Chapter 8
New Developments in the Surgical Management of Spinal Cord Compression Caused by Metastatic Tumor

Roy A. Patchell, M.D.

Metastatic Epidural Spinal Cord Compression (MESCC) occurs when cancer metastasizes to the spine and then secondarily compresses the spinal cord. MESCC occurs in 10 to 20% of patients with lung cancer (5), and it has been estimated that there are over 20,000 new cases each year in the United States (2). If left untreated, virtually 100% of these patients would become paraplegic. Even with the current standard treatment, fewer than 50% of patients ever walk again (3,5,9).

The tumor cells reach the spinal cord by metastasizing from a tumor elsewhere in the body. The most common tumors that cause MESCC are lung, breast, and prostate (in that order) (5,9). Tumor cells from the primary cancer are shed into the bloodstream and carried to the bones of the spinal column. More than 85% of MESCCs are caused by tumors that first metastasize to the vertebral body (located anterior to the spinal cord). The metastasis then grows posteriorly into the spinal canal and compresses the spinal cord. In most cases, the bulk of the tumor remains anterior to the cord. Damage to the spinal cord is caused by both direct compression and interference with the blood supply of the cord. Unless effective treatment is given immediately, the damage becomes irreversible and patients are left paraplegic.

The natural history of MESCC is that virtually all patients become paraplegic without treatment. The first consistent attempts at treatment date from the 1950s when laminectomy was used on a large scale (1,3,15). A laminectomy involves the removal of the posterior elements of the boney spine (the lamina and spinous process) in an attempt to provide posterior decompression for the spinal cord. Few tumors, however, are posteriorly situated, and so laminectomy is, at best, an indirect decompressive method. Laminectomy does not allow the removal of the anteriorly situated tumor mass and usually fails to provide adequate decompression. Also, removal of the posterior vertebral elements by laminectomy may cause the spine to become unstable because the anterior elements (vertebral bodies) may have already been destroyed by the tumor. Results with laminectomy alone were poor, with less than 30% of patients showing any improvement and surgical mortality ranging from 3 to 15%. More than 70% of patients treated with laminectomy alone eventually became paraplegic (3,5,9).

When effective radiation therapy (RT) became available in the 1960s, the two modes of treatment (i.e., laminectomy and postoperative RT) were combined. With the addition of RT, results were improved with approximately 30 to 50% of patients remaining ambulatory after treatment (3,9,10,15). However, retrospective studies suggested that RT alone was as effective as laminectomy plus postoperative RT in the treatment of MESCC (6,7). Nevertheless, combined treatment remained the standard until 1980 when a small randomized trial suggested that RT alone was as effective as laminectomy plus RT in the treatment of MESCC (16).

Radiation alone has been the standard treatment for MESCC, although results with radiation alone are disappointing. Fewer than 50% of patients treated this way ever walk again, and few patients who begin treatment paraplegic ever regain the ability to walk (3,5,9,13). The reasons for these poor results are many: 1) Some tumors are not radiosensitive and are simply not destroyed by radiation therapy (in the doses that can be safely given to the spinal

cord). 2) Even in radiosensitive tumors, it takes several days to deliver a radiation dose large enough to cause destruction of the tumor. During this lag period, RT does not provide decompression and, therefore, spinal cord damage may continue for several days, even after treatment is started. 3) Because the spinal cord is easily damaged by radiation, relatively small (and less effective) doses of radiation are used to treat MESCC, and in many cases, some tumor remains viable after treatment. So, even if there is an initial response to treatment, tumor cells may survive and regrow to cause a recurrence of the cord compression.

To overcome the problems of the current standard treatment, a more rational treatment plan was developed. This treatment plan involves the use of direct decompressive surgery during which the tumor that is actually causing the cord compression is totally removed (or at least substantially debulked). There is the intraoperative stabilization of the spine (in appropriate cases) followed by postoperative radiation therapy (3, 9,8,14). Because more than 85% of spinal metastases arise anterior to the spinal cord, direct attempts at anterior surgical decompression seem logical. In the less common cases when the compressing tumor is located predominantly lateral or posterior to the spinal cord, direct surgical decompression involving removal of the tumor (using lateral or posterior approaches) is also possible and a logical approach to treatment. The advantages to be gained from direct decompression are that 1) the tumor itself is removed, 2) immediate relief of the cord compression results, and 3) immediate stabilization of the spinal column is achieved by the same operation. In addition, there is evidence that surgical debulking followed by postoperative radiation is synergistic, and therefore the odds of completely destroying the tumor are increased.

In preliminary uncontrolled studies using direct surgical decompression, results have been promising, with ambulatory rates of greater than 75% (8). In several series, about 50% of patients who could not walk at the time of treatment regained the ability to ambulate. These generally encouraging results were obtained in small series that contained only surgically treated patients. There were no control groups, and the patients were almost always selected from among those patients with the best overall prognoses. A controlled, randomized trial comparing direct decompressive surgery plus postoperative radiation therapy with radiation therapy alone was needed to determine the true value (if any) of the new treatment.

A randomized trial (11,12) comparing direct decompressive surgery plus postoperative RT with RT alone was recently completed. The study population consisted of patients with known cancer who developed symptoms of MESCC. These patients had magnetic resonance imaging scans to confirm the presence of a true spinal cord compression. Patients were started on dexamethasone, 100 mg initially followed by 24 mg every 6 hours until they began treatment. After that, steroids were decreased, but continued until the completion of radiation therapy. After stratification for primary tumor type, ambulatory status, and presence or absence of spinal stability, patients were randomly assigned to one of two treatment groups. Patients randomized to the radiation alone arm began radiation within 24 hours after study entry and received 3,000 cGy (300 cGy x 10 fractions). Patients randomized to the surgery plus radiation group were operated on within 24 hours after study entry and received radiation within 2 weeks after surgery. The intent of surgery in all cases was to remove as much tumor as possible and to provide immediate decompression and intraoperative spinal stabilization (when needed). The major endpoint of the study was the ability to walk after treatment. This was measured in two ways. The immediate success of treatment was determined by comparing the proportion of patients in each group who were able to walk after treatment. The long-term success of treatment was measured by comparing the length of time patients maintained the ability to walk. Secondary endpoints were post-treatment continence rates and the length of time patients maintained muscle strength and functional status. Survival was also a secondary endpoint.

The original study design called for a sample size of 200 patients. However, after an interim analysis, the study was stopped because the criterion of a predetermined early stopping rule was met. One hundred and one patients were entered into the study. The percentage of patients able to walk after treatment was significantly ($P = 0.001$) higher in surgical patients (84 %) than in the radiotherapy alone patients (57 %). Patients treated with surgery also retained the ability to walk significantly longer than those with radiotherapy alone (median 122 days versus 13 days, $P = 0.003$).

Thirty two patients (16 in each treatment group) entered the study unable to walk; patients in the surgery group regained the ability to walk in a significantly greater proportion than patients in the radiation alone group (10 of 16 [62 %] versus 3 of 16 [19 %], P = 0.01). The need for corticosteroids and opioid analgesics was significantly lower in the surgical group, and muscle strength and functional status were also maintained for significantly longer in patients treated with surgery. Survival times were also significantly (P = 0.033) longer in the surgery group (median, 126 days in the surgery group versus 100 days in the radiation alone group).

The randomized trial shows that patients with MESCC treated with direct decompressive surgery plus postoperative radiotherapy retain the ability to walk longer and regain it more often than patients treated with radiotherapy alone. Surgery permits most patients to remain ambulatory for the remainder of their lives, whereas patients treated with radiation alone spend a large portion of their remaining time paraplegic.

A possible limitation of the study was patient selection bias. Any study that has exclusionary criteria selects a subset of the total number of patients with a disease for study. Our study was designed to reflect the way patients with MESCC were actually being treated in the real world. The patient population studied consisted of those patients for whom surgery would be considered a realistic treatment option. Patients with very radiosensitive tumors, multiple areas of spinal cord compression, or total paraplegia for longer than 48 hours were excluded. Therefore, the results of this trial cannot be used to justify surgery in all patients with MESCC and apply only to those patients who were comparable to those included in the study. Even in this group of patients, reasonable clinical judgment must used in the selection of patients for surgery.

References

1. Arseni CN, Simionescu MD, Horwath L: Tumors of the spine; a follow-up study of 350 patients with neurosurgical considerations. Acta Psychiatry Neurologica Scandinavia 34:398–441, 1959.

2. Black P: Spinal metastases: current status and recommended guidelines for management. Neurosurgery 5:726-746, 1979.

3. Byrne TN: Spinal cord compression from epidural metastases. N Engl J Med 327:614–619, 1992.

4. Cybulski GR: Methods of surgical stabilization for metastatic disease of the spine. Neurosurgery 25:240–252, 1989.

5. Faul CM, Flickinger JC. The use of radiation in the management of spinal metastases. Neuro-oncol 23:149–161, 1995.

6. Gilbert RW, Kim JH, Posner JB: Epidural spinal cord compression from metastatic tumor: diagnosis and treatment. Ann Neurol 3:40–51, 1978.

7. Greenberg HS, Kim JH, Posner JB: Epidural spinal cord compression from metastatic tumor: results with a new treatment protocol. Ann of Neurol 8:361–366, 1980.

8. Klimo P, Thompson CJ, Kestle JRW, Schmidt MH: A meta-analysis of surgery versus conventional radiotherapy for the treatment of Metastatic spinal epidural disease. Neuro-Oncol 7:64–76, 2005.

9. Loblaw DA, Perry J, Chambers A, Laperriere NJ: Systematic review of the diagnosis and management of malignant extradural spinal cord compression. J Clin Oncol 23:2028–37, 2005.
Scandinavia 34:398–441, 1959.

10. Marshall LF, Langfitt TW: Combined therapy for metastatic extradural tumors of the spine. Cancer 40:2067–2070, 1977.

11. Patchell R, Tibbs PA, Regine WF, Payne R, Saris S, Kryscio RJ, Young B: A randomized trial of direct decompressive surgical resection in the treatment of spinal cord compression caused by metastasis. J Clin Oncol 21(23 Suppl):237, 2003.

12. Patchell R, Tibbs PA, Regine WF, Payne R, Saris S, Kryscio RJ, Young B: Direct decompressive surgical resection in the treatment of spinal cord compression caused by metastasis: a randomized trial. Lancet, in press.

13. Rades D, Blach M, Bremer M, et al.: Prognostic significance of the time of developing motor deficits before radiation therapy in metastatic spinal cord compression. Int J Radiat Oncol Phys 48:1403–1408, 2000.

14. Sundaresan N, Galicich JH, Bains MS, et al.: Vertebral body resection in the treatment of cancer involving the spine. Cancer 53:1393–96, 1984.

15. Wright RL: Malignant tumors in the spinal epidural space. Results of surgical treatment. Ann Surg 157:227–231, 1963.

16. Young RF, Post EM, King GA: Treatment of spinal epidural metastases: randomized prospective comparison of laminectomy and radiotherapy. J Neurosurg 53:741–748, 1980.