Adult medulloblastoma

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SUMMARY Twelve cases of adult onset medulloblastoma are presented. Clinical features, treatment and outcome are discussed. It was found that the survival rates for adults are no better than for children. There were no clinical or histological features that distinguished these tumours from those occurring in childhood, except for a higher incidence of hemisphere lesions.

Since its initial recognition as a separate entity by Bailey and Cushing in 1925,¹ medulloblastoma has become well recognised as a malignant cerebellar tumour occurring mainly in childhood. The name medulloblastoma was chosen by Bailey and Cushing to illustrate their view that the tumour arose from a hypothetical primitive pluri-potential stem cell called a medulloblast. This theory has now become traditional. Weight was added to it in 1968 when Zulch and Wechsler² suggested that the tumour arose from the external granular cell layer of Olszewski. This neuro-ectodermal remnant can be readily demonstrated as an external granular layer in the vermis in normal brains up to the age of 16 months. After this age the cells disappear, presumably migrating into deeper granular layers. These tumours have therefore always been considered congenital and most likely to arise within the first 16 months of life. This supposition has even led to the prediction of a period of risk for recurrence which may be calculated by adding nine months to the patient's age at the time of diagnosis.³ The appearance in adults of medulloblastomas histologically indistinguishable from those in children has therefore remained a great puzzle and a challenge to the traditional theory. Cushing and Bailey recognised this in their original paper. Nine of their 61 patients were 18 years old or over at the time their tumours arose. They could find no differences in histology, natural history or response to treatment in patients of differing ages. Since their original paper the literature has become replete with conflicting evidence as to the

relationship of survival to the age of onset. In an effort to define our own experience with these tumours we have reviewed the records of the 12 adult patients with medulloblastoma admitted to Addenbrooke's Hospital after June, 1961. The records were examined with a view to finding any clinical or histological features which might distinguish cases arising after the 18th birthday from those arising in childhood. In addition, treatment and mortality were reviewed.

Material and methods

Between 1961 and 1982 12 cases of medulloblastoma occurring after the 18th birthday have been identified. During this period a total of 37 patients, both adults and children, with medulloblastoma were seen, making adults 32% of the cases. There were two females and ten males. The age of the patients at the time of diagnosis ranged from 18 to 49 years, with an average age of 39 years. One patient was in the second decade of life, three in the third, three in the fourth and five in the fifth.

Clinical features

Most patients presented with very short histories (table 1). In seven (58%) the history was 3 months or shorter. The other five patients had histories of between 3 and 6 months. The longest history was 6 months, the shortest 2 months. The most common symptom was headache, followed by ataxia, nausea and vomiting (table 2). These symptoms usually occurred in combination. Headache occurred in ten (85%) of the patients at some time before their diagnosis. Seven (58%) suffered from ataxia and six (50%) from nausea and vomiting. Two patients (16%) presented with cranial nerve abnormalities. One patient presented with unilateral Vth, VIIth and VIIIth nerve palsies, and another presented with an isolated VIIth nerve palsy. Three patients complained of a stiff neck, it being the sole symptom in one. Papilloedema was found in six patients (50%).

Tumour location

In contrast to the situation in children, nine of the tumours

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Table 1 Clinical features

Age	18–49 years (average 39 years)	
Length of history	Three months or less	7/12
	Between six and three months	5/12
Tumour location	Hemispheric	10/12
	Right	6/12
	Left	5/12
	Midline	4/12
Male/Female	10/2	

were confined strictly to the cerebellar hemisphere, with five on the right and four on the left. One left-sided tumour presented as a cerebello-pontine angle mass in a patient with unilateral cranial nerve signs. Three patients had mid-line tumours.

Histology

The picture was that of a cellular tumour composed of small, dark cells, with scanty cytoplasm. The cell nuclei were small, round or ovoid, and frequently hyperchromatic. Cellular and nuclear pleomorphism were not conspicuous. Mitoses were present in either moderate numbers (five tumours) or large numbers (four tumours). Necrosis was not an outstanding feature. Desmoplastic change was seen in two tumours. Both of these tumours were characteristically lateral in position in the cerebellar hemisphere. As conventional wisdom would predict,⁴ we only found desmoplastic change in those tumours which were laterally placed and superficial enough to pick up a mesenchymal element from the dura. Possible spongioblastic differentiation was present in one tumour. Rosettes were not seen in any of the tumours. Though rosettes are not present in all childhood medulloblastomas, the total absence of rosettes in the present series is the most significant difference from the appearances of the childhood tumour.

Table 2 Signs and symptoms

Symptoms	
Headache	10/12
Vomiting	6/12
Ataxia	7/12
Neck stiffness	3/12
Signs	
Papilloedema	6/12
Cerebellar dysfunction	7/12
Cranial nerve palsies	2/12
VIIth	2/12
VIIIth	1/12

Treatment

All patients underwent some form of direct operative intervention on the tumour. In two cases this was limited to biopsy only, and in a further two cases to what was considered to be a sub-total removal. In eight cases there was considered to be a macroscopic total removal of the tumour. None of the patients was staged by CSF cytology or myelography at the time of original diagnosis. All patients received radical radiotherapy to the brain and spine following surgery. This was given on a 6meV linear accelerator for the brain and a Cobalt gamma 60 machine for the spine. Fifteen to twenty fractions were given over three weeks. Eight patients received a total dose of 4000–4500 cGy to the posterior fossa, with 2000 to the spinal canal. Three patients received 5000–5500 cGy to the posterior fossa, with 2000 cGy to the spinal canal. Eleven patients completed the full course, but one died during radiotherapy. Four underwent a second course of radiotherapy at the time of recurrence, and three patients received chemotherapy with 1-(2-chloroethyl)-3-cyclohexyl-1-nitrosourea (CCNU). One patient received both. Two patients underwent a second posterior fossa exploration at the time of recurrence.

Table 3 Treatment and outcome

Case No	Age at diagnosis	Initial surgery	Initial radiation	Recurrence and treatment	Final outcome from original diagnosis
1	49	Total removal	4500 cGy post. fossa 2000 cGy cord	Post. fossa recurrence Cranial radiation CCNU Reexploration	Died 4 years
2	49	Total removal	5500 cGy post. fossa 1500 cGy cord		Alive and well 5 years
3	26	Total removal	4500 cGy post. fossa	Bone marrow & ribs CCNU	Died 2 years
4	42	Total removal	4500 cGy post. fossa 2000 cGy cord	No recurrence at post mortem	Died 1 year
5	36	Total removal	4500 cGy post. fossa 2000 cGy cord	Post. fossa recurrence Cranial radiation Reexploration	Died 4 years
6	40	Total removal	5000 cGy post. fossa 2000 cGy cord		Alive and well 9 years
7	34	Total removal	4000 cGy post. fossa	Post. fossa and spinal recurrence Craniospinal rad.	Died 2 years
8	21	Biopsy	5500 cGy post. fossa 2000 cGy cord		Alive and well 5 years
9	18	Biopsy	3 fractionations		Died 2 months
10	41	Subtotal removal	4500 cGy post. fossa 2000 cGy cord	Spinal recurrence CCNU	Died 1 year
11	33	Subtotal removal	4200 cGy post. fossa	Spinal metastasis 9 years after DX	Alive with recurrence
12	27	Total removal	2000 cGy cord 4500 cGy post. fossa 2000 cGy cord	Craniospinal rad. Cranial recurrence Cranial radiation	10 years Died 6 years

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Outcome

For the group as a whole there was no operative mortality (death within 6 weeks). The follow up period ranged from 5 to 10 years. The overall one year survival rate was 75%. The five year survival rate in 12 patients is 50%, and at ten years 11% (nine patients). Three patients remain alive and well without recurrence at five, five and nine years from diagnosis. One patient is alive 10 years following diagnosis, but now has widespread cerebral and spinal metastases (table 3). Of the four patients alive now, two underwent biopsy only and radiotherapy and are alive five and ten years later. Two patients are still alive following total surgical removal and radiotherapy five and nine years ago respectively. Of the patients still alive, three had hemispheric lesions and one a midline lesion.

The length of the initial history had no bearing on survival. The average survival was 32 months for those with a history of less than three months, and 27 months in those whose history was between three and six months long. The clinical presentations were broadly similar in all patients except for the two who presented with cranial nerve signs. Of those one died at 11 months and one is alive without recurrence after 5 years.

The type of surgical intervention would appear to have made little difference to survival. There was a 50% five year survival rate in those whose tumours were not completely removed and a 42% five year survival rate in the group whose tumours were macroscopically completely removed.

Unlike surgery, the total dose of radiation to the posterior fossa did appear to affect survival. The three patients who received 5000–5500 cGy to the posterior fossa are alive and well at five, five and nine years respectively, but of the eight patients who received only 4000–4500 cGy to the posterior fossa, only one is still alive at ten years and has widespread spinal metastases. One patient died while undergoing radiotherapy.

In ten patients the histological appearances were classical of medulloblastoma, and in two cases the medulloblastomas were desmoplastic in appearance. One of the patients originally harbouring a desmoplastic tumour is alive and without recurrence at five years. However, the other died of recurrence two years after original diagnosis.

Three patients suffered from spinal metastases at one, two and nine years following their original diagnosis. One patient died without evidence of recurrence. Seven patients had posterior fossa recurrence at the time of death and these recurrences occurred at one to six years from the original diagnosis. As other studies have shown,⁵ once there was recurrence the prognosis was very grave, all but one patient dying within six months. The one exception is a patient who is still alive thirteen months after the diagnosis of spinal metastases. Metastases outside the nervous system were found in only one patient who interestingly did not have a shunt.

Discussion

Although the prognosis for patients with medulloblastoma is generally considered poor, it is quite difficult from the published literature to estimate

exactly how poor it is. Five year survival rates have been reported varying from zero⁶ to 58%⁷ and no clear relationship between the various histological, clinical and surgical factors and survival can be established.

Recent studies in children,^{8,9} have reported five and ten year survival rates of approximately 50–55% and 40% respectively. Comparisons are difficult because, as in our series, radiation therapy modalities have changed in recent years. In addition, reports from radiotherapeutic centres such as those quoted above deal only with patients who survive operation and a full course of radiotherapy. It seems generally accepted that "survival rates of approximately 40% at five years and 30% at ten years are the best that can be expected in children with medulloblastoma. . . ."¹⁰ Within these limitations our survival figures for adults are comparable to those in children, especially considering one of our survivors has only a few more months to go to reach the ten year milestone.

We could not confirm the suggestion of Quest *et al*³ that the time interval between original diagnosis and recurrence would vary directly with the patient's age at diagnosis. For those with tumour diagnosis before the thirtieth birthday the average survival was 53 months, whereas after the thirtieth birthday it was 47 months. Chatty and Earle¹¹ found that patients with hemispheric lesions had increased survival. Our numbers are too small to draw statistically valid conclusions, but tend to support this with three of eight patients with hemispheric lesions surviving, and one of four patients with midline lesions still alive. In this series we could find no correlation between the thoroughness of surgical tumour removal and survival. Our study confirms the data of Kopelson¹² that higher radiation dosage does increase survival.

In conclusion, our series demonstrates that the survival rates for adults with medulloblastoma are no better than for children. Our series showed a higher percentage of hemispheric tumours, which is not found in children, but we could not distinguish any histological factors that would suggest that these tumours are fundamentally different from those to be found in children, nor do there seem to be any features that would allow one to predict which patients will enjoy long survival. The efficacy of higher dosage radiotherapy to the posterior fossa is confirmed.

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