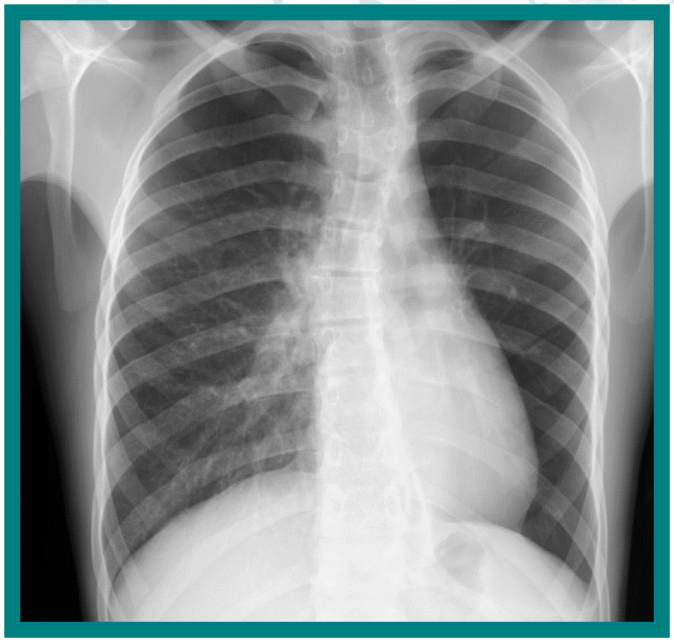
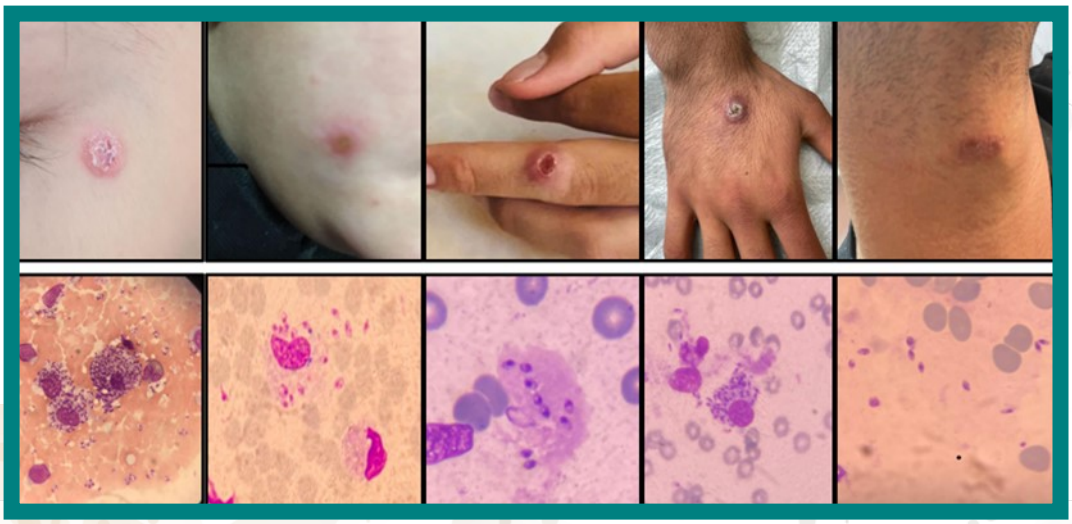
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SINGLE-CENTER EXPERIENCE AND LITERATURE REVIEW OF RADIOTHERAPY OUTCOMES FOR ADULT EPENDYMOMAS

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Abstract

Objective: To retrospectively determine the long-term outcome of adult intracranial and spinal ependymoma patients treated with postoperative radiation therapy after surgery.

Methods: Fourteen adult patients who underwent radiotherapy after surgery at a single center between 1999 and 2022 were included. The endpoints analyzed were overall survival and progression-free survival, together with prognostic factors.

Results: The median (range) age was 29.5 (23–58) years. The majority (71.4%) of the tumors were located in the spinal canal and gross total resection was performed in nine (64.3%) patients. Six patients were irradiated after recurrence (spinal n=4, intracranial n=2) of whom three had myxopapillary and two had anaplastic histology. Patients were followed up for a median duration of 106.5 (13-172) months. Overall, 4 patients (intracranial n=3, spinal n=1) had recurrences and died after radiotherapy as a direct result of disease progression during the follow-up period. All of these intracranial tumors exhibited anaplastic histology and the spinal tumor was myxopapillary type. Patients with intracranial lesions had a 5-year survival of 50% and no patient was alive on the 10th year, compared with 5- and 10-year overall survival of 87.5 % for patients with spinal tumors. Patients with spinal tumors had a 5- and 10-year progression-free survival rate of 52.5%, while those with intracranial lesions had a rate of 25%.

Conclusion: In low-grade spinal ependymomas radiotherapy appears to control disease, even after recurrence. For myxopapillary ependymoma patients, in subtotally resected intracranial and all high-grade tumors, regardless of the extent of resection, adjuvant radiotherapy should be administered.

Keywords: *Ependymoma, adult, radiotherapy, histology.*

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Introduction

In a study conducted in the United States in 2014, ependymomas constituted 1.9% of all brain and Central Nervous System (CNS) tumors in adult patients, and 5.2% in children and adolescents ages 0-19 years.[1] Ependymomas can originate from ependymal cells anywhere in the CNS with an aged-based site areas in all age groups. In the Surveillance, Epidemiology and End Results (SEER) database, ependymomas were found in the spinal cord in 36.2%, infratentorial in 22.2%, supratentorial in 11.8%, and unknown in 29.8% of cases.[2] Adults are more frequently diagnosed with spinal and supratentorial compartment tumors. Ependymomas, regardless of the anatomical locations they originate from, possess a histological uniformity. However, there may be considerable variance in clinical outcomes, and this variability remains unexplained by known clinical and histological factors.[3] A prospective randomized study has not been conducted on the clinical features that predict prognosis in this cohort, largely due to the rarity of these tumors. The most important conventional treatment option is surgery, since the extent of resection was detected as one of the most significant predictors of outcome.[4,5] Radiotherapy (RT) is crucial in treating these tumors with anaplastic histology, improving survival, and reducing recurrence rates. The optimal use of adjuvant RT in low-grade, adult ependymomas after maximal safe resection is unclear. [6-9] The European guidelines recommend adjuvant RT or observation for patients with G2 ependymomas.[6] On the contrary, there is limited information available on the effectiveness of chemotherapy for ependymoma. A randomized phase III trial for infratentorial ependymoma found no improvement in survival rates.[10]

We performed a retrospective analysis of outcomes for this rare tumor following RT. There have only been two previous studies from Turkey concerning this topic reported.[11-12]

Methods

Patients aged 18 years or older with a histological diagnosis of ependymoma and treated with RT after surgery between January 1999- January 2022, at Kocaeli University Hospital were included for analysis. Clinical information, including age at diagnosis, Karnofsky performance status, sex, tumor location and grade, clinical symptoms, the extent of resection, pre-operative and post-operative magnetic resonance imaging (MRI), were all obtained from the hospital database and patient records. Details of RT collected included treatment volume, treatment duration, dose and fraction number, time to postoperative RT, and radiographic response. RT treatment volume was defined as focal for only tumor bed irradiation or whole spine for spinally irradiated patients.

Surgical extent was defined by the absence of a tumor depending on the surgeon's operative record or postoperative MRI and was defined as gross total resection (GTR) when the visible tumor was grossly removed. The surgical procedure was identified as a subtotal resection (STR) if the surgeon saw an unresectable tumor on the operating table or postoperative imaging showed a residual tumor. The extent of surgical resection, use of adjuvant chemotherapy, follow-up duration, and signs of recurrence were also recorded.

The follow-up period was defined as the time from surgery until the patient's last clinic visit. Patients with less than one year of radiological follow-up after RT were excluded from the study. The study was approved by the Non-Interventional Clinical Research Ethics Committee (Approval No: GOKAEK-2023/19.34).

Pathologic Examination

The tumors were carefully re-examined by an experienced pathologist, who made a new diagnosis based on the World Health Organization (WHO) classification of Central Nervous System Tumors 2021.13 The essential diagnostic features for ependymoma were determined to be high nuclear-to-cytoplasmic ratio and high mitotic count.

Statistical Analysis

Statistical analysis was performed using SPSS, version 22 (IBM Inc., Armonk, NY, USA). Data were summarized using standard descriptive statistics such as median, and range for continuous variables; and frequency for categorical variables. Progression-free survival (PFS) and overall survival (OS) were calculated from the date of surgery using Kaplan-Meier estimates. The log-rank test was used for the identification of risk factors. A p-value of 0.05 or less was considered statistically significant.

Results

Patients and Symptoms

A total of 58 patients were diagnosed with adult ependymoma between 1999 and 2022. Fourteen of them, who were irradiated after surgery, were included in our study. Demographic and tumor characteristics are summarized in Table 1. The median (range) age was 29.5 (23–58) years and there were 3 women (21.4%) and 11 men (78.6 %). Presenting symptoms varied according to the location of the tumor. In spinal tumors, pain was the most frequent presenting symptom (57%), followed by sensory deficits (14.3%), motor weakness (14.3%), and sphincter disturbances (7.1%). Patients with intracranially located tumors had headaches (14.3%) and seizures (7.1%). Most patients (90%) were able to walk without assistance before surgery (McCormick grade I and II), with only two patients requiring external assistance (McCormick grade III).

Tumor Characteristics

The median tumor diameter was 2.75 cm (1.0-5.0). Ten of 14 patients (71.4%) had spinal neoplasms, with the other four tumors being located intracranially. The most common histopathology was ependymoma (43%), followed by myxopapillary (28.5%) and anaplastic (28.5%). Of the 10 patients with spinal tumors, only one was classified as Grade 3. Two of the four brain tumors were located above the tentorium, while the other two were infratentorial. Among the intracranially located tumors, three were Grade 3, and the other was Grade 2. The patient with this Grade 2 tumor, who died due to recurrence, was reassessed as Grade 3, after re-consideration by the histopathologist taking part in the study.

Surgery and Adjuvant Therapy

GTR was performed in 9 (64.3%) and STR in 5 (35.7%) patients. After resection, immediate postoperative RT was administered due to residual tumor (n=5), anaplastic histology (n=2), and both anaplastic histology and spinal seeding (n=1). Six patients were irradiated after recurrence (n=4 spinal, n=2 intracranial). Five patients received chemotherapy after RT; four due to local recurrence, and one due to spinal seeding. RT and patient treatment characteristics are summarized in Table 2. The median radiation dose administered was 54 (46-60) Gy. A median of 27 (23-30)

fractions of 1.8–2.0 Gy were delivered with conformal RT in 10 (71.4%) patients, and with intensity-modulated RT(IMRT) in 4 (28.6%). Treatment was given to the tumor volume based on the operative records and imaging findings. For spinal tumors, the RT volume was one vertebra above and below the tumor bed, based on the preoperative and postoperative imaging results and the treating physician's preferences.

Table 1. Patient and tumor characteristics

Characteristic	**No. of patients (%)**
Age (yr)	
Median (range)	29.5 (23-58)
Karnofsky performance status	
≥80	12 (85.7)
<80	2 (14.3)
Sex	
Male	11 (78.6)
Female	3 (21.4)
Tumor location	
Supratentorial	2 (14.3)
Infratentorial	2 (14.3)
Spinal cord	10 (71.7)
Cervical	2 (14.3)
Thoracic	1 (7.1)
Lumbar	7 (50)
WHO 2021 Histologic grade	
WHO Grade 2	10 (71.7)
WHO Grade 3	4 (28.3)
WHO 2021 histopathological classification	
Spinal epandymoma	6 (42.8)
Myxopapillary ependymoma	4 (28.57)
Posterior fossa ependymoma	2(14.2)
Supratentorial ependymoma	2 (14.2)
Tumor size	
<3 cm	9 (64.3)
≥3 cm	5 (35.7)
Presenting symptoms	
Pain	8 (57)
Sensory deficits	2 (14.3)
Motor disturbances	2 (14.3)
Sphincter dysfunction	1 (7.1)
Headache	2 (14.3)
Seizure	1 (7.1)
Extent of resection	
Complete	9 (64.3)
Incomplete	5 (35.7)
Preop McCormick grade	
Grade 1	11 (78.6)
Grade 2	1 (7.1)
Grade 3	2 (14.3)
Grade 4	-

Table 2. Radiotherapy treatment characteristics of all patients

Patient number	Age	Tumor location	Resection Type	Histopathology	RT Timing	Recurrence time after surgery (months)	RT technique	RT dose Gy/frx	Recurrence after RT/Alive or Dead
1	57	Lumbar spine	STR*	Mixopapillary, Grade 2	Postoperative	-	IMRT	54/27	No/Alive
2	29	Lumbar spine and whole spinal metastasis including cauda equina	STR	Anaplastic, Grade 3	Postoperative	-	IMRT	Whole spine:36 Gy/23 Tumor: 54/27	No/Alive
3	23	Thoracal spine	STR	Epandymoma, Grade 2	Postoperative	-	Conformal	50/25	No/Alive
4	25	Lumbar spine	First operation: GTR** Second operation: STR	Mixopapillary, Grade 2	After recurrence due to subtotal excision	55	Conformal	50,4/28	No/Alive
5	26	Lumbar spine	GTR	Mixopapillary, Grade 2	After recurrence	18	Conformal	50/25	No/Alive
6	34	Lumbar spine	STR	Epandymoma, Grade 2	Postoperative	-	Conformal		No/Alive
7	24	Cervical spine	STR	Epanymoma, Grade 2	Postoperative	-	Conformal	46/23	No/Alive
8	58	Cervical spine	STR	Epanymoma, Grade 2	Postoperative	-	Conformal	50,4/28	No/Alive
9	25	Lumbar spine	First operation: STR Second operation: GTR	Epandymoma, Grade 2	After recurrence	5	Conformal	54/27	No/Alive
10	20	Lumbar spine	First operation: GTR Second operation: STR	Mixopapillary, Grade 2 After recurrence Grade 3	After recurrence due to subtotal excision	15	Conformal	52,2/29	Yes/Dead
11	45	Intracranial (temporal)	GTR	Anaplastic, Grade 3	After recurrence	57	Conformal	60/30	Yes/Dead
12	54	Intracranial (temporal)	GTR	Anaplastic, Grade 3	Postoperative	12	IMRT	60/30	Yes/Dead
13	54	Intracranial (4th ventricule)	First operation: GTR Second operation: STR	Ependymoma, Grade 2 After second look; Anaplastic, Grade 3	After recurrence	30	IMRT	54/27	Yes/Dead
14	30	Intracranial (4th ventricule)	GTR	Anaplastic, Grade 3	Postoperative	-	Conformal	54/27	No/Alive

*Subtotal resection,**Gross total resection

Table 3. Summary of important studies with treatment and outcome data for adult spinal ependymomas with and without radiotherapy

First author	Year published	Number	Grade	Outcome predictors	Radiotherapy outcome
Pica et al.[20]	2009	85	All MPE	Improved PFS; -Age > 36 years, -Absence of neurologic symptoms at diagnosis, -Tumor size ≥25 mm - RT	RT improved 5-year PFS; Surgery:50± 11% Surgery+RT:82 ±11% (p = 0.05)
Oh et al.[21]	2013	348	II-337 III-11 (3.4)	Improved OS; - GTR (GTR versus STR + RT group) -Benign ependymomas	RT improved 5-Year PFS; GTR 97.9%, STR + RT 65%, STR 45% (p = .047)
Tarapore et al[22]	2013	134	I-28 II-101 III-3	Improved PFS; -Grade (Low) -Resection type (GTR)	RT did not improve PFS of patients who underwent STR (p=0.36).
Lee SH et al.[23]	2013	88	I -24 II -61 III-3	Improved PFS; -Lower grade histology -Resection type (GTR)	RT was not associated with improved tumor recurrence/progression.
Tsai JC et al.[15]	2014	51	All MPE	Improved PFS; -Resection type (GTR) -Age >35 years at diagnosis -RT	RT was associated with improved PFS (p=0.02) and LC(p=0.03).
Vera-Bolanos et al.[24]	2015	212	I- 30 II -96 III -3	Decreased PFS; -Supratentorial location, -Grade III, -Subtotal resection, followed or not by radiation	PFS of patients with STR+RT better than GTR (p=0 .01).
Lin et al.[25]	2015	1353	III-26 MPE-374 Non-MPE-953	Improved OS; -Lower grade histology -Higher extent of surgical resection	At 5-year follow-up, adjuvant RT did not appear to confer a significant survival advantage following STR (p=0.07) or GTR (p=0.12).
Keil et al.[26]	2016	61	I -25 II -34 III- 2	Improved OS; -Gross total resection -Good preoperative neurological condition	Radiotherapy did not have a significant effect on PFS after STR/biopsy (p = 0.653).
Wostrack.[27]	2018	158	I-44 II-105 III-9	Improved PFS; -GTR, -WHO grade II, -Low Ki-67 index	Adjuvant RT was performed in 15 cases and RT had no effect among patients with incompletely resected patients (p = 0.079).
Wang et al.[28]	2018	169	All classic ependymoma	Improved PFS; -Low grade histology, -Extent of surgical resection -RT	RT patients had a shorter PFS than surgery alone, with a mean of 119.6±14.3 months (P=.000)
Brown et al.[29]	2020	1058	II-1019 III-39	Decreased OS; -Increasing age -High grade	Adjuvant RT did not reduce the hazard of death for the cohort overall (p = 0.810) or for patients with grade II tumors (p = 0.810).
Savoor et al.[30]	2021	65	I- 20 II-42 III-3	Improved PFS; -GTR	For grade II lesions, STR+RT yielded better outcomes than STR alone (10y PFS 77.1% vs 68.2%, LC 85.7% vs 50%) (PFS: p = 0.23, LC: p = 0.21)

MPE;myxopapillary ependymoma, RT;radiotherapy, PFS;progression free survival, OS;overall survival, GTR;gross total resection, STR;subtotal resection

Table 4. Summary of important studies with treatment and outcome data only for adult cranial ependymomas with and without radiotherapy

First author	Year published	N	Grade	Outcome predictors	Radiotherapy outcome
Reni[34]	2003	70	II-51 III-15	Improved OS; -Younger age -Infratentorial tumor location	In grade 2 tumors there's a borderline statistical significance, toward increased OS (p=0.08) and with a significant trend toward increased PFS (p=0.04) with RT.
Rogers[35]	2005	45 (infratentorial)	II-43 III-2	Improved PFS; -Adjuvant RT -Low tumor grade -Extent of resection (GTR)	RT improved 10-year LC: GTR+RT:100%, GTR:50%, STR+RT:36% No difference in OS rate.
Metellus[36]	2007	152	II- 109 III-43	Improved OS; -Low histological grade -Extent of surgery(GTR) -Patient age and patient KPS.	Increased PFS (P <0.05) among low grade tumors with STR vs STR+RT
Guyotat[37]	2009	106 (infratentorial)	II- 88 III-18	Improved OS; -KPS>80, -No recessus lateral extension -Low histological grade (Marseille's grading) -Adjuvant RT	Adjuvant RT was significantly associated with a better OS and PFS in incompletely resected grade II ependymomas
Metellus[38]	2010	114	II-114	Improved OS; -Low histological grade, -Extent of surgery (GTR) -Older age, -Higher KPS -Adjuvant RT	In the subgroup of incompletely resected tumors, adjuvant RT was significantly associated with a better PFS (p= 0.002) and OS (p=0.005)
Dutzmann[39]	2013	64	I-18 II-33 III-13	Decreased OS; -Older age -Supratentorial tumor location	In WHO Grade II tumors RT did not lead to increased PFS (p = 0.888) or OS (p = 0.801) also for incompletely resected tumors.
Nuno[40]	2015	1318	II-1055 III- 263	Decreased OS; -Older age at diagnosis, -High tumor grade, -Large tumor size	Adjuvant RT among grade II and III cohorts did not seem to impact the OS.
Prabhu[41]	2019	1787	II-1471	Decreased OS; -Older age, -Male sex, -Earlier year of diagnosis, -Grade 3 histology	Adjuvant RT was not associated with OS.
Chan Woo Wee[42]	2020	172	II-106 III-66	Decreased OS; -Older age, -WHO grade III -Larger tumor size -STR	Adjuvant RT significantly enhanced LC (p = 0.010) and PFS (p = 0.007).
Zuccato[43]	2022	122	II-95 III-27	Decreased OS; -Grade III histopathology (vs grade II: p = 0.0064) -Undergoing a biopsy/STR	Adjuvant RT improved PFS (p = 0.0147).

RT; radiotherapy, PFS;progression free survival, OS;overall survival, GTR;gross total resection, STR;subtotal resection, LC;local control

Outcomes and Survival Data

The median duration of follow-up was 106.5 (13-172) months. Overall, 4 patients (3 intracranial and 1 spinal) had recurrences and died after RT as a direct result of disease progression during the follow-up period. Three of the four intracranial patients had recurrence. The patient who had an initially graded grade 2 tumor in the fourth ventricle had a first recurrence 30 months later and underwent repeat surgery. After surgery, anaplastic histology was detected and 54 Gy RT was given to the operation cavity. During the follow-up period, 75 months after RT, recurrence was detected on radiographs, which was inoperable, and six cycles of cisplatin, cyclophosphamide, etoposide, and temozolomide chemotherapy were administered. However, the patient died 29 months after the second relapse. The other patient's tumor was located in the temporal lobe. GTR was performed and anaplastic histopathology was reported. RT was administered at a dose of 60 Gy into the resection cavity. A recurrence was detected in the first year. The patient was reoperated but subtotal resection was performed at this time, and chemotherapy was given after surgery. The patient died five months after the second surgery. The third patient with a tumor in the temporal lobe also had anaplastic histopathology reported, and recurrence occurred 57 months after the surgery; he was subsequently irradiated. Sixty-four months after the second surgery the patient died due to a recurrence.

Of the 10 spinal patients, there was only one recurrence which was located in the lumbar region and was diagnosed as myxopapillary ependymoma (MPE). After recurrence subtotal resection was performed and, at this time, anaplastic histology was observed and RT was given. After RT, ICE (Ifosfomide, Carboplatin, Etoposide) chemotherapy was given for six cycles but the patient died after 23 months.

A patient who had a Grade 3 tumor located in the lumbar region had spinal seeding in the early postoperative MRI and was treated with spinal RT, consisting of 36 Gy to the whole spinal canal, and the local site received 54 Gy using the IMRT technique. After the patient underwent RT, chemotherapy using temozolomide was initiated, and at the last follow-up visit, the patient's condition remained stable.

The median OS of all patients was 144 months (95% CI: 95.0-192.9). Five and 10-year OS of the whole group was 83.9% and 71.9%, respectively. Five and 10-year PFS of the whole group was 43%. Patients with intracranial lesions had a 50% 5-year survival rate, with no patients surviving past 10 years. In contrast, patients with spinal tumors had rates of 87.5% for both 5- and 10-year overall survival. The median PFS was 57 months. Patients with spinal tumors had a 5- and 10-year PFS of 52.5%, while those with intracranial lesions had a 5- and 10-year PFS of only 25%.

In univariate analysis, due to low patient number, we did not find any relationship between age, sex, tumor histology, grade, location, tumor size, McCormick grade, RT dose, timing and resection type (p>0.05).

Discussion

Due to the rarity of adult ependymomas, the literature regarding adjuvant therapy is limited to retrospective series and population-based studies with variable results. There is a limited number of patients in order to assess the effectiveness of adjuvant RT in this tumor (Tables 3 and 4).

In this retrospective, single-center study, the spinal cord was the most common location (72%) in keeping with the literature. Spinal ependymomas (SE) are generally benign and slow-growing tumors, mostly classified as Grade 2. GTR is the most important prognostic factor to prevent tumor progression. In a systematic literature review that included 57 articles detailing outcomes for 3,022 patients, the impact of surgical resection and adjuvant therapy on survival for intramedullary ependymomas and astrocytomas was reported. GTR resulted in a 5.37 times increase in OS rate for all tumor grades.[14] In our SE patients, RT was performed due to subtotal resection in 5 low-grade patients (Grade 2 Ependymoma (n=4), Myxopapillary (n=1)), and the 4 patients irradiated after recurrence were mostly Myxopapillary (3) type. Myxopapillary ependymoma (MPE), is a rare variant, commonly found in the lumbosacral region in adults. Tsai et al. reviewed their MPE cases and found that patients receiving GTR plus RT had a median local control (LC) of 10.5 years, compared to 4.75 years for those receiving GTR only (p=0.03).[15] Furthermore, 10-year local control was 0% for 16 patients with STR compared to 65% for those who received adjuvant RT (p=0.008). On multivariate analyses, age older than 35 years at diagnosis and receipt of adjuvant RT was associated with statistically improved PFS and LC (p<0.005).

In the present study, all three of the MPEs irradiated after recurrence were younger than 35 years old. MPEs are also highly recurrent tumors due to the tendency to infiltrate the conus medullaris and spinal cord parenchyma.[16] Notably, the 2021 WHO classification of CNS tumors updated MPE status from grade 1 to the grade 2 category, reflecting the increased recurrence risk.[17] Considering the data, adjuvant RT emerges as an important clinical consideration.

Anaplastic ependymomas (AE) represent only approximately 5% of SEs. In an epidemiologic study, Grade 3 tumor incidence was only 0.6%.[18] In the present study, there was only one AE located in the lumbar spine, with spinal seeding. The clinical outcomes of AEs have demonstrated broad disparities, ranging from long-term progression-free survival to death due to metastases or recurrence with a 5-year OS varying from 60% to 96%. A recent study of a retrospective cohort, and a systemic review, have shown that undergoing GTR and receiving adjuvant RT reduced the risk of tumor progression. In contrast, being 25 years old or younger was found to increase the risk.[19]

The use of adjuvant RT for treating Grade 2 SEs continues to be a subject of controversy. There are both studies showing and not showing that adjuvant RT improved local control after STR. These studies are summarized in Table 3.[15,20-30] Recently, a deep learning algorithm was applied to over 2200 patients in the SEER database to determine predictors of overall survival in SE. The study showed that receiving RT was an independent predictor of survival.[31]

The outcome of intracranial tumors is different from SEs and generally worse, in which the 5-year survival rate does not exceed 70%. In the present case series, there were only four intracranial tumors, all with anaplastic histology and OS was only 50%. Only the youngest patient with a posterior fossa ependymoma (EPF) was still alive after 10 years. The two supratentorial ependymomas displayed different recurrence patterns; one recurred after five years, while the other recurred after just two years. Due to the low patient number, it would be unsafe to draw conclusions about these outcomes but this heterogeneity suggests investigating molecular features of cranial ependymomas which could be responsible. Molecular classification was defined into five groups by WHO: supratentorial ependymoma, ZFTA fusion-positive; supratentorial ependymoma, YAP1 fusion-positive; posterior fossa ependymoma, group PFA; posterior fossa ependymoma, group PFB and spinal ependymoma, MYCN-

amplified.[17] In a recent study investigating the impact of surgery and radiotherapy in EPFs including molecular profiling, it was reported that EPF-PFA ependymomas have poor survival rates with a 5-year PFS ranging from 26.1% to 56.8% and RT after surgery prolonged survival.[32]

Despite the absence of randomized data, the standard treatment for patients with infratentorial and AEs involves the implementation of postoperative adjuvant RT. Both the European Association of Neuro-Oncology (EANO) and the National Comprehensive Cancer Network (NCCN) guidelines recommend adjuvant RT for Grade 3 tumors, regardless of the extent of resection.[6,33] However, there are conflicting recommendations for Grade 2 tumors in these guidelines. The EANO guideline recommends observation for adults with Grade 2 intracranial ependymoma status post-GTR and adjuvant RT for patients with Grade 2 ependymoma status post-STR.[6] However, the NCCN recommends adjuvant RT for Grade 2 intracranial ependymoma regardless of the extent of resection due to the retrospective nature of the studies supporting observation after surgery and until high-quality evidence supporting observation alone becomes available.[33] Although high patient-numbered National Cancer Database and SEER studies did not show any benefit with RT, their results should be interpreted with caution (Table 4).[34-43] This caution is due because of the risk of miscoding, substantial missing data relating to variables such as resection extent and tumor size, and a lack of surviving specific cancer or recurrence data. A central pathology review is further required.[40] Metellus et al. reported that up to 30–60% of intracranial ependymomas may be misdiagnosed as ependymomas based on central pathology review and the histopathological distinction between WHO grades II and III classic ependymomas and AEs was found to exhibit high interobserver variability (up to 69%), even in experienced centers.[36]

Limitations

The main limitation of this study is the small sample size, attributed to the disease's infrequency, a retrospective evaluation approach, and an absence of data gleaned from non-irradiated patients for comparative analysis.

Conclusion

In this single-center study of adult ependymoma, our results were largely consistent with those reported in the literature, despite the limited patient sample size. MPE and AEs should be irradiated after surgery regardless of the extent of resection. Future studies are needed to incorporate molecular changes into management decisions regarding the irradiation of Grade 2 spinal ependymomas after GTR and/or STR.

Ethical Standards Compliance

The study is approved by the Kocaeli University Ethical and Research Committee (Approval No: GOKAEK-2023/19.34).

Declaration of Conflicting Interests

The authors have no conflict of interest.

Author Contributions

A.U.K., B.Y.B.: collected the data and drafted the manuscript. A.U.K., B.Y.B., M.G.A. edited the manuscript, participated in the study design and coordination. All authors (A.U.K., B.Y.B., M.G.A.) read and approved the final manuscript.

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