late treatment had also residual or recurrent low-grade glial tumors.

Although postoperative RT application may vary widely among healthcare centers, it is often preferred in patients who are inoperable as a primary/curative treatment modality, in patients with high-grade glial tumors as an adjuvant therapy and those with residual/recurrent progressive low-grade glial tumors [17,21,24-26]. Similarly, RT was administered to patients with inoperable glial tumors confirmed radiographically, those with recurrent high-grade glial tumors postoperatively, and those with progressive low-grade glial tumors. The median RT dose was 54 Gy in our study. Although it is mostly applied at a dose of 50 to 60 Gy in the literature [25], technological developments in radiation oncology allow to offer new treatment modalities. Hypofractionated and hyperfractionated schedules are particularly used; however, no significant difference in survival rates has been achieved yet [20,21]. We believe, therefore, that such studies should be conducted for further analysis.

In the management of childhood glial tum-

ors RT is typically delivered at 45-60 Gy in 25-30 fractions (1.8-2.0 Gy per fraction) for 5-6 weeks [8,24,25]. Treatment schedules including higher doses or doses at >2 Gy per fraction should be avoided due to possible late CNS toxicity. In a case series involving 90 patients, Mishra et al. [25] performed GTR in 11, STR in 43, diagnostic biopsy in 34, and post-recurrence biopsy in 2 patients. The median RT dose was 54 Gy (range 45-60). In addition, Marcus et al. [11] performed stereotactic RT in 50 patients with low-grade glial tumors. The median total dose was 52.2 Gy (range 50.4-58) with 1.8 Gy/day at 6 MV. In another study involving 9 patients with diffuse brainstem gliomas, Janssens et al. [20] applied a hypofractionated schedule including 3 Gy per fraction (13 fractions total) in 8 patients and 5.5 Gy per fraction (6 fractions total) in one patient for 3 weeks. In another study involving 18 patients with diffuse brainstem gliomas, Marcus et al. [11] applied a hyperfractionated schedule including 1.5 Gy (63-66 Gy total) per fraction in 42-44 fractions at 6-15 MV for 6 hours at least in 3 patients. In our study, we applied conventional RT doses and fractions (1.8-2 Gy/day) for all patients and administered a total of 50-60 Gy at 6 MV or 15 MV alone or in combination for 5-6 weeks for the patients who completed RT.

In the present study, we also delivered RT to patients with residual or recurrent low-grade glial tumors following surgery. The PFS and OS rates were higher in patients who underwent GTR, while prognosis was very poor, particularly in inoperable patients with diffuse brainstem glioma. In a study involving 50 patients with low-grade glial tumors, Marcus et al. [11] administered Cx to 12 patients and performed stereotactic RT in 38 patients with progression following incomplete resection of the tumor. The median total dose was 52.2 Gy (range 50.4-58) with 1.8 Gy per fraction daily at 6 MV. Statistical analysis showed that 5- and 8-year PFS rates were 82.5 and 65%, respectively, while 5- and 8-year OS rates were 97.8 and 82%, respectively. Janssens et al. [20] applied a hypofractionated schedule in 8 patients with brainstem gliomas. The median PFS and OS were 4.9 and 8.6 months, respectively. In another study involving 63 patients with high-grade glial tumors, Hales et al. [23] reported that the median survival was 14 months. The multivariate analysis demonstrated that the following 5 factors had an adverse effect on long-term survival: *(i)* performace status below 80%; *(ii)* bilateral malignancy; *(iii)* tumors of the parietal lobe; *(iv)* non-GRT tumors; and *(v)* RT dose below 50 Gy. In another study involving 128 patients with low-grade glial tumors aged 0-18 years, Fisher et al. [22] reported that OS rate was statistically significant in terms of Karnofsky performance score, RT time (postoperative or delayed) and tumor localization. In a phase II trial including 20 patients who were newly diagnosed with diffuse intrinsic pontine glioma at the age of 3-18 years, Jalali et al. [24] administered temozolomide in combination with RT. The patients received temozolomide 75 mg/m2 in combination with a total of 54 Gy RT in 30 fractions using conventional fractionation between 1-42 days. Following the initial combined regimen, the patients received adjuvant temozolomide for 12 cycles. The median PFS and OS were 6.9 and 9.15 months, respectively. As a result, survival rates were lower in patients with high-grade glial tumors, as confirmed by MRI, compared to those with low-grade glial tumors. In addition, the survival rates were higher in patients with improved neurological status. In this study in which histopathological diagnosis had no significant effect on OS rate, survival was not associated with age, performance status, duration of symptoms and severity of hydrocephalus. In a case series involving 71 patients with low-grade glial tumors of cerebral hemisphere, Pollack et al. [8] reported that the median postoperative PFS rates at 5, 10 and 20 years were 88, 79, and 76%, respectively for 70 survivors, whereas the OS rates were 95, 93 and 85%, respectively. Univariate analysis revealed that tumor resection was strongly associated with PFS and OS rates. On the other hand, the authors reported that RT was not associated with significant improvement in OS rate. They also observed that cognitive and endocrinological disorders were significantly associated with RT application. In our study, we observed that age, surgical procedure, low/high-grade disease and histopathological diagnosis were not statistically associated with PFS and OS. This may be explained by the small sample size, patient population referred from various healthcare centers to our clinic and missing data during follow-up due to incomplete or loss of contact. In addition, the majority of our patients were those who underwent RT due to residual or recurrent disease.

In conclusion, the extent of surgical resection is the most important prognostic factor in patients with childhood glial tumors. It seems that TR/GTR is associated with improved survival outcomes. Of note, adjuvant therapies including RT and/or Cx should be combined with surgery.

References

1. Kutluk MT, On behalf of TPOG. First National Pediatric Cancer registry in Turkey: A Turkish Pediatric Oncology Group (TPOG) Study. Pediatric Blood Cancer 2004;43:452-453.
2. Prayson RA, Goldblum JR. Neuropathology 2005;1:489-494.
3. Louis DN, Ohgaki H, Wiestler OD et al. The 2007 WHO Classification of tumours of the central nervous system. Acta Neuropathol 2007;114:97-119.
4. Statistical Report: Primary Brain Tumors in the United States, 2004–2006. Central Brain Tumor Registry of the United States, 2010.
5. Lanzkowsky P (Ed). Manual of Pediatric Hematology and Oncology 2005 (4th Edn). Marchal Lichtmanm URMC, Rochester, Ch 21: Central nervous system malignancies, pp 647-671.
6. Sandri A, Sardi N, Genitori L et al. Diffuse and focal brain stem tumors in childhood: prognostic factors and surgical outcome. Experience in a single institution. Child Nerv Syst 2006;22:1127-1135.
7. Berger MS. The impact of technical adjuncts in the surgical management of cerebral hemispheric low-grade gliomas of childhood. J Neurooncol 1996;28:129-155.
8. Pollack IF, Claassen D, al-Shboul Q. Low-grade gliomas of the cerebral hemispheres in children: an analysis of 71 cases. J Neurosurg 1995;82:536-547.
9. Lesser GL. Chemotherapy of high grade astrocytomas. Semin Oncol 1994;21:220-235.
10. Soisson ET, Tome WA, Richards GM, Mehta MP. Comparison of LINAC based fractionated stereotactic radiotherapy and tomotherapy treatment plans for skull-base tumors. Radiother Oncol 2006;78:313-321.
11. Marcus KJ, Goumnerova L, Billett AL et al. Stereotactic radiotherapy for localized low-grade gliomas in children: final results of a prospective trial. Int J Radiat Oncol Biol Phys 2005;61:374-379.
12. Epstein F, Constantini S. Practical decisions in the treatment of pediatric brain stem tumors. Pediatr Neurosurg 1996;24:24-34.
13. Kaatsch P, Rickert CH, Kühl J, Schüz J, Michaelis J. Population-based epidemiologic data on brain tumors in German children. Cancer 2001;92:3155-3164.
14. Hirsch JF, Samte Rose C, Pierre-Kahn A, Pfister A, Hoppe-Hirsch E. Benign astrocytic and oligodendrocytic tumors of the cerebral hemispheres in children. J Neurosurg 1989;70:568-572.
15. Palma L, Guidetti B. Cytic pilocytic astrocytomas of the cerebral hemispheres. Surgical experience with 51 cases and long-term results. J Neurosurg 1985;62:811-815.
16. Laws ER Jr, Taylor WF, Clinton MB, Okazaki H. Neurosurgical management of low grade astrocytoma of the cerebral hemispheres. J Neurosurg 1984;61:665-673.
17. Young Jr JL, Ries LG, Silverberg E. Cancer incidence, survival and mortality for children younger than age 15 years. Cancer 1986;58:598-602.
18. Lee BC, Kneeland JB, Walker RW, Posner JB, Cahill PT, Deck MD. MR imaging of brainstem tumors. AJNR Am J Neuroradiol 1985;6:159-163.
19. Steck J, Friedman WA. Stereotactic biopsy of brainstem mass lesions. Surg Neurol 1995;43:563-567.
20. Janssens GO, Gidding CE, Van Lindert EJ et al. The role of hypofractionation radiotherapy for diffuse intrinsic brainstem glioma in children: a pilot study. Int J Radiat Oncol Biol Phys 2009;73:722-726.
21. Mandell LR, Kadota R, Freeman C et al. There is no role for hyperfractionated radiotherapy in the management of children with newly diagnosed diffuse intrinsic brainstem tumors: results of a Pediatric Oncology Group phase III trial comparing conventional vs. hyperfractionated radiotherapy. Int J Radiat Oncol Biol Phys 1999;43:947-949.
22. Fisher BJ, Leighton CC, Vujovic O, Macdonald DR, Stitt L. Results of a policy of surveillance alone after surgical management of pediatric low grade gliomas. Int J Radiat Oncol Biol Phys 2001;51:704-710.
23. Hales R, Shokek O, Burger P et al. Prognostic Factors in Pediatric High-Grade Glioma and the Importance of Accurate Pathologic Diagnosis. ASTRO 2006;66:527 (abstr).
24. Jalali R, Raut N, Arora B et al. Prospective Evaluation of Radiotherapy With Concurrent and Adjuvant Temozolomide in Children With Newly Diagnosed Diffuse Intrinsic Pontine Glioma. Int J Radiat Oncol Biol Phys 2010;77:113-118.
25. Mishra KK, Puri DR, Missett BT et al. The role of upfront radiation therapy for incompletely resected pediatric WHO grade II low-grade gliomas. NeuroOncology 2006;8:166-174.
26. Tai BC, Grundy RG, Machin D. On the importance of accounting for competing risks in pediatric cancer trials designed to delay or avoid radiotherapy. I. Basic concepts and first analyses. Int J Radiat Oncol Biol Phys 2010;76:1493-1499.