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POSTOPERATIVE MANAGEMENT OF PRIMARY SPINAL CORD EPENDYMOMAS

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Abstract

Treatment and final outcome of 11 patients with primary spinal cord ependymomas admitted between 1967 and 1983 have been reviewed. All patients had undergone surgery once or twice before radiation treatment. Six of them are alive and disease-free 78 months to more than 180 months after radiation therapy. A short analysis of the recent literature is presented with special emphasis on the most frequent treatment techniques, extension of radiation fields and doses. The value of postoperative radiation therapy and the complications of both surgery and radiotherapy are analyzed. Some guidelines for treatment are finally discussed and proposed.

Key words: Spinal cord, ependymomas, radiotherapy.

Primary spinal cord ependymoma is rare and its optimal treatment still unclear. Because of its rarity, the effect of various treatments is difficult to assess and meaningful randomized clinical trials are precluded. However, a considerable number of reports has been gathered over a period of many years by surgeons and radiation oncologists employing various treatment techniques.

Until recently the predominant therapeutic methods were those suggested by Wood et al. (21), Greenwood Jr (7), and more recently Scott (18), in which a partial resection or conservative surgery was followed by megavoltage radiation treatment.

This methodology was founded on the firm belief that total removal of intramedullary tumours was impossible. In recent years, however, there have been many reports suggesting the possibility of a total removal of the spinal tumour by modern neurosurgical techniques (1, 2, 6, 9, 16). Three main questions arise from a review of the recent literature:

1) Which is the most favourable management?

2) Does radiation therapy play a role in the postoperative management?

3) If it does, what guidelines can be given concerning the extension of the irradiated volume?

In order to elucidate these problems we present data on 11 patients treated in our department and a review of several recently published series of histologically proven spinal ependymomas.

Ependymomas have traditionally been divided into 4 histologic subtypes with increasing malignancy from grade 1 to 4, but during recent years a tendency to group the cases into low grade (grades 1 and 2) and high grade malignancy (grades 3 and 4) has prevailed. In this paper we have followed the latter type of classification.

Material and Methods

Eleven patients with primary spinal ependymomas were observed and treated in our department from 1967 to 1983. All patients had undergone surgery once or twice before admission to our department. There were 9 males and 2 females, aged 17 to 67 years, mainly with lower spine ependymomas. The main characteristics of our patients as regards age, sex, histology, site of primary involvement, initial management, time to failure, site of recurrence, second management, follow-up and present status are summarized in Table 1.

Pain was generally the first and dominant symptom and frequently preceded the diagnosis by months or years. Urinary dysfunction was also frequently observed. Pain was present 1 month to 6 years before diagnosis. Neurologic deficits and urinary dysfunction appeared as a rule later than pain.

All patients were treated postoperatively by megavoltage photon radiation therapy (RT), with a single posterior

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Table 1

Characteristics of patients observed in the present series

No.	Age Years	Sex	His-tology	Site	Initial treatment	Time to 1st failure Months	Site of recurrence	Manag. of 1st recurr.	Follow-up Months	Outcome
1	46	M	L	L2-L3	S: CR RT: 50 Gy				120	Alive—NED
2	23	M	H	D10-Cauda	S: IR	4	Involved primary site	RT: 40 Gy	12	Dead, brain failure
3	67	F	L	L1-S2	S: IR RT: 51 Gy	12	Involved primary site	RT: 40 Gy	46	Dead, unknown cause
4	42	M	L	D5-D7	S: IR	24	C3-C5	S: IR RT: 40 Gy W.S.	33	Dead
5	28	M	H	D11-L2	S: B	2	D12-L5	S:IR RT: 54 Gy	74	Dead, brain failure
6	37	M	L	D11-L3	S: IR	46	Involved primary site	S: IR RT: 53 Gy	194	Alive with disease
7	17	F	L	L2-L3	S: IR RT: 40Gy	169	L3-S1	S: CR RT: 44Gy	182	Alive—NED
8	40	M	L	L3-S2	S: B RT: 50 Gy				126	Alive—NED
9	25	M	L	L1-Cauda	S: IR RT: 54 Gy				180	Alive—NED
10	32	M	L	D7-L2	S: CR RT: 55 Gy				150	Alive—NED
11	30	M	L	L2-L3	S: IR RT: 54 Gy				78	Alive—NED

L = low grade; H = high grade; S = surgery; B = biopsy; CR = complete resection; IR = incomplete resection; RT = radiotherapy; W.S. = whole spine irradiation; NED = no evidence of disease.

portal directed towards the spine with a margin of one or two vertebral bodies above and below the documented limits of the neoplasm. The whole spine was irradiated in one patient only (No. 4). A cobalt-60 unit was employed. The total doses ranged between 40 and 55.5 Gy with 1.7–2.0 Gy per fraction and 5 fractions per week. The doses were calculated at a depth of 4–6 cm under the skin surface depending on the size of the patient and on the location of the tumour.

Surgery always preceded RT and in several cases (Nos. 2, 4, 5, 6) patients were referred to us after the first surgically managed relapse. Complete resection was performed in 2 cases only (Nos. 1, 10) and biopsy only and decompressive laminectomy in another 2 cases (Nos. 5, 8). More or less incomplete resections were performed in the remaining cases.

The histologic examination showed 2 high grade and 9 low grade ependymomas, mainly of the mixed papillary type.

Results

Six patients (Nos. 1, 7–11) are still alive and free of disease after periods ranging from 78 to more than 180 months after the radiation treatment.

Four patients died of recurrences (Nos. 2, 3, 4, 5). Two of these (Nos. 2 and 5) had high grade ependymoma and were initially treated with incomplete surgical resections only: radiation treatment was given against the involved site after the first recurrence. Both patients had a transient complete recovery of their symptoms, but they died with intracranial failure and diffuse seeding in the central nervous system a few months (No. 2) or years (No. 5) later.

Patient No. 3 was lost to follow-up after a second treatment for recurrence within the primary involved site and died by unknown cause 46 months after the diagnosis.

Patient No. 4 was managed initially by surgery without irradiation. After recurrence the whole spine was irradiated; he died with local recurrence 33 months after the diagnosis.

Patient No. 6 underwent surgical incomplete resection of a tumour involving $T_{11}-L_3$, without postoperative irradiation; 46 months later a recurrence was incompletely resected and postoperatively irradiated. The patient was now paraplegic and survived in this state for about 12 years, when a massive pelvic neoplastic invasion was diagnosed. He is still alive but paraplegic and has a massive recurrence 194 months after diagnosis.

Patient No. 7 relapsed 169 months after the initial treatment. A second operation followed by repeated radiation treatment produced complete recovery of symptoms.

Table 2

Characteristics of some recent series of spinal cord ependymomas

Series		No. of patients	Histology		Sex		Adults	Children	Survival rate (%)	
			LG	HG	M	F			5 years	10 years
Cooper & Epstein	(1)	14	14	0			14	0	72	
Fisher & Mansuy	(2)	16	15	1	10	5	13	3	84	
Garrett & Simpson	(4)	41	39	2	24	17	35*	6*	83	
Kopelson et al.	(10)	12	12	0	8	4	?	?	100	73
Marks & Adler	(12)	15	15	0	5	10	11	4	73	
Mørk & Løken	(13)	53	53	0	28	25	51	2	90	72
Peschel et al.	(14)	9	9	0	4	5	9	0	100	
Read	(15)	26	26	0	?	?	22	4	70	70
Roux et al.	(16)	12	12	0	7	5	12	0		
Schwade et al.	(17)	12	12	0	7	5	12	0	100	
Shaw et al.	(19)	22	21	1	17	5	22	0	81	71
West et al.	(20)	9	8	1	5	4	7	2		
Present series		11	9	2	9	2	11	0	72	60

* Six patients in this series have been indicated as younger than 18, but some of them may have been older.

Discussion

Table 2 summarizes some characteristics including a 5- and 10-year survival of our patients compared with other series published in the last 12 years.

The extreme rarity of high grade spinal ependymoma is obvious and only 7 cases among a total of 252 (less than 3%) have been reported. The male/female ratio in the reviewed literature in Table 2 is 1.42 and the adults/children ratio 10.4. The long term results reported by surgeons (2, 3, 8, 9) are generally good and seem to be equal to those reported by radiation oncologists. Guidetti et al. (9) reported a median survival of 125 months. Fisher & Mansuy (2) reported that 84% of their patients were alive and disease-free after 5 years. Other authors (1, 6) have also reported good results, but the follow-up periods are too short for evaluation of the ultimate outcome. Roux et al. (16) have reported a small series with rather heterogeneous treatment. Mørk & Løken (13) found similar survival rates in patients irradiated and not irradiated after complete surgical resection. Similar data have been reported by Fearnside & Adams (3), Greenwood (7) and Guidetti (8). These data seem fairly convincing and radiation treatment is perhaps unnecessary after complete surgical removal of well differentiated spinal ependymomas. However, even complete surgical resection may be followed by a tumour recurrence, as reported by several authors (3, 8, 10, 16). Moreover, it must be noted that surgery, even in very experienced hands, is associated with complications, that cannot be ignored. A surgical mortality rate of 3–10% has thus been reported (6, 8, 9, 16, 18) and also major complications, such as wound break-down, meningitis, neurological deterioration and progressive kyphosis (1, 11).

In our opinion equally good results may be obtained by a debulking or simply decompressive surgery followed by postoperative radiation therapy, as demonstrated by an abundant literature (3–5, 10, 17–19, 21). We agree with Garcia (4) that 'complete excision should not be attempted if more extensive surgical resection would result in unacceptable neurologic deficit'.

However, radiation therapy too may produce some major complications. Garcia (4) reported one case of radiation induced second malignancy and in another patient severe radiation myelopathy developed 17 years after treatment (in this case both intrathecal administration of colloidal ^{198}Au and external irradiation had been given). Marks & Adler (12) reported 3 cases of radiation myelopathy among 8 patients who received intrathecal colloidal ^{198}Au after external irradiation of the spine, and one case among 25 patients treated with external irradiation alone. As a rule, however, postoperative external irradiation of spinal cord is well tolerated. The high incidence of major complications after intrathecal administration of colloidal ^{198}Au is a strong argument for the abandonment of this method.

Our own patients treated with incomplete surgical resection without postoperative irradiation all suffered relapse (cases Nos. 2, 4, 5, 6). Similar experience has been reported by others (10, 16).

The postoperative radiation treatment of spinal ependymomas is fairly well standardized even if there is a certain variety in the treatments employed. Garrett & Simpson (5) use a single posterior portal against the involved region and a total dose of 50 Gy in 25 fractions. Kopelson et al. (10) use similar techniques but extend the field 2–3 cm cranially and caudally. An analogous technique is used by Peschel et al. (14). Schwade et al. (17) prefer 2 opposed or convergent portals, with a wide margin above and below the tumour. A wide margin (at least 2 vertebral bodies) is recommended by Garcia (4), who employs a single poste-

Table 3

Intracranial failures in spinal cord ependymomas

Series	No. of patients	No. of failures	Histology	
			HG	LG
Fisher & Mansuy (2)	16	2	1	1
Garrett & Simpson (4)	41	3	1	2
Kopelson et al. (10)*	75	5	?	?
Shaw et al. (19)	22	2	0	2
Present series	11	2	2	0

* Kopelson et al. reported 75 cases from a review of several previously published series.

rior field frequently associated with intrathecal colloidal ^{198}Au. The same technique is used by Marks & Adler (12). Shaw et al. (19) have in several cases used a posterior 90° arc therapy, but more often a single posterior portal. All the cited authors have employed conventional fractionation with 1.7–2.0 Gy per fraction, 5 fractions per week, and the dose has been calculated at a depth of 4–7 cm depending on the site of involvement and the size of the patient. A wide range of doses has been reported from 28 to 57 Gy (4, 10, 14, 17, 19). However, the majority of patients in each series has been treated with doses of about 45–50 Gy.

In agreement with some other authors (5, 10) we feel that a minimum dose of 45 Gy is needed for local tumour control. In our series 3 patients out of 11 were treated with doses lower than 45 Gy (Nos. 2, 4, 7) and each of them failed.

The methods of treatment reported above seem to be adequate for low grade spinal ependymomas; actually the majority of failures have been reported within the treatment fields without evidence of seeding (4, 5, 10, 19). Sometimes, however, intracranial failures have been reported as shown in Table 3. Among more than 300 cases of histologically proven tumours only 14 intracranial failures have been observed. This low incidence does not suggest that prophylactic irradiation of the entire central nervous system is necessary. It must be noted, however, that in at least 4 out of 14 cases with intracranial relapse the primary tumour was a high grade spinal ependymoma. This histologic type has been reported in 7 cases only during the last 12 years (Table 2) and 4 of these cases developed intracranial relapse. For this reason we agree with Garrett & Simpson (5) who suggest irradiation of the entire craniospinal axis in high grade tumours. These authors (5) moreover suggested that a poorly differentiated ependymoma in the spinal cord may represent seeding from a primary subclinical cranial ependymoma. Also this possibility justifies irradiation of the entire craniospinal axis.

From the review of the literature and the study of our own series the following conclusions may be drawn:

1) Completely resected spinal ependymoma with low grade malignancy need no further treatment.

2) Complete surgical removal is desirable but it should not be attempted if it is associated with a risk of unacceptable neurologic consequences.

3) Debulking surgery followed by radiation therapy may achieve excellent results as regards survival rate and neurological improvement. The survival rate is similar to that obtained by complete surgical resection.

4) Postoperative radiation therapy should be given to all patients after subtotal resection, even if there is a substantial neurological improvement.

5) Spinal ependymomas with high grade malignancy are very rare and it seems reasonable to irradiate the entire CNS because of the high probability of seeding.

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