Cerebellar medulloblastoma in adults

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From 1960 through 1981, 15 patients with cerebellar medulloblastoma, aged 16 years or over, were referred for irradiation following surgery. All patients received craniospinal irradiation; three patients received adjuvant chemotherapy. Five-year and 10-year survival rates of 63% and 38%, respectively, were obtained. The main cause of treatment failure was tumor recurrence in the posterior fossa. All local recurrences presented late, none developing within the first 3 years. One patient suffered systemic disease. The prognosis following relapse was poor. One patient achieved a prolonged remission following further surgery and radiotherapy, but died of treatment-related complications. The majority of the survivors are free of major deficit. One patient developed paraplegia 10 years after treatment. The possible risk of late damage to the hypothalamic-pituitary axis is discussed.

KEY WORDS • medulloblastoma • radiation therapy • chemotherapy • recurrent tumor • adult

Cerebellar medulloblastoma is usually considered to be a tumor of childhood. A significant proportion of cases, however, have been reported in older patients. In three large series, originating from clinical institutions, approximately one-fifth of the cases occurred in older adolescents and adults. At the Peter MacCallum Hospital, 13 (18%) of the 73 patients registered between 1960 and 1979 were aged 16 years or older. This report examines the results of treatment in this group of patients and includes two additional adults who were treated more recently.

Summary of Cases

Patient Population

From 1960 to 1981, inclusive, 15 patients aged 16 years or older with an unequivocal histological diagnosis of medulloblastoma were registered at the Peter MacCallum Hospital. There were nine male and six female patients. The ages ranged from 16 to 46 years, with a mean of 23.3 years. The age and sex distribution is shown in Fig. 1. The biopsy sections were available for review in 14 cases. In the remaining case the histological diagnosis from the referring hospital was accepted.

Treatment

All patients underwent surgical exploration. In seven patients the primary tumor was laterally placed in the cerebellar hemisphere, and in eight patients it was predominantly midline. Complete macroscopic removal was achieved in four patients, partial removal in 10, and biopsy only in one patient. Two patients required the insertion of arteriovenous shunts.

Following surgery all patients underwent whole craniospinal irradiation. Four patients were treated by orthovoltage equipment and 11 by megavoltage therapy. The majority of patients received irradiation to the whole cranial contents and spinal canal, followed by a "boosting" dose to the posterior fossa. The total dose delivered to the posterior fossa varied from 30.00 Gy (3000 rads) in 5 weeks to 50.00/55.00 Gy (5000/5500 rads) in 5/5 weeks. Three patients received some form of adjuvant chemotherapy. One patient was given intrathecal methotrexate daily for 5 days prior to radiotherapy, two patients received a combination of vincristine and methyl-CCNU (1-(2-chloroethyl)-3-cyclohexyl-1-nitrosourea) for 9 months following completion of radiation therapy.

Treatment Results

The follow-up period ranged from 14 months to 16 years. One patient was lost to follow-up review at 42 months, but a recurrence was suspected. The period of survival and time to recurrence was calculated from the date of commencement of radiotherapy. The summary of patient survival, determined by product limit analysis, is shown in Fig. 2. The 5-year survival rate was 63%, and the 10-year survival rate was 38%.
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Recurrence Disease

Local recurrence in the posterior fossa occurred in four patients over periods ranging from 44 to 100 months (Table 1). Recurrence was confirmed at operation in one patient, at postmortem examination in two, and on computerized tomography scanning in the fourth case. Local recurrence was suspected but unconfirmed in a further patient at 42 months. No patient developed spinal metastasis. One patient developed diffuse metastatic involvement of bone marrow without evidence of local recurrence.

Once the presence of recurrent disease had been established the outlook was poor, with the exception of one patient who underwent further surgery and repeat irradiation of the craniospinal axis. He survived over 5 years after treatment of his recurrent disease before dying of treatment-related complications (see below). At postmortem examination (details of which are incomplete) there was no macroscopic evidence of residual or recurrent disease in the posterior fossa.

Complications of Radiotherapy

There was minimal acute morbidity from craniospinal irradiation. In one patient treatment was temporarily suspended due to myelosuppression.

Major late complications were seen in two patients. One patient, who underwent repeat irradiation of the craniospinal axis following tumor recurrence in the posterior fossa, developed complete paraplegia of gradual onset 2 years after completion of his second course of treatment. The clinical diagnosis was compatible with radiation myelitis, and the patient eventually succumbed to acute suppurative pyelonephritis. A second patient has recently developed paraplegia 10 years after completion of therapy. A diagnosis of "transverse myelitis" has been made and the patient is currently attending a rehabilitation center. Of the remaining survivors none has a major neurological deficit. Three patients

<table>
<thead>
<tr>
<th>Case No.</th>
<th>Time to Recurrence (mos)</th>
<th>Site of Recurrence</th>
<th>Treatment of Recurrent Disease</th>
<th>Result of Treatment</th>
<th>Survival (mos)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>47</td>
<td>posterior fossa</td>
<td>repeat excision, craniospinal irradiation</td>
<td>remained clinically disease-free; died of treatment-related complications</td>
<td>69</td>
</tr>
<tr>
<td>2</td>
<td>100</td>
<td>posterior fossa</td>
<td>emergency ventricular drainage</td>
<td>died postoperatively</td>
<td>—</td>
</tr>
<tr>
<td>3</td>
<td>57</td>
<td>posterior fossa</td>
<td>repeat irradiation of posterior fossa</td>
<td>died before completion of treatment</td>
<td>—</td>
</tr>
<tr>
<td>4</td>
<td>44</td>
<td>posterior fossa</td>
<td>chemotherapy, dexamethasone</td>
<td>transient improvement</td>
<td>2</td>
</tr>
<tr>
<td>5</td>
<td>21</td>
<td>diffuse metastasis to bone marrow</td>
<td>none</td>
<td>—</td>
<td>8</td>
</tr>
</tbody>
</table>

*One patient was lost to follow-up at 42 months with suspected local recurrence.
†Survival time after recurrence.
have minor problems (nystagmus, mild incoordination, and residual cranial nerve paresis), but the quality of life is not seriously impaired. One patient has undergone surgery to correct diplopia.

Two patients have undergone formal testing of pituitary function. One patient, tested 4 years after treatment, showed impaired function but did not require replacement therapy. A second patient who is well 13 years after treatment has normal pituitary function and has undergone three successful pregnancies.

Discussion

With the exception of the recent report by Kopelson, et al., there is little in the literature dealing specifically with the results of treatment of medulloblastoma in older patients. Previously reported series with similar patient selection and treatment techniques quote 10-year survival figures from 16% to 24%, although these series include patients treated over a much earlier period. In their series of 17 patients, Kopelson, et al. obtained a 46% 10-year survival rate. This apparent improvement in survival was attributed to the delivery of higher radiation doses to the posterior fossa.

Chatty and Earle suggested that the location of the primary tumor and its histological type were important prognostic factors. Patients with primary tumors situated in the cerebellar hemispheres that had a desmoplastic histological appearance showed improved survival over the general medulloblastoma population. In this series, four of six patients with laterally placed tumors are alive and well (with a minimum follow-up period of 3 years) compared with three of seven patients with midline tumors. Only two cases showed any degree of desmoplasia. One patient is alive and well at 27 months, the other patient died of disseminated disease at 20 months.

The pattern of relapse was characteristic, with recurrent disease in the posterior fossa being the main indication of treatment failure. Late local recurrence was a feature of this series of patients; no patient had a recurrence in the posterior fossa within the first 3 years. This lends support to Bloom’s observation that the progress of the disease appears to be slower in adults than in children, where 75% of recurrences occur within the first 2 years. It is not possible to draw any valid conclusions regarding local tumor control and radiation dosage delivered to the posterior fossa in this group of patients in view of the small numbers involved, the tendency to late relapse, and the considerable variation in the dosage of radiation prescribed.

The appearance of systemic metastases in medulloblastoma is well documented. A recent comprehensive survey by Kleinman, et al., suggests that approximately 5% of patients with medulloblastoma may be expected to develop distant metastases, with bone being the most common site involved. Once local recurrence or metastasis is established the outlook is poor, and death is usually inevitable. Further radiotherapy and/or chemotherapy may produce useful symptomatic relief and occasionally prolonged survival. Repeat irradiation does carry an increased risk of radiation damage, although the benefits produced are usually considered to outweigh this potential risk. Most cases of gross radiation damage are seen in patients who are heavily re-irradiated to high dosage, as illustrated by the patient who developed radiation myelitis 2 years after his second course of treatment.

The occurrence of paraplegia 10 years after craniospinal irradiation has not, to the author’s knowledge, been previously reported. The risk of impairment of the hypothalamic pituitary axis following cranial irradiation in children has been well documented. Saaman, et al., have recently reported a very high incidence of endocrine abnormalities occurring in a large number of adult patients who had undergone radical radiotherapy for carcinoma of the nasopharynx and paranasal sinuses. Wigg, et al., have attempted to determine the tolerance of the pituitary-hypothalamic region to irradiation and to define the threshold for endocrine complications. It would appear advisable that patients undergoing cranial irradiation, where the pituitary and hypothalamus lie within the irradiated volume and who have a good prognosis, should undergo regular assessment of their endocrinological status.

It is now accepted that the treatment of patients suffering from medulloblastoma by surgery and craniospinal irradiation will yield a substantial number of long-term survivors who are free of major disability. The results currently obtained probably represent the best that can be achieved with these modalities. Whether adjuvant chemotherapy will lead to an overall improvement remains to be determined.

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References


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