The results of the treatment of childhood medulloblastoma with radiotherapy at Kaunas University of Medicine Hospital in 1994–2000

Giedrė Rutkauskienė, Liutauras Labanauskas, Laimonas Jaruševičius
Department of Children’s Diseases, 1Department of Oncology, Kaunas University of Medicine, Lithuania

Key word: brain tumors, medulloblastoma, childhood, radiotherapy, survival.

Summary. Medulloblastoma, a primitive neuroectodermal tumor growing in cerebellum, is one of the most sensitive to radiation therapy childhood brain tumors, therefore, this method of treatments is justly considered to be the standard for the treatment of medulloblastoma. The outcome of this malignant brain tumor differs in standard and high-risk groups of patients.

The aim of the work was to evaluate the survival rate for children with medulloblastoma according to two risk groups.

Patients and methods. Eighteen patients aged from 3 to 18 years with histological proven medulloblastoma treated with standard craniospinal and additional posterior fossa radiotherapy were investigated in our study. Nine patients with disseminated and partial removed medulloblastoma were assigned to the high-risk group and other 9 patients with local and totally removed medulloblastoma were allocated to the standard risk group.

Results. Radiological response of medulloblastoma to the radiation therapy was observed in 15 (83.3%) out of 18 patients: complete radiological response was observed in 6 (67%) out of 9 standard-risk patients and in only 1 (11.1%) out of 9 high-risk patients (p<0.05). Medulloblastoma progressed in 15 (83.3%) patients treated with radiation therapy: relapse rate in the high-risk group was 100% and in the standard-risk group – 66.7% (p>0.05). The mean time to progression for all patients was 18.2 months: 28.9 months in standard and 7.4 months in high-risk group (p=0.02). The overall survival for all investigated patients was 25.8 months: 37.2 and 14.3 months in the standard and high-risk groups, respectively (p=0.01). Five years progression-free and overall survival rate for all patients was 16.7%: 0% in the high-risk group and 33.3% in the standard-risk group (p>0.05).

Conclusion. In our study the difference in survival rate between standard and high-risk patients with medulloblastoma was shown. We observed a statistically significant longer time to progression and better overall survival in the standard-risk group. However, we did not find any significant differences in other survival indices (response, relapse rates, mortality, five years progression-free and overall survival) between those two risk groups.

Introduction

Medulloblastoma is a primitive neuroectodermal tumor growing in cerebellum. It is one of the most malignant and frequently metastasized tumors of central nervous system (CNS). The arising tumor overgrows neighboring brain structures: peduncles of the cerebellum, the fourth ventricle of the brain, brain stem, cervical part of spinal cord; malignant cells can spread by spinal fluid channels into involucres of the spinal cord and brain. Furthermore, medulloblastoma tends to spread hematogenously into bones, bone marrow, lymphatic nodes, liver, and lungs (1).

The prognosis of the children with medulloblastoma is poor. The outcome of the disease is influenced by the spread of the tumor (stage M by Chang’s classification), the age of the patient and extent of resection assessed by the size of the residual post-operative tumor (2–5). According to these criteria the patients with medulloblastoma are divided into two groups: standard and high-risk groups (6). The patients assigned to the standard risk group are older than 3 years old, without metastases of medulloblastoma; the size of residual post-operative tumor is less than 1.5 cm². The patients who are assigned to high-risk group have at least one of the following indicators determined: age is less than 3 years old, spread medulloblastoma,
the size of residual post-operative tumor is more than 1.5 cm\(^2\).

Medulloblastoma is one of the most sensitive to radiation therapy childhood brain tumors, therefore, this method of treatments is justly considered to be the standard for the treatment of medulloblastoma. Modern radiation therapy consists of two stages: 30–36 Gy to craniospinal axis and additional 54–56 Gy irradiation to the posterior fossa of the skull (site of the tumor). E. Paterson and R. F. Farr proposed such treatment protocol in 1953, and their study showed a 5-year survival rate of 41% for the patients treated according to this radiotherapy protocol (7). Since that time craniospinal and additional irradiation to posterior fossa with the dose mentioned above is the conventional treatment of medulloblastoma. It is very important to follow this recommended protocol and doses of irradiation in the treatment of this malignant disease because of high probability of relapse in less irradiated area.

The aim of this study was to evaluate the survival rates for children with medulloblastoma according to risk groups and to establish the influence of prognostic criteria on the outcome of disease.

**Patients and methods**

A total of 18 patients with newly diagnosed medulloblastoma were examined, operated on and treated by radiotherapy at Kaunas University of Medicine Hospital in 1994–2000.

The study inclusion criteria were as follows: patient’s age from 3 to 18 years, histological proven medulloblastoma, and used treatment – standard craniospinal and additional posterior fossa radiotherapy. Children with medulloblastoma less than 3 years of age were not selected considering impossibility of using radiotherapy in so young age because of severe complications.

The diagnosis of medulloblastoma for all patients was made by computed tomography (CT), according to the typical localization of the tumor in the posterior fossa of the skull and was confirmed after the operation by histological analysis.

Patients were operated on 1–3 days after diagnosis of the posterior fossa tumor. The extent of the operation was determined by the entries in the records of the operation as well as the findings of the post-operative computed tomography, during which the size of the residual tumor is determined. The size of 1.5 cm\(^2\) of the residual post-operative tumor was important for the outcome of disease.

Medulloblastoma classification established by C. H. Chang in 1969 is used for the evaluation of the spread of tumor worldwide (8). According to this classification the size of the tumor, its spread into neighboring brain structures (stage T), the spinal fluid channels and hematogenous metastases (stage M) are evaluated (Table 1).

In our study the spread of medulloblastoma was assessed by the help of preoperative computed tomography and/or magnetic resonance imaging, magnetic resonance of the spine, bone scintigraphy, examination of the abdominal organs with ultrasound as well as the x-ray pictures of thorax, and was defined by stages M of Chang’s classification.

The children with medulloblastoma were divided into two groups, standard and high-risk, according to the extent of the operation and spread of medulloblastoma, assessed by stages M according to Chang. The patients without metastases of medulloblastoma and with the size of residual post-operative tumor less than 1.5 cm\(^2\) were assigned to the standard risk group. The patients with at least one of the following indicators – spread of medulloblastoma and size of residual post-operative tumor more than 1.5 cm\(^2\) – were assigned to high-risk group. According to dissemination of disease and extent of tumor resection, 9 patients were assigned to the high-risk and the other 9 to the standard-risk group.

The standard radiation therapy for medulloblastoma was initiated 7–14 (mean 12.4) days after the operation. The standard protocol for medulloblastoma treatment consisting of two stages, craniospinal and additional irradiation to the posterior fossa of the skull (site of the tumor) was applied. A dose of 56–60 Gy was given for the local radiotherapy to the site of the tumor, and a dose of 30 Gy for the craniospinal irradiation. The standard dose fractionation was chosen; an irradiation dose of 1.8–2 Gy once a day and five times per week was given. The duration of radiotherapy was 6 weeks.

Radiological response of the tumor to radiotherapy was evaluated after one month of radiotherapy. For this purpose we repeated the computed tomography of the brain and the magnetic resonance imaging of the spinal cord (particularly if disseminated medulloblastoma had been diagnosed), and the received data were compared to the radiological investigations made before the treatment. According to the results of the investigations, the treatment effect was evaluated as complete response (if the absolute disappearance of the tumor was noticed), partial response (if the diameter of the tumor decreased more than 50% of the size of the primary tumor), stable disease (the tumor
decreased less than 50%) or the progression of the tumor. Patients were regularly observed because of the progression or relapse of medulloblastoma by repeating the computed tomography of the brain and magnetic resonance imaging of the spinal cord every three months during the first 2 years after the treatment and every 6 months during the 3rd–5th year after the treatment. The growth of the tumor mass or the appearance of new tumor formations was considered to be the progression of the disease.

For the assessment of treatment results we used the following indicators: radiological response to the treatment, frequency of relapse and mortality, time to progression (i.e. the period from the diagnosis to the progression of the tumor), overall survival (the period from the diagnosis to death), 5-year progression-free survival and 5-year overall survival (i.e. the percentage of the patients who survived five years without relapse or those who remained alive within five years). We regarded the time to progression and 5-year progression-free survival as the cardinal criteria of assessment.

Wishing to determine the influence of various indicators on the patients’ survival while administering the standard radiation therapy of medulloblastoma we applied Kaplan–Meier method for survival analysis. The log-rank test was applied for the comparison of the survival functions. The survival indices are represented as mean±standard deviation (SD). The independent samples t-test was used to compare mean survival rates between standard and high-risk patients’ groups. The differences were statistically significant if confidence level p was less than 0.05.

**Results**

A total of 18 patients aged from 3 to 15 years (mean age at diagnosis was 7.2 years) were enrolled in this study. Sixteen of them (88.9%) were boys and 2 (11.1%) girls. The characteristics of patients are shown in Table 2.

The first symptoms of the disease typical to all the patients were: increased intracranial pressure (headache, nausea in the morning, vomiting, consciousness disorders); some patients were suffering from the disorder of balance and coordination – cerebellar ataxia and strabismus, diplopia (Table 3).

The diagnosis was made within 6–60 days of the onset of symptoms (the average was 31.5 days).

<table>
<thead>
<tr>
<th>Stage</th>
<th>Definition</th>
</tr>
</thead>
<tbody>
<tr>
<td>T1</td>
<td>Tumor &lt;3 cm in diameter and limited to the midline position in the vermis, roof of the fourth ventricle and less frequently in the hemispheres of cerebella</td>
</tr>
<tr>
<td>T2</td>
<td>Tumor ≥3 cm in diameter, further invading adjacent structure or partially filling the fourth ventricle</td>
</tr>
<tr>
<td>T3a</td>
<td>Tumor invading two adjacent structures or completely filling the fourth ventricle with extension into the aqueduct of Sylvius, foramen of Magendie, or foramen of Luschka, thus producing marked internal hydrocephalus</td>
</tr>
<tr>
<td>T3b</td>
<td>Tumor arising from floor of the fourth ventricle of brain stem and filling the fourth ventricle (may be demonstrated intraoperatively)</td>
</tr>
<tr>
<td>T4</td>
<td>Tumor spreading further through the aqueduct of Sylvius to involve the third ventricle or midbrain, or tumor extending to the upper cervical cord.</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Metastasis</th>
<th>Definition</th>
</tr>
</thead>
<tbody>
<tr>
<td>M0</td>
<td>No evidence of subarachnoid or hematogenous metastasis</td>
</tr>
<tr>
<td>M1</td>
<td>Microscopic tumor cells found in cerebrospinal fluid</td>
</tr>
<tr>
<td>M2</td>
<td>Gross nodular seeding demonstrated in cerebellar, cerebral subarachnoid space, or in the third or lateral ventricles</td>
</tr>
<tr>
<td>M3</td>
<td>Gross nodular seeding in the spinal subarachnoid space</td>
</tr>
<tr>
<td>M4</td>
<td>Extra neural metastasis</td>
</tr>
</tbody>
</table>
The diameter of medulloblastoma determined by preoperative computer tomography ranged between 2 and 5 cm (mean 3.9±0.9 cm). Vermis of the cerebella was the most common place of the localization of the tumor; the tumor was found there in 14 (77.8%) of 18 patients. Medulloblastoma had already outgrown the fourth ventricle and brain stem in 3 patients (16.7%), and 1 (5.7%) had it in the right hemisphere of the cerebellum.

Eight children (44.4%) had metastases of medulloblastoma in the spinal cord. No supratentorial metastases in the brain or evidence of systemic spread of the disease were found in the patients.

Eleven (61.1%) patients had a radical operation, 1 child had a biopsy performed, and the remaining 6 patients had non-radical (less than 90% of tumor mass was removed) or partial (more than 50% of tumor mass removed) operation. The size of the residual tumor on the post-operative CT scan ranged from 0 to 4 cm² (mean 1.2 cm²). The residual tumor size more than 1.5 cm² was observed in 6 (33.3%) patients.

Fourteen (73.7%) patients received the entire planned treatment of 30 Gy craniospinal and the irradiation to the site of the tumor with the radiotherapy dose of 56–60 Gy. However, 4 patients received doses of radiation therapy reduced because of the significant complications of radiotherapy. The doses of craniospinal radiation therapy varied from 20 to 30 Gy, with a mean dose of 25 Gy; additional irradiation to the posterior fossa of the skull varied from 45 to 60 Gy (mean 55.7 Gy). The doses of radiotherapy for the high-risk patients were slightly smaller; this difference was not statistically significant (p>0.05) (Table 2).

Having evaluated the characteristics of standard and high-risk groups of patients, we observed that both groups did not differ in age and sex, the duration of symptoms, size of the tumor and dose of irradiation. However, we found statistically significant difference in spread of tumor, rate of radical operation and size of residual tumor between standard and high-risk groups of patients (Table 2).

Response to the radiation therapy was observed in 15 (83.3%) out of 18 patients with medulloblastoma (Table 4).

Despite good initial response to radiotherapy, medulloblastoma progressed in 15 (83.3%) of 18 patients treated with radiation therapy. The time to progression varied from 2 to 60 months (mean 18.2) in both groups of patients. Ten (55.6%) of 18 patients with medulloblastoma relapsed during first year after diagnosis. The median time to progression (i.e. the period during which the patient remained disease-free) was 12 months.

Table 2. The comparison of patients’ characteristics between standard and high-risk groups (mean±SD)

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>All patients (n=18)</th>
<th>Standard-risk group (n=9)</th>
<th>High-risk group (n=9)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, months</td>
<td>87.6±12</td>
<td>96.6±13.3</td>
<td>78.6±6.3</td>
<td>&gt;0.05</td>
</tr>
<tr>
<td>Sex, male/female ratio</td>
<td>16/2</td>
<td>9/0</td>
<td>7/2</td>
<td>&gt;0.05</td>
</tr>
<tr>
<td>Duration of symptoms, days</td>
<td>31.5±4</td>
<td>36.2±3</td>
<td>26.7±8</td>
<td>&gt;0.05</td>
</tr>
<tr>
<td>Diameter of primal tumor, cm</td>
<td>3.9±0.9</td>
<td>3.8±0.2</td>
<td>4.1±0.3</td>
<td>&gt;0.05</td>
</tr>
<tr>
<td>Disseminated disease (M1–M4 stage), %</td>
<td>44.4</td>
<td>0</td>
<td>88.9</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Radical resection, %</td>
<td>61.1</td>
<td>88.9</td>
<td>33.3</td>
<td>&lt;0.02</td>
</tr>
<tr>
<td>Residual tumor, cm²</td>
<td>1±0.1</td>
<td>0.2±0.06</td>
<td>1.4±0.2</td>
<td>&lt;0.03</td>
</tr>
<tr>
<td>Irradiation dose to posterior fossa, Gy</td>
<td>55.7±1.2</td>
<td>56.4±1</td>
<td>55±1.5</td>
<td>&gt;0.05</td>
</tr>
<tr>
<td>Craniospinal irradiation, Gy</td>
<td>25±2</td>
<td>26.4±3.3</td>
<td>23.5±3.3</td>
<td>&gt;0.05</td>
</tr>
</tbody>
</table>

Table 3. The symptoms of medulloblastoma

<table>
<thead>
<tr>
<th>Symptoms</th>
<th>Number of patients</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Increased intracranial pressure</td>
<td>18</td>
<td>100</td>
</tr>
<tr>
<td>Cerebellar ataxia</td>
<td>6</td>
<td>33.3</td>
</tr>
<tr>
<td>Pathological eyes movement</td>
<td>2</td>
<td>11.1</td>
</tr>
</tbody>
</table>

Table 4. Different radiological response among patients with medulloblastoma

<table>
<thead>
<tr>
<th>Radiological response</th>
<th>Number of patients</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Full response</td>
<td>8</td>
<td>53.3</td>
</tr>
<tr>
<td>Partial response</td>
<td>4</td>
<td>26.7</td>
</tr>
<tr>
<td>Stable disease</td>
<td>3</td>
<td>20</td>
</tr>
<tr>
<td>Total</td>
<td>15</td>
<td>100</td>
</tr>
</tbody>
</table>

Medicina (Kaunas) 2006; 42(1)
which a half of patients relapsed) was 9 months. All relapses were diagnosed during the first two years. After that period no relapses occurred. Five years progression-free survival was 16.7%. The progression-free survival for patients treated with radiotherapy is represented by Kaplan–Meier curve in Fig. 1.

The dissemination of medulloblastoma in the central nervous system was observed in 7 (46.7%) of 15 patients at the time of relapse. Local relapse was diagnosed for 6 (40%) patients and 2 (13.3%) systemic metastases in the long bones were observed.

Three (6.7%) of 18 patients survived and are free of disease for five years; all of them were from the standard-risk patients’ group. The mortality rate of medulloblastoma patients treated with radiotherapy alone was 83.3%.

The overall survival for patients varied from 6 to 60 months (mean 25.8 months). The median overall survival was 18 months. More than a quarter (27.8%) of patients died during first year, all other patients died during the period of three years after diagnosis. The five years overall survival was 16.7%. The Kaplan–Meier curve in Fig. 2 represents the overall survival for all patients with medulloblastoma.

**Fig. 1.** The time to progression of all patients with medulloblastoma treated by radiotherapy

**Fig. 2.** The overall survival of all patients with medulloblastoma treated by radiotherapy
Evaluating all survival indices mentioned before separately for the patients of the two risk groups, we noticed that the radiological response of the standard-risk patients’ group was more frequent, but the difference was not statistically significant. Complete radiological response was observed in 6 (67%) of 9 standard-risk patients and only in 2 (22.2%) of 9 high-risk patients (p<0.05) (Table 5). The higher incidence of relapse was observed in the high-risk group, though this difference was not statistically significant. The mean time to progression between these two groups differs statistically significantly (28.9 months and 7.4 months, respectively). The 5-year progression-free and overall survival rates were lower for the high-risk patients than the standard-risk patients.

Differences in the majority of survival indices (radiological response, relapse rate, mortality, 5-year progression-free and 5-year overall survival) are not statistically significant, most likely because of the small number of patients (Table 5).

The Kaplan–Meier curves in Fig. 3 and 4 represent the progression-free and overall survival for the standard-risk and high-risk patients.

Wishing to assess how various factors influence the survival of patients with medulloblastoma we divided patients into groups according to age, the size of tumor in the posterior fossa of the skull, the dissemination of medulloblastoma in the central nervous system (stages according to Chang; local (stage M0) or disseminated (stage M1-M4) tumor), the extent of the operation (radical or non-radical operation), the size of the residual tumor (larger or smaller than 1.5 cm²). The time to progression and the progression-free survival were chosen as the cardinal criteria of

Table 5. The comparison of treatment results of patients with medulloblastoma according to the groups (mean±SD)

<table>
<thead>
<tr>
<th>Survival index</th>
<th>Standard-risk group (n=9)</th>
<th>High-risk group (n=9)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Response to treatment, %</td>
<td>78</td>
<td>22</td>
<td>&gt;0.05</td>
</tr>
<tr>
<td>Complete response, %</td>
<td>67</td>
<td>22</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>Relapse, %</td>
<td>66.7</td>
<td>100</td>
<td>&gt;0.05</td>
</tr>
<tr>
<td>Mortality, %</td>
<td>66.7</td>
<td>100</td>
<td>&gt;0.05</td>
</tr>
<tr>
<td>Time to progression, months</td>
<td>28.9±8</td>
<td>7.4±1.7</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>Overall survival, months</td>
<td>37.2±6.5</td>
<td>14.3±2.5</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>5-year progression-free survival and 5-year overall survival, %</td>
<td>33.3</td>
<td>0</td>
<td>&gt;0.05</td>
</tr>
</tbody>
</table>

Fig. 3. The time to progression in patients of two risk groups

Medicina (Kaunas) 2006; 42(1)
To determine the influence of various criteria on the patients’ survival we used the methods of survival analysis.

The patient’s age was not a statistically significant criterion, which determined the outcomes of medulloblastoma. The size of the primary and residual tumor also did not have any influence on survival rates (data not shown).

The mean time to progression for the patients with non-disseminated medulloblastoma (Chang’s stage M0) was 27±7 months and the overall survival 36±6 months, whereas the same indices for patients who had disseminated disease were 8±2 and 13±2 months, respectively. The progression-free and overall survival for the patients with local and disseminated medulloblastoma are shown in Fig. 5 and 6.

**Discussion**

The CNS tumors are the second most frequent of childhood malignancy after leukemia and leading...
cause of death from the tumors at this age (1). Every year 2.5 to 4 new cases of CNS tumors per 100 000 children are diagnosed worldwide. Around 18–20% of these cases are medulloblastoma, one of the most frequent malignant childhood CNS tumors (1). In Lithuania the annual incidence of medulloblastoma among children (according to the data of Lithuanian Registry of Cancer) is 0.45 cases per 100 000 children and does not differ from morbidity in other European countries or USA (0.2–0.7 new diagnosed cases per 100 000 children per year (9–12)). Only the treatment results of 18 patients who had medulloblastoma diagnosed in 1994–2000 were assessed during our study. Such small number of cases is due to the rarity of the disease.

According to research data medulloblastoma is usually diagnosed in the first ten years of age (13). Among patients with medulloblastoma a male to female ratio of about 3:1 is reported (13). In our research we also observed this tendency – 78% of patients were between the ages of 3 to 10 years, but the male to female ratio (8:1) was a bit higher in our research than in other scientific studies. The symptoms of increased intracranial pressure, morning nausea and vomiting, headache and lethargy, were the most common complaints recorded more frequently in our study (100%) than in foreign (75–90%). The symptoms of ataxia (34%) and pathological eye movements (11%) were less common in our patients comparing to foreign research (60% and 20%, respectively) (14). This phenomenon may be due to the little number of investigated.

Medulloblastoma is one of the most frequently metastasized CNS tumors. The disseminated disease is found in 11–43% of the cases (1). The same results were obtained in our study. Metastases of the tumor were diagnosed in 44% of investigated patients. All these patients had a stage M3 tumor according to Chang’s classification.

According to many authors, the most important three factors influencing the results of treatment are the spread of the tumor outside the posterior fossa, age of patient and residual tumor (2–5). Due to these criteria the patients with medulloblastoma are divided into two groups: standard and high-risk groups (6, 15). This dividing of patients with medulloblastoma into the risk groups has a great importance not only for the outcome of disease but also for the choice of the method of treatment observing that the survival rate for these patients’ groups differs. In our investigation the patients were assigned to risk groups according to the same criteria, except patient’s age because children less than 3 years of age were not included in our study.

Standard-dose radiation therapy warrants a good control of the disease in the group of local medulloblastoma (stage M0 according to Chang). However, in the case of disseminated disease these results are much worse (5-year progression-free survival rate varies respectively 50–65% of M0 and 0–30% of M1–4 stages of medulloblastoma according to Chang) (16–19).

After comparing the results of radiotherapy treatment of children with medulloblastoma at Kaunas...
University of Medicine Hospital with the results of foreign hospitals, it is observed that despite the same principles of treatment (local and craniospinal radiotherapy) and the same doses of irradiation, our hospital showed much worse results of treatment – 5-year progression-free survival rate was only 16.7% among patients treated at our institution, whereas according to the data of foreign authors this number was approximately 30–45%. This can be conditioned by the reduction of the dose of local and craniospinal irradiation due to one of the complications of radiotherapy – myelosuppression. Five years progression-free survival rate was also lower (33.3 %) in the standard-risk group patients treated with radiotherapy at our institution in comparison with the results of foreign pediatric centers (50–65%). The 5-year survival rate for patients in the high-risk group was low both in foreign (0–30%) and our (0%) institutions.

After comparing the results of the treatment in standard and high-risk groups we observed that statistically significant longer time to progression (p= 0.02) and the overall survival (p=0.01) were in the standard-risk group, what is comparable to the data of the other articles (16). Even though we did not find any statistically significant difference between these two patients’ groups while assessing other indicators, such as the frequency of response to radiation therapy, the risk of death and relapse, 5-year progression-free survival and total survival, we have observed the tendency of better results in the standard-risk group (p=0.06). The small number of patients may condition the absence of statistically significant difference.

The spread of medulloblastoma is the most important criterion that helps to evaluate the prognosis of medulloblastoma. During our study it was ascertained that the only one of the previously mentioned prognostic criteria had influence on the rate of survival. Statistically significant shorter time to progression (p= 0.02) and overall survival (p=0.01) were observed among the patients with metastasized medulloblastoma.

The size of primary tumor did not influence the results of the treatment not only in our research, but also in other foreign studies. Controversial data was published concerning influence of extent of resection and size of residual tumor on outcome of medulloblastoma. It was shown that size of residual tumor is important prognostic factor only if local disease (M0 stage of Chang’s classification) is diagnosed (20, 21). In our investigation both extent of the operation and size of residual tumor did not influence the patients’ survival.

The patient’s age over 3 years did not influence the prognosis of medulloblastoma (6). However, according to data of foreign research, only age less than 3 years is important for survival of patients with this tumor. Since the patients younger than 3 years were not included in our study, we could not verify this fact.

Although there was a good initial response to the radiation therapy, medulloblastoma relapsed in 15 (83.3%) out of 18 cases. After the relapse of the disease mortality rate was 100%, irrespective of the tactics of the relapse treatment. The cause of death for all patients was the progression of tumor, which resulted in brain edema, brain stem disorder, and the disorder of vital functions.

Despite the newest radiotherapy technology, standard doses of local and craniospinal irradiation, the prognosis for medulloblastoma, especially in the advanced stages, remains very poor. Medulloblastoma can spread not only to nearby parts of the brain and spinal cord but also outside the central nervous system. Because of inability to cure the patient with medulloblastoma with radiation therapy only, the perspective of the treatment of this tumor is combined treatment (surgery, irradiation and chemotherapy). So, the identification of the exact stage of medulloblastoma, the evaluation of the risk group help not only to foresee the possible outcomes of the disease but also to choose the more correct method of treatment.

Conclusions
1. Prognosis of children with medulloblastoma treated with the radiation therapy alone is poor: the overall survival is 25.8 months, while only 16.7% of the patients survived five years after the diagnosis.
2. All patients with recurrent medulloblastoma relapsed during the two years after diagnosis; two-third of them relapsed during the first year.
3. The time to progression between the high and standard-risk patients (28.9 and 7.4 months, respectively) also as the overall survival (37.2 and 14.3 months, respectively) statistically significant differs (p=0.02 and p=0.01, respectively).
4. The mortality rate of patients with medulloblastoma was 83.3%.
5. The principal prognostic criterion that influences the survival rates is the spread of medulloblastoma (M stage).
Vaikų meduloblastomos gydymo radioterapija Kauno medicinos universiteto klinikose rezultatai 1994–2000 metais

Giedrė Rutkauskienė, Liutauras Labanauskas, Laimonas Jaruševičius
Kauno medicinos universiteto Vaikų ligų klinika, ¹Onkologijos klinika

Raktąžodžiai: galvos smegenų navikai, meduloblastoma, vaikai, radioterapija, išgyvenimas.


Darbo tikslas. Ištirti pacientų, sergančių meduloblastomą, išgyvenimą didelės ir standartinės rizikos grupėse gydant juos standarine radioterapija.

Pacientai ir metodai. 18 pacientų nuo 3 iki 18 metų, kuriems buvo histologiskai patvirtinta meduloblastoma, gydymo metu laikomi Kauno medicinos universiteto klinikose kraniospinaline radioterapija su papildoma užpakalinės kaukolės daubos apšvita. Devyni iš šių pacientų, kuriems nustatytą metastazavusi ir (ar) neradikalaišai pašalinta meduloblastoma, priskirti didelės rizikos meduloblastomos grupei. Kitiems devyniems, kuriems diagnozuotas lokalus navikas radikalaišai pašalintas, priskirti standartinės rizikos grupei.

Rezultatai. Radiologinis meduloblastomos atsakas į spindulinį gydymą konstatuotas 15 iš 18 (83,3 proc.) pacientų. Laukiamos radiologinis atsakas konstatuotas 6 iš 9 (67 proc.) standartinės ir tik 1 iš 9 (11,1 proc.) didelės rizikos grupės pacientų (p<0,05). Meduloblastomos progresija nustatyta 15 iš 18 (83,3 proc.) pacientų, gydymo metodai: 100 proc. didelės ir 66,7 proc. standartinės rizikos grupės (p>0,05). Didutinė trukmė iki progresijos – 18,2 mėn. Abiejose tiriamose grupėse: 28,9 mėn. standartinės ir tik 7,4 mėn. didelės rizikos grupės (p>0,02); gyvenimo trukmė – 25,8 mėn. Abiejose: 37,2 – standartinės ir 14,3 mėn. didelės rizikos grupės (p=0,01). Penkerių metų laisvas nuo progresijos ir bendras išgyvenimas buvo 16,7 proc.: didelės rizikos grupėje – 0 proc. ir standartinės rizikos grupėje – 33,3 proc. (p>0,05).

Išvados. Mūsų atliktoje studijoje įrodytas išgyvenimo rodiklių skirtumas tarp standartinės ir didelės rizikos grupių pacientų. Apskaičiavome statistiškai reikšmingai ilgesnį laiką iki progresijos ir gyvenimo trukmę standartinės rizikos grupėje. Tačiau kiti išgyvenimo rodikliai (atsako ir ligos atsinaujinimo dažnis, mirtimamumas bei penkerių metų laisvas nuo progresijos ir bendras išgyvenimas) reikšmingai nesiskyre tarp dviejų grupių pacientų – standartinės ir didelės rizikos.

Adresas susirašinėti: G. Rutkauskienė, KMU Vaikų ligų klinika, Eivenių 2, 50009 Kaunas
El. paštas: giedre.rutkauskiene@takas.lt

References

Medicina (Kaunas) 2006; 42(1)


Received 14 September 2005, accepted 12 December 2005

Straipsnis gautas 2005 09 14, priimtas 2005 12 12