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RADIATION THERAPY FOR SPINAL EPIDURAL METASTASES WITH COMPLETE BLOCK

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Spinal epidural metastasis resulting in spinal cord compression is a medical emergency requiring prompt medical evaluation and decompression of the cord should permanent neurologic sequence be prevented. This is particularly true when myelography discloses a complete spinal block in which the spinal cord is undergoing maximum pressure within a narrow spinal canal. The neurologic outcome of patients with a complete block is significantly different from those with no block (YOUNG et coll. 1980). A complete block results from a conjunction of several factors such as the presence of an epidural tumor, bony fragments or intervertebral discs resulting from a pathologic fracture or cord edema.

Currently, two treatments for epidural metastasis are practised: radiation therapy alone and surgical decompression followed by radiation therapy. Great controversies in the contemporary neurosurgical practice exist as to which treatment modality is most effective and beneficial. The most reliable course for prompt decompression may be surgical. Several criteria for a decompressive laminectomy have been described in the literature (APUZZO et coll. 1977, CRUE & FELSOORY 1977, BRUCKMAN & BLOOMER 1978, BLACK 1979, RODRIQUEZ & DINAPOLI 1980, SHAW et coll. 1980): acute progressive neurologic deficits, partial paralysis, complete myelographic block, unknown primary, and tumors resistant to radiation. However, a conventional laminectomy not infrequently fails to achieve neurologic improvement postoperatively (WRIGHT 1963, WHITE et coll. 1971, COBB et coll. 1977). Total eradication of the epidural metastasis is virtually impossible by surgery, thus requiring postoperative irradiation (WILD & PORTER 1963, WRIGHT). During the past decade reports supporting radiation therapy as a primary treatment have appeared to an ever increasing extent. However, no supportive evidence has been presented that carcinomas or sarcomas respond to ionizing radiation with a significant decrease in size within an acceptable time when a prompt cord decompression is essential. When the cause of a cord compression is mainly osseous or structural, irradiation per se fails to decompress the cord even though neoplastic cells may be eradicated. The previous literature (COBB et coll., RAICHLE & POSNER 1970, MARSHALL & LANGFITT 1977) reported that results are similar for both treatments, whether the patient underwent decompressive laminectomy followed by irradiation or was given radiation therapy alone.

A series of patients with complete myelographic block treated primarily with a uniform protocol of irradiation and a high dose of dexamethasone was carefully reviewed. Particular attention was paid to correlate the objective findings at spine radiography and myelography, the nature of the primary tumor, and pre-treatment status of each patient, to the neurologic outcome in order to establish guide lines

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for the selection of treatment mode in prospective patients.

Materials and Methods

From January of 1979 to December of 1979, 535 patients underwent myelography at the Memorial Sloan-Kettering Cancer Center; a complete block was demonstrated in 110; 78 of these had a myelographic complete block due to epidural spinal metastases and constitute the basis for the present review. The remaining 32 with a comlete block were excluded because of insufficient clinical data available in 9, an intradural lesion in 8, epidural spinal metastasis surgically treated before radiation therapy in 7, primary benign tumors of the spine in 3, previous treatment by radiation or surgery in the same region in 3, spinal epidural hematoma confirmed by autopsy in one and spondylosis in one. Among the 78 patients with complete block secondary to spinal epidural metastasis, 36 were male and 42 were female. Ages ranged from 7 to 81 with a mean average of 53.0 (Table 1). All patients had a previous history of malignant tumor (Table 2).

The ability of the patient to walk was the focus to evaluate the results of treatment. Group I consisted of patients able to walk without support (34 patients), Group II patients able to walk with support (19), Group III patients unable to walk (18), and Group IV paraplegics (7 patients).

Myelography after both lumbar and cervical puncture to determine the longitudinal extension of the block was performed. After completion of the myelography, uniform treatment was applied using the previously described protocol of radiation therapy with 5 Gy for 3 consecutive days, followed by a 4-day rest, then 3 Gy daily for 5 consecutive days to a posterior port centered on the site of the block extending to two vertebral levels above and below (GREENBERG et coll. 1980). High doses of dexamethasone, 100 mg intravenously, were begun either before or immediately after myelography, followed by tapering doses of dexamethasone either orally or intravenously. Seven patients did not complete the radiation therapy: refusal 1, early deaths 2, and persistent paraplegia in 4. Myelographic findings were single complete block (1 spinal level) in 36, single complete block plus a separated incomplete block in 14, multiple contiguous block (2 spinal levels) in 8, multiple contiguous block (3 or more) in 9, multiple contiguous block plus a separated incomplete block in 5, and extent of the complete block unevaluable at myelography in 6.

The cause of compression of the spinal cord or cauda equina was classified as tumoral or structural.

Table 1

Age distribution

Age (years)	No. of cases
0– 9	1
10–19	1
20–29	4
30–39	2
40–49	14
50–59	29
60–69	16
70–79	10
80–	1

Table 2

Primary site of tumor in 78 patients with epidural metastases causing complete block. Per cent in parentheses

	No. of cases
Breast	20 (25.6)
Lung	11 (14.1)
Prostate	10 (12.8)
Kidney	9 (11.5)
Melanoma	3 (3.8)
Colon	3
Myeloma	3
Head and neck	3
Other sites	11
Unknown	5 (6.4)

Table 3

Results of irradiation of epidural metastases

Before irradiation	After irradiation				No. of cases
	I	II	III	IV	
I	15	10	5	4	34
II	1	11	4	3	19
III	0	1	13	4	18
IV	0	0	0	7	7
Total	16	22	22	18	78

Table 4

Results after irradiation correlated to nature of primary tumor

Before irradiation	After irradiation			No. of cases
	I+II	III	IV	
Breast				
I+II	10	3	2	15
III	1	4	0	5
IV	0	0	0	0
Lung				
I+II	5	0	2	7
III	0	2	2	4
IV	0	0	0	0
Prostate				
I+II	8	1	0	9
III	0	1	0	1
IV	0	0	0	0
Kidney, colon, melanoma				
I+II	5	4	1	10
III	0	5	0	5
IV	0	0	1	1
Myeloma, lymphoma, leukemia, neuroblastoma, seminoma, medulloblastoma				
I+II	2	0	0	2
III	0	1	0	1
IV	0	0	5	5

Table 5

Development of symptoms and signs

Before irradiation	After irradiation			No. of cases
	I+II	III	IV	
No weakness, stable or slow progression for more than a week				
I+II	34	7	5	46
III	0	6	1	7
IV	0	0	0	0
Rapid progression for less than a week				
I+II	3	2	2	7
III	1	7	3	11
IV	0	0	7	7

Table 6

Results of irradiation correlated to site of block

Before irradiation	After irradiation			No. of cases
	I+II	III	IV	
Cord (cervical and thoracic)				
I+II	25	6	7	38
III	0	9	4	13
IV	0	0	7	7
Cauda equina (lumbar)				
I+II	12	3	0	15
III	1	4	0	5
IV	0	0	0	0

Table 7

Results of irradiation on bone lesions

Before irradiation	After irradiation			No. of cases
	I+II	III	IV	
Normal				
I+II	3	1	0	4
III	0	1	2	3
IV	0	0	3	3
Involvement of pedicle(s) only				
I+II	3	2	0	5
III	0	2	0	2
IV	0	0	0	0
Spinal body involvement without collapse				
I+II	8	1	0	9
III	0	1	0	1
IV	0	0	1	1
Spinal body collapse less than 25 per cent				
I+II	13	1	1	15
III	0	5	1	6
IV	0	0	2	2
Spinal body collapse more than 25 per cent				
I+II	10	4	6	20
III	1	4	1	6
IV	0	0	1	1

Structural causes were wedging or dislocation of the spinal body, or presence of bony fragments or herniated intervertebral discs within the spinal canal leading to direct compression of the spinal cord. Tumoral indicated the cause of compression to be the tumor within the intraspinal canal.

The neurologic outcome was evaluated one month after treatment or the longest follow-up period if the patient died before that time. The grouping of the patients after irradiation compared with that before treatment appears in Table 3. Several factors

Table 8

Results of irradiation. Multiplicity of spinal involvement

Before irradiation	After irradiation			No. of cases
	I+II	III	IV	
No or single spinal lesion				
I+II	17	7	1	25
III	0	6	4	10
IV	0	0	5	5
Multiple spinal lesions				
I+II	20	2	6	28
III	1	7	0	8
IV	0	0	2	2

Table 9

Results of irradiation correlated to cause of block

Before irradiation	After irradiation			No. of cases
	I+II	III	IV	
Tumoral				
I+II	27	4	2	33
III	0	8	2	10
IV	0	0	6	6
Structural				
I+II	10	5	5	20
III	1	5	2	8
IV	0	0	1	1

Table 10

Results of repeat myelography

Before irradiation	After irradiation			No. of cases
	I+II	III	IV	
Incomplete block				
I+II	14	4	1	19
III	0	6	0	6
IV	0	0	3	3
Persistent complete block				
I+II	9	3	3	15
III	1	1	2	4
IV	0	0	0	0

Table 11

Extent of metastatic disease in 78 patients. Per cent in parentheses

	No. of cases
No metastasis, other than at block	14 (17.9)
Systemic bone metastasis and block	33 (42.3)
Soft tissue* metastasis	18 (23.1)
Soft tissue* and systemic bone metastasis	13 (16.7)

*Lung (n=14), liver (n=14), brain (n=8), CSF (n=6; sample from myelography), pleura (n=5), other (n=2; adrenal 1, testis 1).

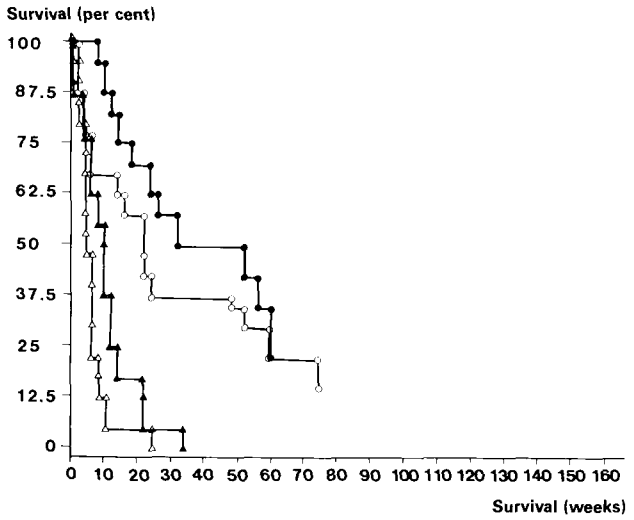
were analyzed that influenced the neurologic outcome after treatment. These include pathologic type (Table 4), rapidity of onset (Table 5), level and extension of block (Table 6), spinal changes demonstrated at spine radiography (Tables 7, 8), cause of compression of the spinal cord or cauda equina (Table 9), and results of repeat myelography (Table 10). All paraplegias appeared in the patients with cord lesions but not with cauda equina lesions.

Only 10 patients had normal spine films and 7 disclosed only involvement of the pedicles (Table 7). The multiplicity of spinal involvement did not influence the outcome (Table 8).

Forty-seven patients were evaluated with repeat myelography 1 to 30 days after the first myelography (8 during treatment). Most of the patients underwent repeat myelography utilizing the residual pantopaque which was introduced at the first myelography, but some required a re-injection of pantopaque because of an insufficient amount of contrast medium in the subarachnoid space. Twenty-eight patients had relief of the complete block, resulting in complete or partial block, the causes of compression of the spinal cord or cauda equina being tumoral in 20 and structural in 8. Nineteen patients had persistent complete block at the same level as at the first myelography; in these cases the block was tumoral in 7 and structural in 12. The repeated myelography results and the respective outcome appear in Table 10.

Seven patients underwent decompressive laminectomy during or after completion of the radiation therapy. The laminectomy was indicated because of increasing neurologic deficits, intractable pain and persistent myelographic block. Six of 7 patients (1 Group I, 3 Group II, 2 Group III) had benefit from the decompressive laminectomy and changed to Group I or II. One patient in Group III remained in the group postoperatively.

The extent of the metastatic disease is shown in



Survival of patients with spinal epidural metastasis according to the ambulatory status after treatment. Ambulatory without support (●), ambulatory with support (○), non-ambulatory (▲), paraplegia (△).

Table 11. Cytology of the cerebrospinal fluid drawn at the myelography was routinely carried out. Six cases (7.7%) had malignant cells in the CSF.

In June 1981 62 patients were known to be dead, 9 to be alive, between 54 and 155 weeks after the treatment. Seven patients were lost to follow-up. Cumulative proportion survival curves in each group of the spinal epidural metastases classified by the ability of ambulation after treatment (7 after laminectomy) are illustrated in the Figure; 18 patients belonged to Group I, 23 patients to Group II, 19 patients to Group III, and 18 patients to Group IV. The median survival after myelography of the respective groups was 52.7 weeks in Group I, 21.4 weeks in Group 2, 9.3 weeks in Group 3, and 4.6 weeks in Group 4. The cause of death was known in 41 patients. The most common cause of death was systemic spread of the malignant disease which was confirmed by clinical signs or postmortem examination. The other known causes of death were: 10 of brain metastases, 4 of disseminated intravascular coagulopathy or gastrointestinal hemorrhage, 5 of sepsis, 2 of myocardial infarction, and 1 of pneumonia.

Discussion

This relatively large series, specifically dealing with epidural spinal metastases with a myelographic complete block, revealed several important factors possibly predicting the neurologic outcome of the patients after non-surgical treatment with irradiation and high doses of dexamethasone. The present results may be different from previously reported series with a similar treatment protocol since others included those with incomplete block (MONES et coll. 1966, KHAN et coll. 1967, FRIEDMAN et coll. 1976, GREENBERG et coll., YOUNG et coll.).

The status of the patient before treatment affected the outcome; those who were unable to walk or were paraplegic remained so after the treatment. Particularly, paraplegic patients benefited the least. This observation was supported in the literature by those using either surgical or non-surgical treatment (WRIGHT, HALL & MACKAY 1973, MARSHALL & LANGFITT, BRUCKMAN & BLOOMER, GREENBERG et coll., SHAW et coll.). Whereas the patient who was able to walk with or without assistance remained so in 70 per cent of the present series. However, 7 (13%) of these 53 patients became paraplegic following the treatment.

The nature of the individual tumor was another factor influencing the neurologic outcome. Patients with metastases from a prostate carcinoma had the best outcome; reports on such patients treated surgically have also shown excellent results (WILD & PORTER, MERRIN et coll. 1976). However, the patients whose primary sites were the colon or kidney and those with melanoma which was resistant to radiation often developed neurologic deterioration during or after the treatment. Metastases from breast carcinoma have been considered to be good clinical responders to irradiation (GREENBERG et coll.). However, the present series indicated that 30 per cent became non-ambulatory; the majority of these patients had associated bony destruction and the cause of compression of the spinal cord was structural. The high radiation sensitivity of tumors arising from the hematopoietic tissues, such as leukemia, lymphoma or myeloma, is well known (MILLBURN et coll. 1968, BRUCKMAN & BLOOMER) and in these patients radiation therapy is of value (FRIEDMAN et coll.). However, paraplegia rarely responded to irradiation or surgical decompression (WRIGHT, SHAW et coll.). This is also applicable to the other tumors sensitive to radiation, such as seminoma, medulloblastoma or neuroblastoma.

The rapidity of progression and longevity of duration of symptoms may be an indicator of the outcome. Acute progressive symptoms are associated with poor compensation of the spinal cord to either acute proliferation of the neoplastic cells or acute

spinal structural changes. Cases with more rapid progressive symptoms had a poorer neurologic outcome in the present series, as in previous reports (WILD & PORTER). Also, the presence of urinary bladder dysfunction was a less favorable sign (WILD & PORTER, BANSAL et coll. 1967, KHAN et coll., SHAW et coll.).

The nature of the block and associated spinal abnormalities are important. Patients with cord lesions had a poorer outcome than those with cauda equina lesions, particularly those with high thoracic lesions (WILD & PORTER, WHITE et coll., BATEN & VANNUCCI 1977). Associated spinal changes, such as compression fracture or dislocation, and presence of bony fragments in the spinal canal which causes structural compression on the cord, were featured to produce refractory response to radiation therapy, since theoretically, the osseous cause of compression did not respond to radiation therapy. These results were comparable to those of the repeat myelographic results: 74 per cent of the comlete block by tumoral causes whereas only 40 per cent of those by structural causes changed after treatment to incomplete block. The reopening of the spinal subarachnoid space, however, did not necessarily coincide with the ability to walk after treatment. One-half of the patients with an incomplete block disclosed at repeat myelography and 47 per cent of those with a persistent block were unable to walk or were paraplegic. Acute myelographic improvement may be due to the irradiation, but substantial use of dexamethasone probably played a major role.

Most important is a prompt shrinkage of the tumor mass. Since the majority of carcinomas do not respond immediately to irradiation, probably the rapid myelographic improvement within a few days is secondary to decrease of the spinal cord edema due to the administration of dexamethasone. Multiple publications exist supporting the efficacy of adrenal corticoid hormone to improve, though temporarily, the neurologic symptoms of human patients or experimental animals with cord compression due to spinal epidural metastases (CANTU 1968, MARSHALL & LANGFITT, USHIO et coll. 1977a, BRUCKMAN & BLOOMER, GILBERT et coll. 1978). This is attributed to the decrease of cord edema and possibly oncolytic effects of the adrenal cortical hormone (POSNER et coll. 1977).

Repeat myelography not only demonstrates the response to the treatment, but the extent of the block and the exact location of the mass in the spinal canal may also be accurately evaluated.

The data revealed a good correlation of survival to the ambulatory status after treatment of the respective patient: the patient with better ability to walk lived longer, while the bedridden patients, particularly when paraplegic, had extremely poor survival. Sixty per cent of all patients with systemic bone metastasis died 6 months after diagnosis of a fracture in a bone destruction (NUSSBAUM et coll. 1977). SHAW et coll. reported that 70 per cent of the surgically treated patients with epidural metastases died within 6 months. Irrespective of the presence of systemic metastases, other than spinal or epidural space involvement, those who were non-ambulatory or paraplegic had shorter survival than ambulatory patients (APUZZO et coll.). This result may not only be due to less intensive treatment, but also to associated complications, such as infectious processes from an enduring urinary catheter or decubitus, neurodynamic ileus and thrombophlebitis secondary to prolonged immobilization, and possibly psychologic depression. However, prolonged survival, more than 5 years, in paraplegic patients due to metastatic spinal tumor was reported by JAMESON in 1974 (the majority of his patients had Hodgkin's lymphoma, myeloma, or carcinoma of prostate and breast). Among surgically treated patients, survival of those with lymphoreticular malignancy or myeloma was best, followed by breast and prostate carcinomas, while those with lung tumors were worse (WILD & PORTER, BANSAL et coll., WHITE et coll., USHIO et coll. 1977b). It is certain that metastases to vital organs such as the brain, liver and lung limit the patient's life expectancy.

Although RODRIQUEZ & DINAPOLI stated that it is extremely rare to have both epidural and intradural carcinoma concomitantly, 6 of the present patients had malignant cells in the CSF (2 with breast carcinoma, 2 with prostate, 1 with oat cell of the lung and 1 with head and neck carcinoma). The presence of the malignant cells in CSF may be related with coincidental meningeal spread from the primary tumor or dural involvement of the epidural tumor extending into the subarachnoid space.

Based upon the results of the present series, it may be concluded that radiation therapy may be indicated for patients with a stable neurologic condition, a tumoral cause of the compression of the spinal cord, subtle or no spinal bony changes, and tumors responsive to radiation such as hematopoie-

tic, prostate or breast neoplasms. The systemic condition of the patient should be carefully evaluated. In the case of coexisting multiple systemic metastases to vital organs or hematogenous metastasis of lung carcinoma (MARSHALL & LANGFITT, GILBERT et coll.) in which a short survival time is expected, surgical treatment is not in the patient's best interest. Evidence of bone marrow depression or hypercalcemia discourages surgical decompression.

Patients with acute progressive disease, but not paraplegic, the major cause of compression being structural, with tumors non-sensitive or non-responsive to radiation, and in good systemic condition, are candidates for surgical decompression. In children, metastases should be treated intensively since they often improve dramatically after surgical decompression (TRAGGIS et coll. 1977). The patient who deteriorates acutely during or after irradiation should be considered for surgical decompression if systemic conditions are acceptable and prolonged survival is expected (MARSHALL & LANGFITT). However, it must be remembered that surgical procedures are often complicated by delayed wound healing, wound dehiscence, and postoperative infection after irradiation. Pre-existing spinal instability may progress after radiation therapy, leading to a severe kyphosis and neurologic deficits, even though the metastatic disease is controlled.

Once surgical decompression is planned, extensive decompression of the spinal cord should be performed along with the spinal stabilization. Computed tomography is useful to disclose bone destruction and the presence of a para spinal mass, and to establish a surgical plan (GIANNOTTA & KINDT 1978, RODRIQUEZ & DINAPOLI). Conventional laminectomy may lead to further spinal instability, acute posterior shift of the spinal cord due to the ventrally located mass (either tumor or osseous segment), or incomplete decompression of the spinal cord. The laminectomy should include resection of the diseased articular facets, pedicles and part of the vertebral bodies. The posterior-lateral portion of the vertebral bodies are readily accessible posteriorly once articular facets and pedicles are resected (DOHN 1981). Underlying spinal nerve roots should be decompressed to relieve pain associated with root compression. If the tumor is localized in the vertebral body or ventral to the spinal cord (incidence is low, HALL & MACKAY), an anterior approach to resect the affected vertebral body would be chosen. Several reports indicated that trans-thoracic vertebral body resection significantly improved the results (LARSSON 1979, HARRINGTON 1981). The main concern after extensive decompression either dorsally or ventrally to the cord, is postoperative instability of the spinal column. Currently, available techniques using Harrington rods, methylmethacrylate fusion or autogenous bone grafts will counter these problems (DUNN 1977, BLACK 1979, LARSSON, HANSEBOUT & BLOMQUIST 1980).

Despite increasing efficacy of multi-modal treatments of malignant tumors, the prognosis of patients with systemic metastases is generally poor, given that survival of these patients is limited an extensive surgical procedure may be unacceptable. PARRISH & MURRAY (1970) stated that the patient with a fracture in a pathologic bone is a candidate for surgery, if the total life expectancy is 6 weeks or more. Particularly, patients with spinal metastasis leading to a major functional disturbance should be carefully evaluated and selection of treatment modes should be made individually.

In conclusion, complete spinal block secondary to epidural metastasis requires immediate medical attention. After confirmation of the spinal block by ascending and descending myelography, a quick decision should be made to treat these patients either with irradiation or surgical decompression. High doses of dexamethasone improved coexisting spinal cord edema (CANTU, MARSHALL & LANGFITT, POSNER et coll., USHIO et coll. 1977a, b, BRUCKMAN & BLOOMER, GILBERT et coll.).

SUMMARY

Myelography was performed in 535 patients at the Memorial Sloan-Kettering Hospital from January 1979 to December 1979. In 110 cases a complete block was demonstrated and of these, 78 had epidural metastases. A uniform treatment was applied using radiation therapy and high dose steroid. The neurologic outcome for each patient was evaluated, correlating pre-treatment neurologic status, pathologic type, nature of block (level, structural versus tumoral), and result of repeat fluoromyelography. Only 2 patients improved, but 11 became completely paraplegic. The survival was influenced by the ambulatory status after treatment (median survival: 52.7 weeks in the ambulatory group and 4.6 weeks in the paraplegic). Based on this series, rational approach and management of complete block secondary to spinal epidural metastases are discussed.

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