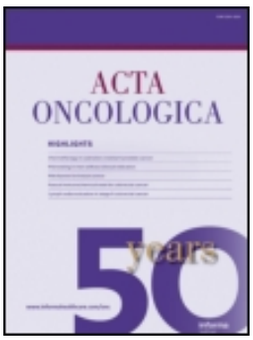

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Intracranial Ependymomas in Childhood

A Retrospective Review of Sixty-two Children

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Of the 818 tumours of the central nervous system diagnosed between 1972 and 1991, 62 patients (35 males and 27 females) with histopathologically confirmed ependymomas were treated and followed-up at the Children's Hospital of Hacettepe University during that period. The median age was 6 years (range 1–17 years). Headache, nausea and vomiting were the most frequent symptoms; papilledema was the most common sign in our patients. Tumour sites were in the posterior fossa in 47 patients and supratentorial in 15 patients. All patients underwent surgery. Gross- total resection was performed in 27 patients, subtotal resection in 32 patients and biopsy in the remaining 3 patients. Initially, 53 patients were given postoperative radiotherapy. Four patients did not receive radiotherapy because of their young age, whereas five patients died prior to starting radiotherapy. Two slightly different types of chemotherapy protocols were applied for an average of one year in 47 patients. Event-free and overall survival rates at 10 years were 36% and 50%, respectively. Twenty children suffered relapse 4 to 55 months after diagnosis (median 16 months). Relapses were distant in 3 cases and local in 17. Age was the only statistically significant prognostic factor, patients younger than 5 years of age having a poorer outcome. Sex, histopathologic type, localization of the tumour, extent of surgery, and chemotherapy did not influence the prognosis in our study. Because the majority of recurrences were local, better local tumour control is required. New treatment strategies should be developed in order to improve local control.

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Ependymomas are rare tumours that constitute about 10% of all primary intracranial tumours in childhood (1–3). They arise from the ependymal cells lining the ventricular system and the central spinal canal. In about 60% of patients, the tumour is located in the posterior fossa while the remainder are located supratentorially (4, 5). Ependymomas can also occur in the spinal cord and constitute 25% of all spinal cord tumours. More than half the patients with ependymomas are under the age of five years at diagnosis. Ependymomas may seed through the cerebrospinal fluid pathways. The true incidence of this complication is not completely clear (6, 7).

There are significant disagreements concerning optimal postoperative treatment. Surgery and radiotherapy (RT) have been used in the management of these patients (8, 9). In contrast to surgery and radiotherapy, the use of chemotherapy in the treatment of childhood ependymoma is controversial (10, 11). The aim of this retrospective study was to analyse the clinical characteristics and presentation, factors influencing prognosis and treatment results of 62 patients with intracranial ependymomas at the Children's Hospital of Hacettepe University during a 20-year period (1972–1991).

MATERIAL AND METHODS

Retrospective identification of patients with a diagnosis of intracranial ependymoma accrued in the 20-year period was carried out from medical records. The following data were collected: patient age at diagnosis, sex, presenting symptoms, duration of symptoms, examination at presentation, radiographic evaluations, location of tumour, extent of surgical resection, pathology, presence of leptomeningeal dissemination, radiotherapy, chemotherapy, evidence of recurrent tumour, and survival. All pathological diagnoses on admission were made almost exclusively by the same pathologist at our pathology department.

Owing to the long time period, diagnostic methods differed with time. Computed tomography (CT) was routinely used after 1985. Survival curves were calculated by

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the Kaplan-Meier method. Groups were compared with respect to time, local failure and survival duration using the log-rank test.

RESULTS

The study group included 35 males and 27 females. The median age at diagnosis was 6 years (range: 1–17 years) and the mean duration of symptoms was 60 days; 43% of the patients were under 5 years of age. The presenting symptoms were headache (69%), nausea and vomiting (74%), and vertigo (32%). The most common neurological signs were papilledema (56%), and ataxia (43.5%). Twenty-two patients had ependymoblastoma and 40 had ependymoma; 4 patients had features of leptomeningeal dissemination. In all of them, the primary tumour was localized infratentorially. Spinal seeding was observed at diagnosis in three out of four patients.

All the patients had surgical excision of their tumours. Total resection was performed in 27 patients, 32 patients had subtotal resection and 3 patients underwent biopsy only. Four patients died of early postoperative complications and meningitis one month following surgery. After surgery, complications developed in 22.5% of patients (n = 14) meningitis being the most frequent of these (n: 11). The other complications were cerebrospinal fluid (CSF) fistula, pneumonia and uncal herniation.

According to tumour site, most of the patients received 30 Gy irradiation to the whole brain or spinal cord after surgery. Booster dose radiotherapy (20–25 Gy) was directed at the primary area. Nine patients did not receive any radiotherapy, 4 because of their younger age, while 5 patients died prior to starting radiotherapy, within one month after surgery.

Forty-seven patients were treated with a combination of vincristine and CCNU with or without procarbazine.

When the records of the 62 patients were analysed, it was found that 23 patients had died, 17 were alive and 22 patients were lost to follow-up; 10 of the 22 patients were lost after relapse, while the remaining 12 were lost when there was no evidence of disease. The overall (OAS) and event-free survival (EFS) of 62 patients with intracranial ependymoma at 5 and 10 years was 50% and 36%, respectively (see Fig. 1). At the time of analysis 23/62 patients had died. In all of these patients, death was related to their ependymoma: 14 of these 23 patients died of progressive disease, 5 of infection, while for the remaining 4 patients, the cause of death was surgical complications. Twenty patients were documented to have recurrent tumour (median 16 months).

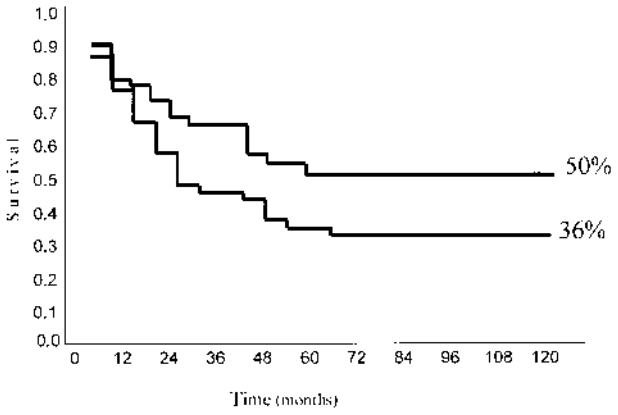

Fig. 1. Overall and event-free survival in ependymomas

Nine out of 20 patients with recurrent tumour died of their disease between 1 and 12 months following recurrence. Only one patient responded to the treatment and was alive while the remaining 10 patients were lost to follow-up. Spinal seeding was observed in 3 patients. All of them were ependymoblastoma and localized infratentorially. In two patients, cranial seeding was observed. One of the patients was localized infratentorially while the other was localized supratentorially.

The influence of both clinical and treatment variables on survival was examined: age, sex, tumour location, histopathologic subtype, extent of surgery, radiotherapy, and chemotherapy. The influence of these variables on both EFS and OAS is summarized in Table 1. There was no survival difference according to sex, histopathological subtype, tumour localization and extent of surgery. There was a statistically significant difference according to age (p: 0.05 for EFS, p: 0.02 for OAS) The outcome for patients above 5 years of age was found to be better. When the impact of different chemotherapy regimens on patient outcome was compared, no statistical difference could be found.

DISCUSSION

Ependymomas are relatively rare intracranial tumours in children, with a particularly poor prognosis. Despite improvements in the treatment of childhood brain tumours, survival rates for children with intracranial ependymoma are generally poor.

In our series, the 5-year event-free and overall survival rates are 36% and 50%, respectively Other series have reported 5-year survival rates of 56%, 46%, 51%, and 44.6% (1–3, 5). Our group demonstrates an outcome similar to that reported in previous studies. An increase in the number of lost patients might have had an influence on our survival rates. The actual survival rates of our patients may be lower than the present results show. These results suggest that the prognosis for children with ependymoma is still poor. In our series, 15 of the tumours occurred in the supratentorial localization and 47 in the infratentorial localization. The predominance of the infratentorial location has also been reported by others (1, 2). For the supratentorial region, there was an insignificantly better prognosis than infratentorial localization, with a 5-year

Table 1

Univariate analysis of influence of clinical and treatment variables on survival

Variable	No of pts	EFS at 10 years	p-value	OAS at 10 years	p-value
Age (yrs)					
≤5	27	21	0.05	33	0.02
>5	35	47		63	
Sex					
Male	35	38	0.77	63	0.28
Female	27	33		38	
Tumour site					
Infratentorial	47	30	0.10	45	0.34
Supratentorial	15	54		60	
Histhopathology					
Ependymoma	40	34	0.89	44	0.19
Ependymoblastoma	22	37		67	
Extent of surgery					
Total resection	27	32	0.76	46	0.91
Subtotal resection	32	34		50	
Chemotherapy					
VCR+CCNU	23	33	0.06	53	0.08
VCR+CCNU+Proc	24	36		55	

Abbreviations: EFS = event-free survival; OAS = overall survival.

event-free survival rate of 54%, compared with 30%. Similarly, authors who reported ependymomas previously had found higher survival rates for supratentorial localization. Recently, Needle et al. reported that the only significant prognostic factor identified in their study was the location of primary tumour (11). In their study, all treatment failures occurred in patients with posterior fossa tumour. However, there are also some reports supporting the opinion that location is not of prognostic importance. Salazar reported that there was no difference in survival time between 31 patients with infratentorial tumours and 20 patients with supratentorial ependymomas (9). Similarly, Perilongo and Goldwein reported that tumour location has no clear prognostic significance (12, 2).

The report of 93 adults and children by Vanutysel and colleagues mentioned that female patients had 5- and 10-year survival of 59% and 49% compared with 39% and 32% survival in men (3). Evans reported that they found a better outcome for female (10). However, our findings did not show a similar female advantage. Contrary to the previous studies, there was a better prognosis for males with 5-year, event-free and overall survival rates of 38%, and 63% compared with 33% and 38% for females in our patients, respectively. This result was probably due to the impact of male predominance in our country; parents attach more importance to boys and they strictly comply with therapy.

In our study the most important prognostic factor for outcome was age of the patient. Patients younger than 5 years fared significantly worse than older children. The 5-year event-free survival rate for children under 5 years was 21% vs. 47% for children aged 5 years or older. Similarly, in most of the series in the literature, age has been considered an important prognostic factor (2, 4, 5). All reported that older age was associated with favourable outcome. However, the definition of older age varied between over 2 and 10 years. We accept above 5 years as the older age group in this analysis.

Although, several authors have advocated the radical removal of ependymomas to decrease the tumour burden prior to radiotherapy and for a better prognosis, we could not verify the importance of complete resection of the primary tumour. In our series, gross total removal was possible in 43.5% of patients. This number is according to the operative reports. Postoperative CT or MRI (magnetic resonance imaging) was not available for most of our patients. Healey pointed out that there were significant discrepancies between the clinical and radiological determinations of the extent of resection (13). This observation might explain our finding. Postoperative imaging should be done routinely to decide the extent of surgery. Several series of patients with ependymomas have revealed seeding in 3–15% of cases. In infratentorial ependymomas, a higher incidence has been reported. The risk of developing spinal metastasis plays an important role in the formulation of radiotherapy protocols. In our series, spinal seeding was observed in 6.4% of patients. Three of these patients had evidence of leptomeningeal dissemination at diagnosis. In only one case, seeding developed at his course of disease. No spinal seeding was observed in the supratentorial location. All of the patients who showed seeding were localized infratentorially. Therefore, prophylactic spinal irradiation can only be considered for infratentorial location. Several authors identified a risk factor for seeding. It is shown that infratentorial high-grade tumours are associated with a higher risk for seeding. On the other hand,

Vanuytsel reported that prophylactic spinal irradiation did not influence the incidence of spinal seeding (14).

In this analysis, we found no correlation with outcome between ependymomas and ependymoblastomas. This finding does not provide sufficient evidence for modifying therapy based on histopathology. Recurrent disease was documented in 20 treated patients. Local recurrence was the major pattern of failure, with 17/20 recurrences occurring in the primary site. A similar pattern of relapse has been noted in other all retrospective series (1–5) Now, it is widely accepted that ependymomas recur predominantly at the site of the primary diseases.

Radiotherapy is generally accepted as part of the standard treatment for ependymomas, but optimal irradiation treatment modalities are not well defined. The use of prophylactic spinal irradiation is controversial. It has not been shown conclusively that craniospinal irradiation decreases the risk of spinal seeding. Craniospinal irradiation is generally the treatment of choice for patients with high-grade lesions and those with positive cerebrospinal fluid cytological findings. Healey et al. reported that they had found no difference in outcome for patients treated with craniospinal, whole-brain or involved-field radiotherapy (13). Despite these controversies, the role of radiotherapy in the treatment of childhood intracranial ependymomas is firmly established.

In contrast to surgery and radiotherapy, the use of adjuvant chemotherapy in the treatment of ependymomas is controversial. Recently, Needle reported that the 5-year, event-free survival estimate of 80% for patients with postoperative residual ependymoma was higher than all previous reports (11). These results suggest that the use of chemotherapy gives an important survival advantage to patients with postoperative residual tumours. The Child's Cancer group reported the results of a randomized trial comparing RT alone with RT plus Lamustine and VCR in children with posterior fossa ependymoma (15). In that study, additional treatment with chemotherapy did not improve the survival rates. Similarly, Goldwein et al. reported that they found no statistically significant benefit from using chemotherapy (2). However, their findings showed a chemotherapy advantage. They found that the event-free survival rate of 47% at five years for the adjuvant chemotherapy group was different from the 41% EFS rate for patients given no chemotherapy.

In our patients, two different chemotherapy regimens were used. Procarbazine did not give any treatment benefit to the patients with ependymoma. Chemotherapy may be useful for high-grade tumours in patients with recurrences. Further studies should be designed to determine the role of adjuvant chemotherapy in ependymomas.

In conclusion, survival rates for children with intracranial ependymomas in this study were similar to published survival results. However, the high percentage of lost patients might have had an impact on the survival results. It is advisable to bear this fact in mind, when reviewing this study. The only statistically significant prognostic factor is the age of the patients. Survival was better for those older than 5 years. Other factors, such as, histopathology, location, sex, extent of resection and use of chemotherapy were not found to be statistically significant. Further investigational studies such as intensive adjuvant chemotherapy are needed to determine the management of these children with ependymomas, since current therapies have not led to clear improvement.

REFERENCES

1. Rousseau P, Habrand JL, Sarrazin D, et al. Treatment of intracranial ependymomas of children: review of a 15-year experience. Int J Radiat Oncol Biol Phys 1994; 28: 381–6.
2. Goldwein JW, Leahy JM, Packer RJ, et al. Intracranial ependymomas in children. Int J Radiat Oncol Biol Phys 1991; 19: 1497–502.
3. Vanuytsel LJ, Bessel EM, Ashley S, Bloom JG, Brada M. Intracranial ependymoma: Long term results of surgery and radiotherapy. Int J Radiat Oncol Biol Phys 1992; 23: 313–9.
4. Lyons KM, Kelly JM. Posterior fossa ependymomas: report of 30 cases and review of the literature. Neurosurg 1991; 28: 659–65.
5. Nazar GB, Hoffman HJ, Becker LE, Jenkin D, Humphreys RP, Hendrick EB. Infratentorial ependymomas in childhood: prognostic factors and treatment. J Neurosurg 1990; 72: 408–17.
6. Goldwein JW, Corn BW, Finlay JL, Packer RJ, Rorke LB, Schut L. Is craniospinal irradiation required to cure children with malignant (anaplastic) intracranial pendymomas? Cancer 1991; 67: 2766–71.
7. Wallner KE, Wara WM, Sheline GE, Davis RL. Intracranial Ependymomas: results of treatment with partial or whole brain irradiation without spinal irradiation. Int J Radiat Oncol Biol Phys 1986; 12: 1937–41.
8. Garrett PG, Simpson WJK. Ependymomas: results of radiation treatment. Int J Radiat Oncol Biol Phys 1983; 9: 1121–4.
9. Salazar OM, Castro-vita H, VanHoutte P, Rubin P, Aygun C. Improved survival in cases of intracranial ependymoma after radiation therapy. J Neurosurg 1983; 59: 652–9.
10. Evans AE, Anderson JR, Lefkowitz-Boudreaux IB, Finlay JL. Adjuvan chemotherapy of childhood posterior fossa ependymoma: cranio–spinal irradiation with or without adjuvant CCNU, vincristine, and prednisone: a Children's Cancer Group study. Med Pediatr Oncol 1996; 27: 8–14.
11. Needle MN, Goldwein JW, Grass J, et al. Adjuvant chemotherapy for the treatment of intracranial ependymoma of childhood. Cancer 1997; 80: 341–7.
12. Perilongo G, Massimino M, Guido S, et al. Analyses of prognostic factors in a retrospective review of 92 children with ependymoma: Italian pediatric neurooncology group. Med Ped Oncol 1997; 29: 79–85.
13. Healey EA, Barnes PD, Kupsky WJ, et al. The prognostic significance of postoperative residual tumor in ependymoma. Neurosurgery 1991; 28: 666–72.
14. Vanuytsel L, Brada M. The role of prophylactic spinal irradiation in localized intracranial ependymoma. Int J Radiat Oncol Biol Phys 1991; 21: 825–30.
15. Lefkowitz I, Evans A, Sposto R, Wilson C, Hammond D. Adjuvant chemotherapy of childhood posterior fossa (PF) ependymoma: craniospinal irradiation with or without CCNU, vincristine (VCR) and prednisone (P). Proc Am Soc Clin Oncol 1989; 8: 87.