Ependymoma in childhood: prognostic factors, extent of surgery, and adjuvant therapy

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Object. The aim of this study was to investigate the effect of patient-related factors, extent of surgery, and adjuvant therapy on survival in children presenting with intracranial ependymoma.

Methods. Between 1980 and 1999, 83 children (mean age 36 months) underwent surgery for intracranial ependymomas. Complete resection, verified on postoperative computerized tomography scans, was achieved in 73%. Adjuvant therapy modalities have changed over the years: before 1990 all patients received radiotherapy, whereas after 1990 the children younger than 3 years of age and later those younger than 5 years of age were treated first with chemotherapy and received radiotherapy only after their first tumor recurrence. The follow-up period averaged 70 ± 49 months.

Conclusions. Overall survival, intraoperative deaths excluded, was 73 ± 11% and 51 ± 14% at 5 and 10 years, respectively. The event-free survival rate at 5 and 10 years was 48 ± 12% and 46 ± 12%, respectively. Most of the events were local recurrences. Despite multiple reinterventions, the overall survival rate in this group dropped to 14%. On univariate analysis, the only significant prognostic factors were complete resection and radiotherapy. Both of these factors combined increased the 5- and 10-year survival rates to 93 and 75%, respectively. Age of the patients was not a statistically independent prognostic factor. The patients in the chemotherapy group did not fare as well as those in the radiotherapy group. A subgroup (36%) within the chemotherapy group, however, survived tumor free after a mean follow-up period of 67 months. It is not clear whether this subgroup either responded well to chemotherapy or needed no adjuvant therapy. Further research is warranted to answer this question.

Key Words • ependymoma • tumor recurrence • resection • radiotherapy • chemotherapy • children
of age, and later those older than 5 years received routine surgical removal of the tumor. Children older than 3 years was administered only in the event of a recurrence, and after chemotherapy as the only adjuvant therapy. Radiotherapy after 1995. Children younger than this age limit received irradiation. In addition, some of the malignant lesions were treated with different regimens of additional chemotherapy.

For example, before 1990 all ependymomas were treated with primary adjuvant therapy, and the chemotherapy regimens included in the radiotherapy group because this was the primary adjuvant therapy and chemotherapy (eight children) were included in the analysis. Patients who received both postoperative radiotherapy. In the event of a recurrent tumor, these children underwent reoperation and were treated with chemotherapy, which was administered according to the BBSFOP. This protocol consists of seven cycles of three chemotherapy courses, alternating two drugs at each course (procarbazine and carboplatin, etoposide and cisplatin, vincristine and cyclophosphamide). Before 1991, patients routinely received spinal irradiation, either combined with whole-brain or posterior fossa irradiation. After 1991, patients received only focal irradiation of the tumor bed, usually between 50 and 55 Gy.

The follow-up period was censored on July 1999, and survival rates were calculated according to the Kaplan–Meier analysis. The event-free survival rate was calculated by taking the occurrence of an event as the end point. Events were defined as either regrowth or recurrence, the recurrence being local or distant. Log-rank and Cox proportional hazards tests were used to evaluate patient characteristics and treatment parameters.

The effect of adjuvant therapy was analyzed by comparing patients treated with the BBSFOP regimen (who did not undergo radiation therapy) with those who had received radiotherapy with or without other chemotherapy regimens. There were several reasons to choose this method of comparison. First of all, the BBSFOP regimen was intended to replace radiotherapy. Furthermore, the BBSFOP regimen was well defined and controlled, and the group treated with this regimen (25 patients) was large enough to allow statistical analysis. Three patients underwent chemotherapy only, but not with the BBSFOP regimen; this group was not included in the analysis. Patients who received both postoperative radiotherapy and chemotherapy (eight children) were included in the radiotherapy group because this was the primary adjuvant therapy, and the chemotherapy regimens were too diverse to allow separate analysis.

### Results

#### Patient Characteristics

The patient characteristics are listed in Table 1. The median age at surgery was 36 months (0–196 months). The majority of the lesions (78%) were infratentorial, most in the fourth ventricle. Of the 18 supratentorial ependymomas, 16 were hemispheric, one was located within the third ventricle, and one was in the pineal region. Of 37 patients in postoperative radiotherapy. In the event of a recurrent tumor, these children underwent reoperation and were treated with chemotherapy, which was administered according to the BBSFOP. This protocol consists of seven cycles of three chemotherapy courses, alternating two drugs at each course (procarbazine and carboplatin, etoposide and cisplatin, vincristine and cyclophosphamide). Before 1991, patients routinely received spinal irradiation, either combined with whole-brain or posterior fossa irradiation. After 1991, patients received only focal irradiation of the tumor bed, usually between 50 and 55 Gy.

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whom adequate pre- or postoperative images of the spine were obtained to determine the absence of metastasis two (5%) had spinal metastases, both from primary infratentorial tumors.

**Presence of Hydrocephalus**

Of the 56 patients (67%) with preoperative hydrocephalus, 22 were treated before tumor surgery: 14 had a ventriculostomy, seven underwent shunt placement, and in one an external drain was inserted. In 12 patients a progressive hydrocephalus developed after tumor removal and they were treated appropriately.

**Extent of Surgery**

A gross-total resection was achieved in 73% of patients and was more frequent with supratentorial tumors (83%) than with infratentorial ones (69%). Among the latter, gross-total resection was more frequent in CPA lesions (80%) than in lesions arising from the floor of the fourth ventricle or the brainstem (66%). In two giant neonatal supratentorial ependymomas only biopsy sampling was performed. Otherwise, the percentage of gross-total resections was even higher in the patients younger than 3 years of age (83%) compared with those older than 3 years of age (70%).

**Perioperative Deaths and Complications**

The perioperative mortality rate was 7.2% (six patients). After 1990 this figure dropped considerably, to 2.5% (one of 40 patients). This drop was probably caused by the increasing experience of surgeons and anesthesiologists, because no specific changes in the procedure were introduced. Air embolus, tumor bleeding, and cardiovascular instability were serious complications in this series. An air embolus occurred once and it was fatal. Serious bleeding was observed in five cases and was responsible for the death of two very young infants and an incomplete tumor removal in the other three patients. Cardiovascular instability developed intraoperatively in eight cases, each time during removal of the tumor attached to the floor of the fourth ventricle. One of these patients died of a sudden cardiac arrest. In the other seven, surgery was interrupted until normalization of the blood pressure and cardiac rhythm was observed. In three of these seven patients, surgery was restarted, in one case after approximately 30 minutes, and the tumor was finally totally removed with no further problem. In the remaining four patients, recurrence of the same problem forced the cessation of surgery before we could achieve complete tumor removal. Two patients died of medical complications within 30 days postsurgery.

**Postoperative and Long-Term Complications**

Postoperative complications developed in 47 patients (Table 2); most of these complications were easily treatable. Surgery was necessary for one frontal extradural hematoma, and three patients with subdural hematomas needed temporary subduralperitoneal drainage. Thirty-three patients suffered from immediate neurological deficits (Table 3); cranial nerve palsies were the most frequent. More than 50% of these deficits resolved with time, and only one of these patients is actually severely disabled. It is worth noting that swallowing difficulties regressed in all patients in whom follow up was longer. Three patients required a tracheotomy, one of which was removed after 9 months; the other two children died within 6 months of surgery. Epilepsy developed in three children with supratentorial ependymomas. Gross-total resections were associated with a higher complication rate than incomplete resections (43% and 25%, respectively).

**School Performance**

Information about school performance was available in 46 patients. In 27 of them an IQ was also known. Of the school-age children, 60% were attending a regular school without a delay, 30% were in a regular school with a delay, and 10% were attending either a special school or institute. The kind of schooling was related to the occurrence of postoperative neurological complications; that is, complications were noted in 30% of the children who attended a regular school without a delay, in 60% of the children with delayed school attendance, and in 75% of the institutionalized children. Interestingly, cranial nerve deficits were not found to influence school performance. The mean IQ was 89 ± 20 (mean ± SD, range 48–131). There was no relationship between IQ and the patient’s age at presentation or any type of adjuvant therapy.

**Adjuvant Treatments**

After the initial surgery, 72 patients received adjuvant therapy; 44 of them (61%) received radiation therapy, with (eight patients) or without (36 patients) additional chemotherapy. Twenty-eight (39%) received chemotherapy only, mostly BBSFOP (90%). Three patients had “sandwich” chemotherapy, and six received other types and combinations of chemotherapeutic agents (Table 4).

Nineteen patients underwent spinal irradiation: in 10 patients this was combined with whole-brain irradiation, and in nine it was combined with posterior fossa irradiation. After 1991, 25 patients received only focal irradiation to the tumor bed, usually between 50 and 55 Gy.

**Follow-Up Duration and Recurrences**

The mean follow-up period was 70 ± 49 months (mean ± SD), and it ranged from 4 to 217 months (median 59 months). At the date of censoring, 48 patients (58%) were alive and 35 (42%) had died; one of these 35 deaths was unrelated to the disease.

Thirty-nine patients (47%) had a first event at a mean of 27 months postoperatively; these events consisted of local
recurrence in 33, local recurrence and metastasis in three, and metastasis only in three. Twenty-eight patients underwent reoperation for local recurrence, 12 more than once, with a maximum of five reoperations in one patient. The average interval between reoperations dropped progressively, from 27 months between the first and second interventions to 12 months between the third and fourth interventions. Of the 39 patients with recurrence, only 11 (28%) survive and only two are free of tumor. One of these patients had a lesion of the brainstem that recurred 44 months after complete resection and radiotherapy. He underwent a second complete resection followed by chemotherapy, and now has reached a follow-up duration of 109 months. The second patient had a lesion of the CPA; this lesion recurred three times, at 5, 8, and 14 months after the first operation, despite gross-total removal at each surgery. Interestingly, the tumor stopped recurring, and the boy is still alive 57 months after his first surgery.

Data about worsening of neurological status were available in 26 of the 28 patients who underwent reoperation. Twenty-three percent suffered neurological worsening after reoperation, compared with 43% after the first intervention. A gross-total resection could be obtained in only 47% of reoperations, however, compared with 73% of first interventions.

Incomplete Resections

An incomplete resection was performed in 18 patients;
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TABLE 5
Univariate and multivariate analysis of patient-related factors*

<table>
<thead>
<tr>
<th>Factor</th>
<th>Median Survival (mos)</th>
<th>95% CI for Exp (B)</th>
<th>5-Yr Survival Rate (%)†</th>
<th>Univariate Analysis; Log-Rank Test (p value)</th>
<th>Multivariate Analysis; Cox Regression Test</th>
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<tr>
<td></td>
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<td>OS EFS</td>
<td>p Value Exp (B) OS EFS 95% CI p Value Exp (B) OS EFS 95% CI</td>
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<td>112–137</td>
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<td>female</td>
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<td>69–117</td>
<td>70 ± 19</td>
<td>45 ± 18</td>
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<td></td>
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<td>≤3</td>
<td>110</td>
<td>78–142</td>
<td>66 ± 17</td>
<td>37 ± 18</td>
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<td>&gt;3</td>
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<td>55–235</td>
<td>80 ± 14</td>
<td>57 ± 16</td>
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<td>supratentorial</td>
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<td>61–229</td>
<td>83 ± 22</td>
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<td>brainstem/4V</td>
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<td>74 ± 14</td>
<td>49 ± 16</td>
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<tr>
<td>CPA</td>
<td>75</td>
<td>22–128</td>
<td>60 ± 28</td>
<td>27 ± 24</td>
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<td>benign</td>
<td>93</td>
<td>53–133</td>
<td>74 ± 22</td>
<td>47 ± 26</td>
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<td>malignant</td>
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<td>gross-total</td>
<td>145</td>
<td>117–173</td>
<td>80 ± 12</td>
<td>53 ± 14</td>
<td>&lt;0.03 4.2† 1.5–11.8 &lt;0.004 4.2† 1.7–10</td>
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<td>incomplete</td>
<td>63</td>
<td>27–99</td>
<td>51 ± 26</td>
<td>33 ± 22</td>
<td>&lt;0.04 0.002 &lt;0.02 2.9 1.2–6.8 &lt;0.0002 4.1 1.9–8.6</td>
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<td>adjuvant treatment</td>
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<td></td>
<td></td>
<td></td>
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<td>RT/chemo</td>
<td>148</td>
<td>119–177</td>
<td>80 ± 12</td>
<td>64 ± 15</td>
<td>&lt;0.04 0.002 &lt;0.02 2.9 1.2–6.8 &lt;0.0002 4.1 1.9–8.6</td>
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<tr>
<td>BBSFOP</td>
<td>69</td>
<td>60–78</td>
<td>69 ± 22</td>
<td>25 ± 20</td>
<td>&lt;0.04 0.002 &lt;0.02 2.9 1.2–6.8 &lt;0.0002 4.1 1.9–8.6</td>
</tr>
</tbody>
</table>

* CI = confidence interval; EFS = event-free survival; Exp (B) = exponent (B), hazard ratio; NC = not calculated; NS = not significant; OS = overall survival; RT/chemo = radiotherapy with or without chemotherapy; 4V = fourth ventricle.
† Survival rate calculated according to the Kaplan–Meier method; mean ± 2 SDs.
‡ Hazard ratio for location in CPA compared with supratentorial and brainstem/4V location.

eight (44%) are alive, with a mean follow-up time of 63 months (range 33–129 months). Of these eight patients, three have progressive disease and five have stable disease. They all received adjuvant treatment; in the group with progressive disease, two patients received radiotherapy and one had BBSFOP. In the group with stable disease, three received radiotherapy and two had BBSFOP. In the five patients with stable disease the follow-up duration is 42, 98, 98, 121, and 129 months, respectively.

**Statistical Analysis**

Overall survival, including perioperative deaths, was 68 ± 11% at 5 years and 47 ± 13% at 10 years (Fig. 1 upper left). Overall survival without perioperative deaths was 73 ± 11% after 5 years and 51 ± 14% after 10 years (Fig. 1 upper right). The event-free survival rate was 48 ± 12% after 5 years and 46 ± 12% after 10 years (Fig. 1 lower left). All recurrences but three (92%) occurred in the first 5 years after surgery (one patient presented with a recurrence after 18 years). Recurrences had a particularly bad prognosis: after their treatment, the survival rate dropped to 14% at 5 years.

No patient-related factors were identified as significant on univariate or multivariate analysis (Table 5), except tumor location in the CPA compared with all other locations. Children older than 3 years of age had better overall and event-free survival rates than those younger than this age, but the difference was not statistically significant. On the other hand, treatment-related factors, which included resection as well as adjuvant treatment, were significant on both univariate and multivariate analysis (Table 5; Figs. 2 and 3). Age was included in the multivariate analysis, although it was not significant on univariate analysis to adjust for the effect of age when analyzing adjuvant treatment. Infratentorial location of tumor was associated with a slightly worse prognosis (5-year survival rate 71 ± 12%) than supratentorial location (83 ± 22%), but this difference was not significant. The histological grade of the tumor was not related to outcome.

The extent of surgery was highly significant. The overall survival and especially the event-free survival rate improved significantly after gross-total compared with incomplete resections (Fig. 2).

The patients treated with radiotherapy also had a significantly better outcome than those treated with the BBSFOP regimen (Fig. 3). At 5 years, the event-free survival rate for the chemotherapy group was only 33%, compared with more than 60% in the radiotherapy group. Although the latter group fared worse, one third of these patients were alive without tumor after a mean follow-up duration of 67 months. We could identify no patient characteristics that differentiated this subgroup from the whole group. After adjustment for the extent of resection, radiotherapy remained significantly better than BBSFOP in terms of outcome (Table 6).

When spinal irradiation was compared with local irradiation, three metastases without local recurrence were noted after local irradiation, but none after spinal irradiation. The overall survival rate after 5 years was 90 ± 20% after spinal irradiation and 70 ± 20% after local irradiation. This difference is not statistically significant. The event-free survival
rate was 74 ± 20% after spinal irradiation compared with 54 ± 20% after local irradiation. This difference was statistically significant, with a probability value of 0.03.

Discussion

Although some progress has been made in the last decade, the prognosis for patients with ependymomas remains rather poor. Survival rates for childhood intracranial ependymoma reported in the literature vary from 30 to 60% at 5 years.4,8,25,28,35 In series containing infratentorial lesions in children only,4 the survival rates tend to be lower, whereas in series including adult and spinal ependymoma,28,39 much better survival rates are reported. In our patient population, the 5-year survival rate of 68% with and 73% without the perioperative deaths included compares favorably. This population includes patients with infratentorial as well as supratentorial lesions, but the survival rates in both groups were not significantly different.

In this population the younger children had a slightly worse outcome, but the difference was not significant. Younger age has been shown to be a negative prognostic factor in only half of the reported series (Table 7).11,18,21,23,25,28,33,34,35–37 This lack of conformity might, in part, be caused by the considerable variation in cut-off age between studies.

It is often assumed that the absence of radiotherapy in the younger group causes the difference in outcome, but other factors might also be important. Nazar, et al.,25 and Perilongo, et al.,28 report an association of younger age with malignant lesions, infratentorial location, and subtotally resected lesions. On the other hand, Lyons and Kelly23 and Pollack, et al.,29 found that younger age was a negative prognostic factor regardless of histological findings, extent of resection, and radiotherapy. In our study anaplasia was not predominant in the younger children, and the percentage of gross-total removal was even higher in this age group than in the older children.

In the recent literature most authors, as in our study, have found no correlation between prognosis and histological grade of the tumor.s.7,13,14,23,25–28,34,36,37,41 This may be explained by the use of many different grading systems and the difficulty in differentiating between benign and malignant lesions, but also by histological variability within the tumor. Better-defined histological criteria as well as wider use of mitotic index markers2,8,30,31 and identification of genetic subtypes17,42 are probably necessary to identify a prognostically valuable differentiation between tumors. This would also be very helpful in selecting patients who will benefit from adjuvant therapy.

A gross-total resection seems to be the most important prognostic factor in the treatment of ependymomas.6,8,18,19,25,28,29,34,40 A complete resection was obtained in 73% of our patients. Once the perioperative deaths were excluded, the 5-year overall survival rate was 80 ± 12% after a gross-total resection, compared with 51 ± 26% after an incomplete one. Also, the event-free survival rate was better after a gross-total resection (53 ± 14%) than after an incomplete one (33 ± 22%). This means that a complete resection lowers the risk of recurrences. Considering the dismal prognosis after a recurrence, a complete resection seems to provide the best chance for survival. The concept of second-look surgery is, therefore, completely justifiable.19

In this group of patients, only two underwent a two-stage procedure. In one patient a subtotal resection was enlarged to a gross-total resection, and in the other the initial subto-

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**TABLE 6**

*Extent of resection and use of adjuvant treatment*

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Gross-Total Removal</th>
<th>Incomplete Removal</th>
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<tbody>
<tr>
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<td>No. of Patients</td>
<td>Survival Rate (%)</td>
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<td>radiotherapy</td>
<td>32</td>
<td>93 ± 9</td>
</tr>
<tr>
<td>5-yr overall survival</td>
<td>75 ± 16</td>
<td>33 ± 27</td>
</tr>
<tr>
<td>5-yr event-free survival</td>
<td>63 ± 24</td>
<td>100 ± 70</td>
</tr>
<tr>
<td>BBSFOP</td>
<td>21</td>
<td>21 ± 19</td>
</tr>
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**FIG. 2.** Graphs showing survival curves. *Left:* Overall survival rate after gross-total removal (solid line) is compared with subtotal removal (dotted line). *Right:* Event-free survival rate.
nal resection was enlarged, but not to the extent of a gross-total resection. The most important arguments for reoperation were the resectability of the tumor rest as estimated by the surgeon and the patient’s good clinical condition after the first surgery. The degree of difficulty of second interventions depended on where the rest or regrowth was located and whether it was easily identifiable as tumorous tissue. Both aspects are usually more complicated in second interventions, for a rest as well as for a recurrence. The Société Internationale d’Oncologie Pédiatrique protocol for ependymoma gives the surgeon the interesting option to retry a complete resection of residual tumor that remains after postoperative chemotherapy.

In our series, tumor location in the CPA was identified as a negative prognostic factor, although the percentage of gross-total removals for these lesions was similar or even better than for those in other locations. Ikezaki, et al., found a significantly reduced survival rate for patients with lesions located in the CPA compared with fourth ventricle and brainstem lesions, but they supposed that these bad results were associated with residual tumor.

The complication rate and neurological status in patients at the last follow-up review receive little or no attention in most studies. Complications are hardly inevitable, even in a difficult to treat tumor such as ependymoma. More than half of our patients suffered from complications, but the majority of these resolved. Persistent complications were associated with worse school performance. Are these results good enough to continue to pursue complete resection? In our study, gross-total resections were associated with a higher complication rate than incomplete ones. The patient pays a price for a gross-total resection that provides a better chance of survival. It is difficult to say whether this increased chance of survival is in proportion to the complications that arise and the resulting quality of life. Further quality-of-life assessments are required, especially in long-term survivors, to get a clear insight into the effects of our treatment.

The indications for adjuvant treatment are not clear, and protocols vary from institution to institution. Although it has never been tested in randomized studies, radiotherapy seems to be effective. It is not clear from the literature, however, if radiotherapy is indicated after a complete resection. In our series, patients received radiotherapy regardless of the completeness of the resection, except after 1990, when children younger than 3 years of age began to receive chemotherapy instead of radiotherapy. Radiotherapy significantly improved survival rates compared with chemotherapy, even after correction for patient age. Radiotherapy administered after a complete resection improved the 5- and 10-year survival rates to 93 and 75%, respectively (Table 6). After several studies in which it was suggested that local radiotherapy would provide similar survival rates compared with spinal radiotherapy, the protocol was changed to local radiotherapy only. In this study the chance of a distant recurrence developing was slightly higher after local radiotherapy. On statistical analysis, only the event-free survival rate was significantly better after spinal radiotherapy; the overall survival rate was not. Therefore, there might be a small advantage of spinal over local radiotherapy; however, in children this must be judged against

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<th>Authors &amp; Year</th>
<th>Patient Sex</th>
<th>Tumor Grade</th>
<th>Location†</th>
<th>Patient Age (p value)</th>
<th>Cut-Off Age (yrs)</th>
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<td>Ross &amp; Rubinstein, 1989</td>
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<td>Ikezaki, et al., 1993</td>
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<td>&lt;0.01‡</td>
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<td>Rousseau, et al., 1994</td>
<td>NS</td>
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<td>3</td>
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<td>Pollack, et al., 1995</td>
<td>—</td>
<td>NS</td>
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<td>&lt;0.003</td>
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<td>Foreman, et al., 1996</td>
<td>NS</td>
<td>NS</td>
<td>—</td>
<td>&lt;0.04</td>
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<td>Perilongo, et al., 1997</td>
<td>NS</td>
<td>NS</td>
<td>S</td>
<td>5</td>
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* NS = not significant; S = significant, p value not given; — = not tested or not given.
† Supratentorial compared with posterior fossa location.
‡ CPA compared with 4V and brainstem.
the major side effects. Based on these results we would not suggest the reintroduction of spinal radiotherapy for ependymoma. It is probably much more important and effective to identify patients who are really at risk of experiencing a recurrence, for example by genetic subtyping of the tumor.

The patients in the chemotherapy group did not fare as well as those in the radiotherapy group. The event-free survival rate was significantly worse after chemotherapy than after radiotherapy, indicating that the BBSFOP protocol had little effect on the prevention of recurrences. The fact that at 2 and 5 years postsurgery, 46 and 25% of patients, respectively, had no recurrence and therefore did not receive radiation therapy may simply represent the effect of surgery or favorable histological findings. It is not possible to ascertain the efficacy of the chemotherapy from our data. Similarly, the subgroup of patients (36%) within the chemotherapy group who survived tumor free after a mean follow-up period of 67 months could either represent good responders to chemotherapy or a group that might not need any adjuvant therapy. We could not identify preoperative patient characteristics that might differentiate this subgroup from the whole group. It is worth noting that the overall survival rate is significantly better for the radiotherapy than for the chemotherapy group. To our minds, this means that radiotherapy given at the time of recurrence is less effective than at the time of primary treatment. For all these reasons, the efficacy of chemotherapy as a replacement for radiotherapy, but also as an adjuvant treatment for residual tumor, must be tested, preferably in randomized studies. This could be done in the group of patients younger than 5 years of age; in these patients radiotherapy is contraindicated. Not only would such a randomized study allow investigators to evaluate the effect of chemotherapy, but at the same time they could identify patients who need no adjuvant therapy.

The management of recurrences has not received much attention in the literature. It is an important aspect of ependymoma, because at least half the patients will eventually experience a recurrence. Prevention is obviously the best option. Because the majority of recurrences are local, initial treatment must be focused on maximum local control. Once there is a recurrence the prognosis worsens dramatically. Based on the present data we suggest that a second intervention can have a slight chance of generating long-term survival, but only if a complete resection can be achieved. Second interventions are also effective in early recurrences (< 1 year), probably because they treat overlooked residuals and in fact serve as second-look surgery. In this study second interventions were less likely to achieve gross-total resection than first interventions; however, the complication rate was also considerably lower. This shows that second interventions are not necessarily more difficult but that the surgeon prefers to incur less risk to achieve a gross-total resection in these cases. Incomplete second resections and three or more interventions can prolong survival time, but only to a limited extent.

Almost all recurrences occur within 5 years after the initial surgery. The event-free survival rate after 5 years is 48% and drops only to 46% after 10 years. Surprisingly, this is true for all patient categories and treatment groups. The risk of recurrence or progression becomes quite small once the first 5 years after the initial surgery have passed uneventfully, regardless of whether initial surgery was complete or incomplete or whether the patient received radiotherapy or BBSFOP. This accounts for the incidental survival of more than 10 years, even after an incomplete resection treated adjuvantly with either radiotherapy or BBSFOP. The interpretation of this finding is not easy. It might indicate the existence of an as yet unidentified histological subgroup of tumors with a more indolent character.

Conclusions

The aim of treating ependymomas should be to achieve maximum local control. A gross-total removal is essential in preventing recurrences and thus providing a chance for cure. Radiotherapy is effective: complete removal followed by focal irradiation at a minimum dose of 45 Gy appears to be the best combination to prevent recurrences. Radiotherapy is contraindicated, however, in children younger than 5 years of age. In these children, the choice after surgery is between chemotherapy and no adjuvant treatment. The efficacy of chemotherapy remains to be proven, and in a few patients, chemotherapy and perhaps even radiotherapy might not be necessary. Further research should be directed at identifying patients who might need no adjuvant treatment. This could be done in a multicenter, randomized study, comparing chemotherapy with no adjuvant treatment in patients younger than 5 years of age.

References

Treatment of childhood ependymoma


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