Epidural Spinal Cord Compression from Metastatic Tumor: Diagnosis and Treatment

Robert W. Gilbert, MD, Jae-Ho Kim, MD, and Jerome B. Posner, MD

The clinical findings in 130 consecutive cases of spinal cord compression by metastatic extradural tumors were analyzed. These 130 patients were combined with a previous survey of 105 patients to compare the effectiveness of radiation therapy (RT) alone with that of surgical decompression followed by RT. Ambulation after treatment was considered a successful outcome. The most common primary tumors producing spinal cord compression were (in order) breast, lung, prostate, and kidney. In 68% of these tumors the thoracic region was involved. Pain was the primary symptom in 96% of the patients, while motor or sensory deficits (or both) were found in 82% of them. Therapy consisted of surgery and RT in 65 patients and RT alone in 170 patients. There were no differences in outcome between those treated by surgery combined with RT and those managed by RT alone. Patients with radiosensitive tumors and those ambulatory at the onset of treatment benefited whether treated by surgery or by RT. Seventy-five percent of living patients who improved from treatment remained ambulatory at 6 months, and approximately 50% of living patients were ambulatory at 1 year. We conclude that RT without decompressive laminectomy is as effective as decompressive laminectomy in treating epidural spinal cord compression from systemic cancer.

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Metastatic epidural tumor compressing the spinal cord is a common neurological complication of cancer [4, 24]. At Memorial Sloan-Kettering Cancer Center (MSKCC), a 560-bed cancer hospital, there are 40 to 50 new cases of symptomatic epidural spinal cord compression annually. If not treated, the symptoms progress inexorably to complete loss of spinal cord function below the compression site. The treatment of metastatic epidural spinal cord compression is unsatisfactory, however. Most texts and reports recommend immediate decompressive laminectomy even though that procedure produces clinical improvement in only 30 to 40% of the patients [6, 25, 37, 40]. Some investigators advocate radiation therapy (RT) as the primary treatment; good results have been reported, particularly in highly radiosensitive tumors (e.g., lymphoma) [12, 25, 29].

We have undertaken a retrospective analysis of 235 patients treated at MSKCC in the last several years in order to review the clinical findings and to compare the results of decompressive laminectomy followed by RT with those of RT alone. Our results indicate that RT alone is as effective as decompressive laminectomy.

Materials and Methods

Two separate retrospective analyses of patient records were done at two different times. An earlier series, consisting of 109 episodes of spinal cord compression in 105 patients evaluated between 1964 and 1970, has been reported in abstract form by Raichle and Posner [27]. The present series consists of 130 consecutive patients evaluated by neurologists at MSKCC from January, 1974, through December, 1976. The clinical diagnosis was supported by myelographic evidence of complete or almost complete (>80%) extradural block in all 130 patients of the recent series and in all but 2 patients in the old series. In most patients, when a complete block was present on lumbar myelogram, cisternal myelography was also performed to locate the upper margin of the tumor. Pantopaque was used in most patients, but in a few, Pantopaque lumbar myelography was combined with metrizamide cisternal myelography [13] so that the contrast material above the block would be absorbed. In all patients, contrast material was left in the subarachnoid space so that follow-up myelography could be performed without repeated lumbar punctures.

In the recent series, dexamethasone (16 mg daily in divided doses) was started at the time of diagnosis. In the old series, prednisone (60 mg daily in divided doses) was usually given, but in that series the use of steroid drugs and their dosage varied from patient to patient. Definitive therapy was begun as soon as possible after the diagnosis was established and consisted of either RT alone or decompressive laminectomy followed postoperatively by RT. There was some variation in the dose of RT, but in all the patients in the recent series who had not peviously been irradiated to the area, a tumor dose of 400 rads daily for the first three days was given to a port 8 cm wide encompassing two vertebral

From the Departments of Neurology and Radiation Therapy, Memorial Sloan-Kettering Cancer Center, and Departments of Neurology and Radiology, Cornell University Medical College, New York, NY.

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Address reprint requests to Dr Posner, 1275 York Ave, New York, NY 10021.

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bodies above and below the block. A single posterior field was treated, and the tumor dose was calculated at a depth of 6 to 8 cm. The first dose was given immediately (30 min to 2 hr) following myelographic definition of the lesion. After the first three doses the patient was treated with 200 rads daily to a total dose of 2,000 to 4,000 rads, depending on the nature of the tumor and the history of previous RT. Decompressive laminectomy was carried out by the usual techniques with an attempt to remove as much tumor as feasible. RT was generally begun five days after surgical decompression. At the end of the course of RT, steroids were tapered to the patient's tolerance level but maintained or increased if neurological symptoms worsened. All surgically treated patients received RT in the postoperative period except for a few who had been irradiated previously and could receive no further RT to the involved area.

No predetermined criteria were applied to decide which patients would receive RT only and which would have surgical decompression prior to RT. In each case, the decision to operate or irradiate was based on the clinical judgment of the neurologist or neurosurgeon seeing the patient. Thus, this study was not controlled and the patients were not randomized. Certain general rules, however, were followed: If the patient was not known to have an underlying cancer, or if the nature of the primary cancer was not established (10 cases), surgical decompression was carried out with the aim of establishing a definitive diagnosis as well as treating the compressed spinal cord. Patients with lymphoma usually received RT because of the known radiosensitivity of that tumor. Patients who were paraplegic at the time they were first seen usually received RT since the chances of recovery after surgical decompression were so low.

The patients were divided into three grades, based on motor function: *Grade 1* patients were ambulatory, with or without weakness of the lower extremities or ataxia. *Grade 2* patients were not ambulatory but were able to lift their legs when recumbent. *Grade 3* patients were paraplegic or were unable to move their legs against gravity. Successful treatment was defined as ability of the patient to walk when discharged from the hospital, usually two to four weeks following the beginning of therapy. Sphincter function, sensation, and pain were not considered in determining the success of therapy because the retrospective chart review did not permit accurate assessment of minor improvement in those symptoms. On the other hand, the patient's ability to walk was clearly documented in the chart.

In the old series, epidural lesions involving the cauda equina, below the L1 vertebral body, were not included in the definition of spinal cord compression. Because in both series there were no differences in outcome between spinal cord and cauda equina compression, in the recent series the two are considered together under the term *epidural spinal cord compression.*

Results

Primary Tumors

Table 1 lists the primary cancers causing metastatic epidural spinal cord compression. The incidence of primary tumors generally reflects the overall tumor incidence at MSKCC, with some exceptions: Gastrointestinal tumors, i.e., carcinoma of the colon and stomach, are underrepresented because such tumors metastasize to vertebral bodies less commonly than do carcinomas of the lung, prostate, and breast [33]. Lymphomas and myelomas are slightly overrepresented because of the frequent paravertebral lymph node localization of the former and the high incidence of vertebral body involvement in the latter. Lymphomas, however, were less frequent in the recent series because more patients with lymphoma now receive total nodal irradiation, which includes the spine, as their initial treatment [12].

Table 1. Primary Tumors Causing Epidural Spinal Cord Compression

Primary Tumor	Old Series (1964–70)	Recent Series (1974–76)	Total
Breast	20	28	48
Lung	9	21	30
Prostate	7	14	21
Kidney	5	12	17
Lymphoma	18	8	26
Myeloma	1	8	9
Melanoma	1	7	8
Sarcoma	16	6	22
Head and neck	8	6	14
GI	4	5	9
Embryonal cell carcinoma	0	5	5
Female reproductive tumor	4	1	5
Neuroblastoma	5	0	5
Miscellaneous (thyroid, bladder, thymus, etc)	7	5	12
Unknown primary	0	4	4
Total	105	130	235

The interval between diagnosis of cancer and development of spinal cord compression varied from 0 to 19 years in the recent series of 130 patients. Ten patients presented with spinal cord compression as the initial symptom of cancer; the tumors included lymphoma in 4, myeloma in 3, and teratoma, carcinoma of the prostate, and carcinoma of the lung in 1 patient each. In the other 120 patients a primary diagnosis of cancer had been established weeks to years before. The longest interval between diagnosis of the primary neoplasm and onset of neurological symptoms was 19 years in a patient with carcinoma of the breast. Two other patients with carcinoma of the breast developed epidural spinal cord compression 12 and 14 years following mastectomy. Two patients with chondrosarcoma developed cord symptoms 13 years after their initial operation.

There were 80 male and 50 female patients in the recent series. The average age was 58 years with a

Table 2. Site of Spinal Cord Compression by Primary Tumor in Recent Series

Primary Tumor	Cervical		Thoracic		Lumbosacral		Total
	No.	%	No.	%	No.	%	No.
Breast	4	14	22	79	2	7	28
Lung	8	38	12	57	1	5	21
Prostate	2	14	10	71	2	14	14
Kidney	1	8	9	75	2	17	12
Lymphoma	1	13	5	63	2	25	8
Myeloma	1	13	5	63	2	25	8
Melanoma	1	14	4	57	2	29	7
GI	0	0	2	40	3	60	5
Others	2	7	20	74	5	19	27
No. of patients	20	15	89	68	21	16	130

range of 4 to 85 years (peak incidence, 56 to 60 years). The site of epidural tumor defined by the vertebral body was cervical in 20 (15%), thoracic in 89 (68%), and lumbar or sacral in 21 (16%) (Table 2). Twenty-two of the 130 patients had compression at more than one site at some time during the course of their illness. The site of compression varied somewhat with the primary cancer. Colon cancers metastasized more frequently to the lumbosacral spine, and lung and breast tumors to the thoracic spine (Table 2).

Clinical Findings

Four symptoms characterized the clinical features of spinal cord compression: pain, weakness, autonomic dysfunction, and sensory loss, including ataxia (Table 3). Symptoms were present for 5 days to 2 years (median, 2 months) before the diagnosis was established by myelography.

PAIN. The initial symptom in 125 of the 130 patients (96%) was pain (Table 3). In 12 patients, pain was the only symptom present when the diagnosis was established and treatment was begun. In the 113 patients in whom pain was the initial symptom but who later developed other neurological symptoms or signs, pain preceded the other symptoms by 5 days to 2 years (median, 7 weeks).

Table 3. Signs and Symptoms of Epidural Spinal Cord Compression in 130 Patients

Sign/Symptom	First Symptom		Symptoms at Diagnosis	
	No.	%	No.	%
Pain	125	96	125	96
Weakness	2	2	99	76
Autonomic dysfunction	0	0	74	57
Sensory loss	0	0	66	51
Ataxia	2	2	4	3
Herpes zoster	0	0	3	2
Flexor spasms	0	0	2	1

Pain was of two types: local and radicular. Almost all the patients who experienced pain complained of local pain, usually close to the site of the lesion subsequently identified at myelography. The incidence of radicular pain varied with the location of the tumor, being more common in cervical (79%) and lumbosacral (90%) regions and less common in thoracic (55%) area. Radicular pain was either unilateral or bilateral when it occurred in the cervical or lumbosacral areas, but almost always bilateral when it occurred in the thoracic area. Thus, 47 patients complained of a band or girdle of pain or tightness radiating from back to front around the chest or abdomen. Radicular pain, when present, usually localized the lesion within one or two vertebral segments.

In occasional instances the site of the pain was misleading. Local pain occasionally occurred a distance from the site of cord compression, usually because other vertebral bodies were involved by cancer, causing independent pain. In rare instances radicular pain was falsely localizing, with the typical thoracic or abdominal band of pain representing a false localizing sign of cervical cord compression [14]. We did not encounter in this series any cases of "cervical sciatica" [18].

Several patients had pain that was neither prominent nor clearly localized. In such cases, localization could be elicited by various maneuvers in the examination. Vertebral tenderness at the site of spinal cord compression was specifically noted in 42 of the 130 patients. Neck flexion often produced pain of a local or radicular nature at the site of the lesion, particularly if the lesion was thoracic. Straight leg raising at times produced local or radicular pain in the lumbar or thoracic area, also helping to localize the lesion.

The pain was usually constant, relieved to some degree by analgesic agents and exacerbated by movement, coughing, sneezing, or the Valsalva maneuver.

In the majority of patients the quality of the pain was typical of that described for epidural tumors and different from that of herniated intervertebral discs [19]. The pain became worse when the patient was recumbent, thus causing him to get up several times during the night and frequently to sleep in a sitting position.

WEAKNESS. In 2 patients, 1 with chondrosarcoma and 1 with carcinoma of the breast, weakness was the first symptom of spinal cord compression. By the time of diagnosis, 99 of the 130 patients (76%) complained of weakness. On neurological examination, however, 113 patients (87%) were weak. The degree of weakness at the time of presentation is indicated in Table 4, and the old and recent series are compared. The greater proportion of grade 1 patients in the recent series suggests that increased awareness of the problem of spinal cord compression by oncologists has led to earlier neurological consultation and diagnosis. Still, however, 15% of these patients are paraplegic at the time the diagnosis is first suspected. Of the 19 patients in the recent series who were paraplegic at the time of diagnosis, 9 had experienced "rapid" onset of paralysis (less than 48 hours). The primary tumors in these 9 patients included carcinoma of the prostate in 3, carcinoma of the lung in 2, and carcinoma of the ovary, breast, unknown primary, and head and neck in 1 each. All these patients had pain prior to the onset of paraplegia. Four of the 9 patients were treated by decompressive laminectomy; hemorrhagic tumor was not found.

SENSORY LOSS. Sensory complaints were never a presenting symptom in this series. By the time of diagnosis, however, numbness or paresthesias were complaints in 66 of the 130 patients (51%). Sensory deficits on examination were noted in 101 patients (78%). In 84 patients (65%) the upper limits of the sensory disturbance corresponded to within two vertebral bodies of the site of the lesion. In only 3 patients was the sensory level misleading: in 2 it was far below the site of the lesion, and in 1 it extended several segments above the lesion. Sensory loss to pinprick was as frequent as that to vibration or position. Although no attempt was made to quantify the sensory loss, its severity tended to parallel that of motor weakness. In patients who were paraplegic, pinprick sensation, vibration, and position loss were usually complete, although some appreciation of gross touch (i.e., squeezing the leg lightly with one's whole hand) was frequently felt even by totally paraplegic patients.

AUTONOMIC DYSFUNCTION. In no instance was autonomic dysfunction the presenting complaint. However, bladder and bowel dysfunction were present in 74 patients (57%) when they were first seen. Autonomic dysfunction in the absence of motor and sensory loss was found in a few patients whose lesions subsequently were located at the T10 to T12 vertebral bodies. Characteristically, these patients complained of pain, sometimes with radiation into the groin or low abdomen, but without weakness or sensory loss, and they presented with rapid onset of urinary retention and severe constipation. The neurological examination was usually normal except for a lax anal sphincter, an enlarged bladder, and some vertebral tenderness over the lower thoracic and upper lumbar area. The myelogram usually revealed complete block between the T10 and T12 vertebral bodies.

Autonomic dysfunction was an unfavorable prognostic sign. Of 65 patients with urinary incontinence or retention at the time of diagnosis, 43 (66%) either were or became nonambulatory, whereas this was true of fewer than 50% of the patients without autonomic dysfunction.

OTHER CLINICAL FEATURES. Unusual clinical features occasionally made the diagnosis difficult. Ataxia without pain or motor or sensory loss was a presenting complaint in 2 patients. In 7 additional patients severe gait ataxia was the most striking sign on examination. In these patients, proprioceptive loss under direct

Table 4. Grade of Weakness at Time of Diagnosis

	Old Series (109 cases)[a]		New Series (126 cases)[b]		Total (235 cases)	
Grade of Weakness	No. of Patients	%	No. of Patients	%	No. of Patients	%
Grade 1 (ambulatory)	18	17	62	49	80	34
Grade 2 (paraparetic)	70	64	46	37	116	49
Grade 3 (paraplegic)	21	19	18	14	39	17

[a] 105 patients; 4 patients suffered two separate episodes.
[b] 130 patients; 4 were not treated.

examination was absent or mild and not sufficient to account for the striking gait difficulties. One such patient was subjected to diagnostic tests to assess cerebellar disease before spinal cord compression was recognized as the causative factor.

In most cases the spinal cord signs were relatively symmetrical. Asymmetrical cord signs suggesting the Brown-Séquard syndrome were present in 3 of our patients. In all 3, however, careful examination revealed signs of bilateral cord disease—usually bilateral extensor plantar responses—and occasionally bilateral proprioceptive loss.

Three of our patients were affected with herpes zoster at the site of extradural cord compression. This unusual symptom has been reported before [4] and is believed to be due to activation of a latent virus by tumor involvement of the posterior root ganglion.

Myelographic Findings

Lumbar myelograms were performed in all 130 patients of the recent series. Complete block to the passage of contrast material was found in 97 patients and a high-grade partial block in 33. In most patients with complete block, cisternal myelography was performed in order to identify the upper end of the block. The block extended one or two segments in the majority of patients but occasionally was considerably longer, in which case the differentiation of a long lesion from a second, separate lesion was not possible. The block was discovered to be at the site of a vertebral body involved by tumor in 85% of the patients, but no bony involvement could be identified at the site of the epidural block in the remainder. In all instances in which a block was encountered, the myelographic contrast material was left in the subarachnoid space for repeat myelograms to assess the results of treatment (Figs 1, 2). In those patients who received RT to the lumbar and lumbosacral areas the radiopaque substance was sometimes found to be fixed and immobile on attempted repeat myelography. In these patients a radiological diagnosis of arachnoiditis was made, but we encountered no patients in whom the clinical signs and symptoms of adhesive arachnoiditis were present.

Treatment

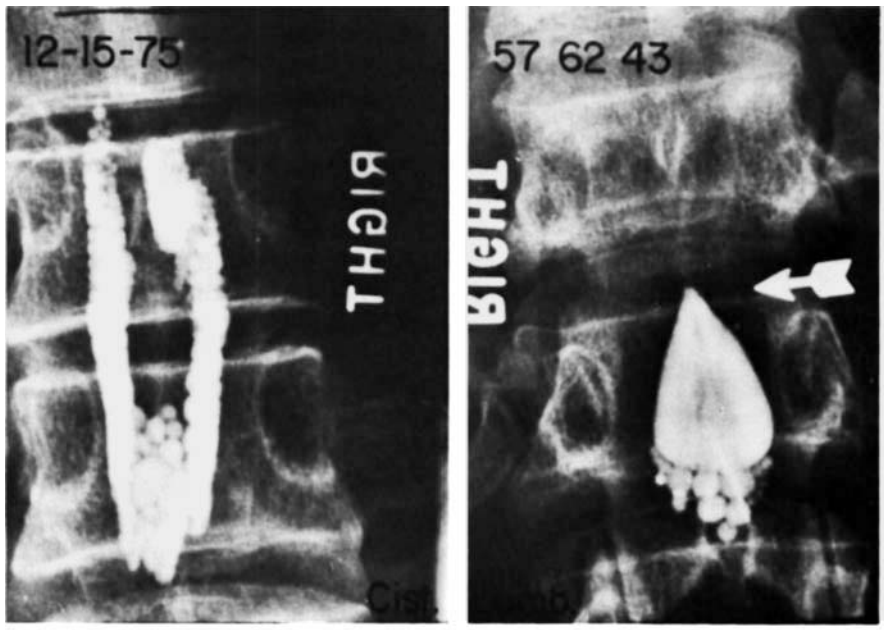
Of the 235 patients in the two series, 65 underwent surgical decompression followed by irradiation and 170 were treated by RT without surgery. The reasons for surgical decompression in the 31 patients in the recent series included uncertain diagnosis in 8, prior RT in 7, rapid progression of symptoms in 9, and other reasons in 7.

The results of treatment are summarized in Table 5. The old and recent series are grouped together since there was no significant difference between them. (Statistical analysis of patient groups was performed by the chi-square test except where otherwise noted.) After treatment, 46% of the patients operated on walked, compared with 49% of those who had irradiation. There was no significant difference between the two treatment groups. Those patients who were ambulatory at the onset of treatment had the best outcome, whether treated by surgery or RT, and those patients who were paraplegic at the onset of treatment generally did poorly. Only 2 of 39 paraplegic patients (<5%) became ambulatory. However, there was no significant difference between those patients who had surgical decompression and those treated by RT, even when each grade of weakness at the onset of treatment is considered individually.

Table 5 also compares the results of treatment in those patients whose primary tumors fell into a group

Table 5. Short-Term Results of Treatment for Epidural Spinal Cord Compression

	Total Series (235 cases)				Radiosensitive Tumors (54 cases)				Less Radiosensitive Tumors (181 cases)			
	Surgery + RT		RT Only		Surgery + RT		RT Only		Surgery + RT		RT Only	
Pretreatment Condition	No. Ambulatory / No. Treated	%	No. Ambulatory / No. Treated	%	No. Ambulatory / No. Treated	%	No. Ambulatory / No. Treated	%	No. Ambulatory / No. Treated	%	No. Ambulatory / No. Treated	%
Grade 1 (ambulatory)	14/22	64	46/58	79	5/6	83	10/12	83	9/16	56	37/47	79
Grade 2 (paraparetic)	15/33	45	37/83	45	5/8	63	14/19	74	10/25	40	22/64	34
Grade 3 (paraplegic)	1/10	10	1/29	3	1/1	100	1/8	13	0/9	0	0/20	0
Total	30/65	46	84/170	49	11/15	73	25/39	64	19/50	38	59/131	45



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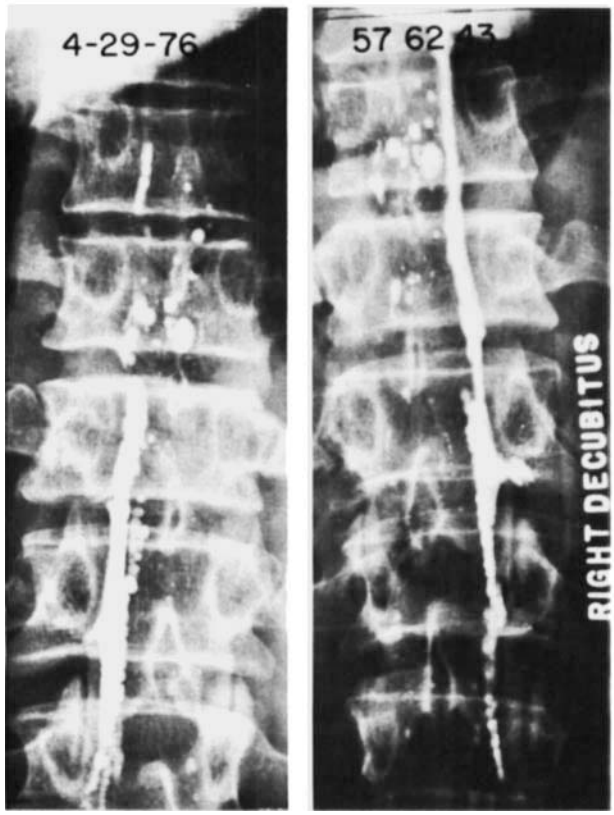

B

Fig 1. Successful resolution of spinal cord compression after radiation therapy. This patient, who had a seminoma of the testis, developed low back pain early in December, 1975. When he was admitted on December 15 he had been unable to walk for 2 days, and myelography (A) revealed an extradural block at both the lumbar (right) *and cisternal* (left) *regions at T11. The symptoms resolved rapidly with steroid and radiation therapy, and he left the hospital fully ambulatory. A repeat myelogram (B) in April, 1976, using the contrast material remaining from the first myelogram, revealed only a minimal extradural mass on the left decubitis film* (left). *The right decubitis film* (right) *was normal.*

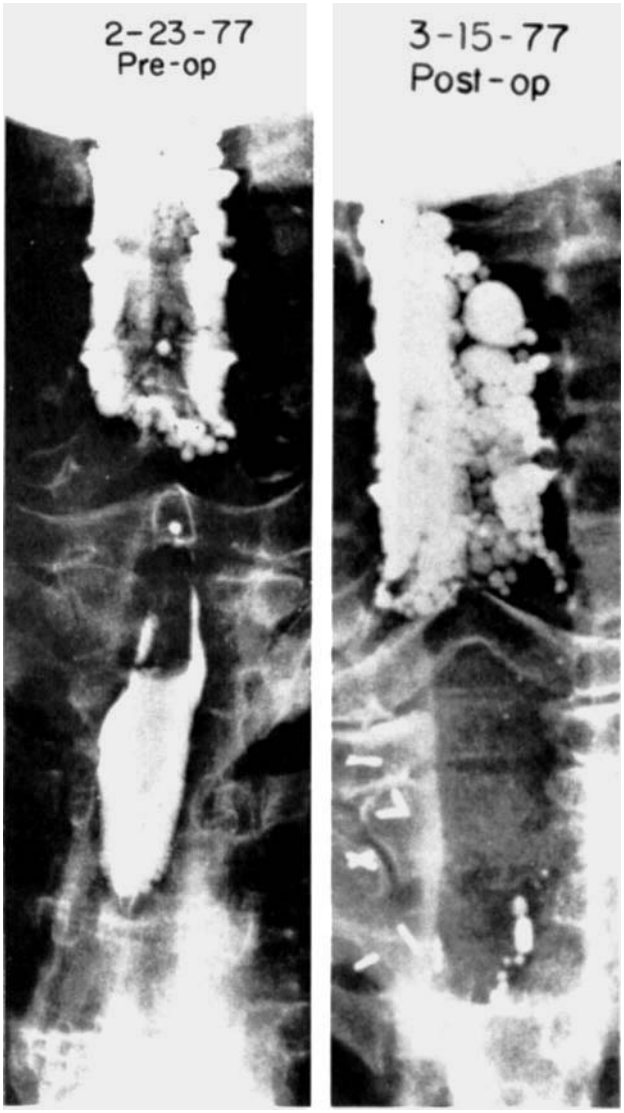

Fig 2. Failure of decompression laminectomy to relieve an extradural block. This 47-year-old man with anaplastic carcinoma of the lower lung developed pain in his upper back and weakness of the lower extremities. Cisternal and lumbar myelography on February 23, 1977 (left) *revealed a complete extradural block from T1 to T3. Because of previous RT to the area, a decompressive laminectomy was performed. A postoperative myelogram* (right) *revealed that the block was still present. The patient was clinically unimproved. He died of his primary disease 10 days later.*

generally considered highly sensitive to RT (i.e., seminoma, lymphoma, myeloma, Ewing's sarcoma, neuroblastoma) and those whose tumors were generally considered less sensitive to RT (carcinomas, melanomas, soft tissue sarcomas). There were 54 patients in the former group and 181 in the latter. Those patients with radiosensitive tumors had a better response whether treatment was decompressive laminectomy followed by RT or RT alone. There was no significant difference between the two treatment groups, however. Those patients whose tumors were considered less radiosensitive had a poorer outcome than the more radiosensitive group whether treatment was by decompressive laminectomy or by RT alone.

Because rapid progression of spinal cord dysfunction is often considered an indication for surgery, we analyzed the results in the 22 patients who had weakness that developed over less than 48 hours (Table 6). Of the 9 patients who underwent surgical decompression, none improved. Of the 13 patients irradiated without surgery, 7 improved. The difference in response was significant ($p < 0.02$ by Fisher's test).

Table 7 illustrates the duration of improvement after the two forms of therapy. Of the 12 surgically treated patients who maintained or regained ambulation, 9 (75%) remained ambulatory for 6 months or longer. Of the 47 patients successfully treated by RT alone, 31 (78%) of those alive after 6 months remained ambulatory. The relapse rate in less than 6 months of 22% in the RT-treated group and 25% in the surgically treated group is not significantly different. At 1 year, 6 of the 11 patients successfully treated by surgery who remained alive were still ambulatory. Thirteen of 28 patients successfully treated by RT alone and still alive remained ambulatory for more than a year. Only 1 of the 12 patients who had successful surgery died of his primary cancer in the first year. Many more patients who had RT alone (17 of 47) died of their primary disease during the year without relapse in their spinal cord signs.

The nature of the primary tumor was more important in determining long-term improvement than was the nature of the treatment. Patients with myeloma, lymphoma, or carcinoma of the breast comprised 26 (65%) of 40 patients who remained ambulatory for more than 6 months, and 14 (74%) of 19 who remained ambulatory for more than a year. The initial response rate of these patients with various primary tumors is presented in Table 8.

In the recent series there was 1 postoperative death, from sepsis, among the 31 operated patients. Thirteen other patients suffered some postoperative complications, including epidural hemorrhage in 2, instability with subluxation of the spine in 4, wound infection in 4, and wound dehiscence or delayed closure in 3.

Table 6. Response to Treatment of Rapidly Progressing Patients

Mode of Treatment	Total No. of Patients	Pretherapy		Posttherapy	
		Grade 2	Grade 3	Grade 1 or 2	Grade 3
Surgery and RT	9	5	4	0	9
RT alone	13	8	5	7	6

Table 7. Duration of Improvement

Duration	Surgery plus RT				RT Alone			
	No. Ambulatory No. Treated	%	No. Ambulatory No. Alive	%	No. Ambulatory No. Treated	%	No. Ambulatory No. Alive	%
Immediate	12/31	39			47/95	49		
≥ 6 mo	9/31	29	9/12	75	31/95	33	31/40	78
≥ 12 mo	6/31	19	6/11	54	13/95	13	13/28	46

Discussion

Extradural spinal cord compression is one of the more common neurological complications of systemic cancer. Barron et al [4] have estimated that 5% of the patients with systemic cancer who come to autopsy have pathological evidence of a tumor invading the extradural spaces. The proportion of intramedullary spinal metastases is less than 1 in 20 [10]. At MSKCC, spinal cord compression is second only to metastatic brain tumor as a cause of structural disease of the nervous system in cancer patients. In addition to being common, spinal cord compression is devastating. Virtually all the patients suffer pain, and, if not successfully treated, all inexorably become paraplegic. However, spinal cord compression per se is not fatal, so many patients live for extended periods. Thus, 30% of the patients in this series were still alive after a year, and 4-year and 5-year survivals after the development of cord compression are known to occur. Major efforts to relieve the signs and symptoms of this complication and reverse or prevent paraplegia are warranted because the disorder is common, serious, and often chronic.

Most physicians treating this disorder assume that surgical decompression is the only logical approach. Thus, most large series evaluating treatment of extradural malignant tumors have been surgical; patients are subjected to laminectomy with or without postoperative RT. These data are summarized in Table 9.

Surgery

Several conclusions concerning surgical decompression can be drawn from Table 9. The overall results are poor. With ambulation as the end-point, most series report less than a 50% response rate. Our own surgical results of 50% are better than any previous series reported except for the 61% of Brady et al [5]. Those patients whose signs of spinal cord compression are least severe recover best. Thus, 58% of our patients who were ambulatory continued to be ambulatory after treatment, whether that treatment was surgical decompression or RT. Only 5% of our patients who

Table 8. Initial Response to Treatment by Tumor Type

Tumor	Surgery plus RT			RT Alone		
	No. of Patients	No. Ambulatory	% Improved	No. of Patients	No. Ambulatory	% Improved
Myeloma	3	3	100	5	3	60
Lymphoma	3	2	67	5	4	80
Breast	1	1	100	26	17	65
Kidney	2	0	0	10	6	60
Lung	5	1	20	16	8	50
Prostate	5	1	20	8	2	25
Melanoma	2	0	0	5	1	20

Table 9. Results of Treatment for Epidural Spinal Cord Compression in Major Published Series

Treatment	Series	No. of Patients	No. Improved (%)	No. Worse (%)	Operative Mortality (%)
Surgical	Mullan 1957 [22]	36	8 (22)	12 (33)	...
decompression	Perese 1958 [23]	30	4 (13)	...	1 (3)
± RT	Barron 1959 [4]	38	11 (29)	7 (18)	...
	Wright 1963 [40]	86	28 (33)	...	...
	Brice 1965 [6]	139	44 (32)	10 (7)	8 (6)
	Smith 1965 [31]	51	13 (25)	7 (14)	2 (4)
	Vieth 1965 [36]	34	13 (38)	3 (9)	3 (9)
	Auld 1966 [2]	41	15 (37)	9 (22)	...
	Bansal 1967 [3]	51	20 (39)	...	...
	Chade 1968 [8]	162	62 (38)	25 (15)	...
	Haerer 1968 [15]	65	20 (31)	2 (3)	...
	White 1971 [37]	226	78 (35)	23 (10)	20 (8.7)
	Posner 1971 [25]	34	17 (50)		
	Hall 1973 [16]	129	39 (30)		
	Brady 1975 [5]				
	Surgery alone	24	7 (29)		
	Surgery + RT	90	55 (61)		
	Present series	65	29 (45)		
RT only	Mones 1966 [21]	41	14 (34)		
	Khan 1967 [17]	82	34 (41)		
	Posner 1971 [25]	75	35 (47)		
	Brady 1975 [5]	19	9 (47)		
	Present series	170	84 (49)		

were paraplegic regained ambulation after therapy, no matter what the therapy. The depressingly low rate of recovery after treatment of a patient who is paraplegic is recapitulated in most series. The apparent exception is the 37% recovery rate from "marked paresis" after surgery plus RT reported by Brady et al [5]. That this rate is much higher than those reported in other series, including our own, may be due to their definition of terms, since their category of marked paresis referred to complete paralysis or paresis to such a degree that patients were unable to support their body weight. This definition would include many of our patients in grade 2 as well as many in the other series who were considered paraparetic rather than paraplegic. Despite these differences, which may explain their better overall outcome, Brady and associates also noted that the more severe the degree of involvement, the less good the recovery. Most series that have taken into account differences between patients treated by decompressive laminectomy followed by RT and those not irradiated postoperatively have reported that RT following operation has a salutary effect on outcome. Wright [40] achieved a 50% ambulatory rate among 17 patients treated with postoperative RT but only 14% in patients treated by surgery alone. Wild and Porter [38] reported that 44% of their patients irradiated after surgery became ambulatory, whereas only 26% of those not irradiated did so. Brady's patients who had surgery alone had a 29% response rate as opposed to 61% with postoperative RT.

Surgical morbidity and mortality also constitute a problem. At one time the prognosis after decompressive laminectomy for epidural metastases was so poor that Elsberg [11] and Shenkin et al [30] considered laminectomy contraindicated in patients with metastatic epidural tumor. As late as 1959, Arseni et al [1] emphasized that surgery was probably useful only for relief of pain, and that paresis and paralysis were rarely improved by operation. Törmä [32], in the largest series to date, 250 cases reported in 1957, concluded that if the patient was known to have extradural metastases from systemic cancer, decompressive laminectomy was not warranted. However, advances in surgical technique and improved postoperative RT have changed this picture [8, 31, 36, 37], and most textbooks discussing the problem currently recommend decompressive laminectomy. Surgical mortality is now low; in our recent series, the 1 death in 31 patients (3%) is the lowest incidence in the literature. Surgical morbidity, however, continues to be an important factor. Mullan and Evans [22] found 12 of 36

operated patients to be worse following surgery; White et al [37] reported 23 of 226 patients to be worse, and Arseni and co-workers [1] considered 60% either worse or unimproved following surgery.

Why are the results of surgical decompression so poor? The reason lies in the anatomy of metastatic spinal cord compression. The majority of epidural tumors arise in a vertebral body [1, 4, 32], invade the epidural space anteriorly, and remain largely anterior to the spinal cord. The vertebral body at the level of the cord compression is often destroyed. This creates a difficult problem for the surgeon attempting decompressive laminectomy. He approaches the tumor posteriorly and is usually unable to remove substantial parts of the mass without damaging the spinal cord. If the cord is not decompressed, worsening compression eventually causes spinal cord infarction, usually within the white matter [20]. There is also the risk of producing an unstable spine, since the anterior elements supporting the spine may already have been destroyed by the tumor, and the surgeon removes the posterior elements. Since most of the tumor remains following decompression, it is not surprising that symptoms persist, that myelographic block often remains (see Fig 2), and that postoperative RT is required to shrink the tumor. Thus, at best, surgical decompression should be thought of as a temporizing measure to buy time while slower but more definitive antitumor therapy is delivered. Unfortunately, our results indicate it does not even accomplish that.

Whether certain groups of patients—e.g., those rapidly developing neurological symptoms, those with tumors less sensitive to RT, or those with involvement of posterior vertebral elements rather than the vertebral body—represent subgroups that respond to both surgical decompression and RT is unclear.

One specific subgroup of patients, those with rapidly progressing neurological dysfunction (< 48 to 72 hours), is particularly controversial. Most authors agree that the more rapid the progression of spinal cord dysfunction, the less favorable the prognosis. In 1968 Chade [8] confirmed this observation and concluded that patients with a short history and rapid progression should not be subjected to surgery. However, most neurosurgeons concur with Wild and Porter's [38] recommendation that "immediate surgical decompression is indicated in cases with progressing paresis." Very little data actually support this contention, however. In recommending surgical therapy for patients with rapid progression, Smith [31] noted significant improvement in only 1 of 9 patients, whereas Mullan and Evans [22] noted "fair" recovery in 1 of 8 such patients. Our data showed that none of 9 patients with rapidly progressing weakness who were subjected to emergency surgery improved, whereas 7 of 13 such patients treated with RT alone improved. These results suggest that patients with rapidly progressing symptoms respond best to RT rather than to surgical decompression.

An additional reason often cited for surgical decompression prior to RT is that RT may increase edema of the spinal cord and thus worsen neurological signs. Hall and Mackay [16] "assumed that radiation therapy initially causes swelling and oedema which in the presence of a complete block may determine paraplegia." Rubin [29], however, in the only extant experimental approach to this assumption, presented compelling evidence in both animals and patients that RT delivered to the spinal cord does not render the cord edematous nor, when delivered in high dose, does it increase the symptoms of cord compression. Our own experimental results [35] as well as the clinical findings reported here support this conclusion.

Radiation Therapy

The nonsurgical treatment of extradural malignant disease has received much less attention in the literature. Mones et al [21] in 1966 reported 41 patients from this institution who were treated with RT. They found that 14 became ambulatory after RT and suggested that this response rate of 34% compared well with the previous surgical series, questioning the need for surgical decompression. Khan et al [17] in 1967 reported 82 patients, 58 of whom had either breast carcinoma or lymphoproliferative disorders. Radiation therapy to their area of epidural cord compression produced a response rate of 42%. Myelograms, however, were not done in most of the patients, and some had RT despite negative myelography. Other RT series have been concerned primarily with the treatment of cord compression by lymphoma. Williams et al [39] reported on 103 patients with lymphomas and found that the patients treated by decompressive laminectomy responded well (75%) but no better than those treated by RT alone (70%). Many of the patients in their series did not undergo myelography. Recently, Friedman et al [12] analyzed 73 patients with malignant lymphomas producing spinal cord compression and found 75% improvement in those treated with RT alone.

Only one other study addresses itself to comparing surgery with RT from the same institution. Brady et al [5], using a somewhat different classification from ours, noted a response rate of 61% in 90 patients treated with surgical decompression followed by RT and compared that with a response rate of 29% in 24 patients receiving decompressive laminectomy alone and 47% in 19 patients receiving RT alone. They concluded that the combination of surgery and RT was likely to yield the best response. These findings differ from ours in that their outcome for the surgical and RT series was much better than our RT alone or

combined surgery and RT. The reason for these differences is not clear, but it may be that their patients who were operated on were in generally better condition than ours (and those previously reported in the literature). The small number of patients in their group having RT alone precludes effective comparison with combined surgery plus RT.

In the absence of a prospective controlled study, the treatment of choice for epidural spinal cord compression from metastatic tumor remains unknown. Even if one were to do a controlled series, questions about the treatment of individual patients with unique problems would still arise. Our data, however, suggest that RT alone is as efficacious as decompressive laminectomy followed by RT. Both treatments at this institution have had as good (or as bad) an outcome as previously reported series, suggesting that it is not a failure of either RT or surgery that yields the results presented.

Are there prospects for improving RT of spinal cord compression? Over the years, radiotherapeutic technology and methods have considerably improved so that more effective tumoricidal doses can be delivered without excessively impairing overlying normal tissues. The use of megavoltage radiation and of the simulator to locate the treatment field precisely have both helped to increase control of local cancer with a reduction of normal tissue complications. More recently, various attempts have been made to improve therapeutic ratios by varying the dose/time fractionation schedules. In our old series (1964–1970), some of the patients were treated using a conventional and repetitive fractionation schedule of 1,000 rads per 5-day week. This may not be the optimal fractionation for any given tumor. It is probably not optimal for spinal cord compression, in which rapid cytolysis and reduction in tumor volume are required. While the optimum schedule for any given cancer is unknown, some schedules appear better than others in experimental radiological studies [35]. All the patients in our new series (1974–1976) were treated with 1,200 rads in the first 3 days, followed by 200 rads daily until the total dose was reached. The radiobiological rationale for this fractionation scheme was based on the concept that high dose fractions are more efficient in inducing rapid tumor cell cytolysis and in improving cell reoxygenation, which would help eliminate radioresistant hypoxic fractions of solid tumors. The success of this fractionation scheme in treating radiosensitive tumors has led us recently to increase the dosage, in the hope of improving our success with more radioresistant tumors. We currently deliver 500 rads daily on 3 consecutive days (priming dose), followed by a 4-day rest, and then deliver 300 rads per day on 5 consecutive treatment days. The results of this change in fractionation are not yet known. We hope that a marked improvement can be achieved, particularly with radioresistant tumors.

Steroids

The role of edema in producing the signs and symptoms of spinal cord compression is unknown. Ushio et al [34] have reported that spinal cord compression by epidural tumor in an animal model produced edema in the cord that partially resolved after treatment by glucocorticoids. Weakness in these animals also was improved by steroids, leading us to conclude that the edema was responsible for some of the weakness. Others [7, 9] have reported definite amelioration of signs of spinal cord dysfunction in human beings after steroid treatment and have assumed that edema must have played a role in producing the initial signs. Relief of symptoms of spinal cord compression by steroids, however, does not guarantee that the symptoms were caused by edema, and steroids may have oncolytic as well as antiedema effects [26].

We have no systematic human data on the effects of steroids in treating spinal cord compression because we believe spinal cord compression is a neurological emergency requiring immediate and definitive therapy. Thus, we have been unable to assess the results of steroid treatment alone. Despite this, the few cases in the literature and the animal experiments seem to show that steroids are indicated.

The dose of steroids to treat spinal cord compression is not established. In our initial series we used approximately 60 mg of prednisone a day, and in the later series we used 16 mg of dexamethasone daily. Because the optimal dose is not established and because there is some evidence from brain tumor therapy that higher doses may be more effective than lower doses [28], we have recently increased the dosage to 100 mg of dexamethasone daily for 3 days with rapid tapering as tolerated. This dose appears to be well tolerated, but whether it is more effective than standard dosages is still not established.

Conclusions

The results of the studies reported here suggest that RT is the treatment of choice for most patients with extradural spinal cord compression from systemic cancer. Adrenocorticosteroids also appear indicated based on experimental evidence and anecdotal patient reports, but the optimum dose of such steroid hormones is not established. Decompressive laminectomy is indicated when: (1) the nature of the primary tumor is not known or the diagnosis is in doubt; (2) relapse occurs weeks, months, or years after RT and the patient cannot be given further radiation; and (3) perhaps when symptoms progress inexorably during RT after several doses have been delivered. It is unclear to

us whether certain patients with known radioresistant tumors will benefit from surgical decompression. As reported in the literature and in our series, the outcome in this group appears not to be very good. Based on our data, we doubt that surgical decompression is necessary or desirable as the initial therapy for most patients with epidural spinal cord compression. All lymphomas should be treated primarily by RT, and our results indicate that most patients with carcinoma of the breast and myeloma will also respond well. In patients with other primary tumors the outcome is dismal, but it is unfavorable no matter what treatment is undertaken. Whatever the modality early diagnosis and aggressive therapy are mandatory since the outcome is clearly better in those patients who are treated promptly.

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