Intramedullary Spinal Cord Metastases, Mainly of Nonneurogenic Origin

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The clinical data and imaging studies of 12 patients with intramedullary metastases were reviewed retrospectively to see if these lesions had a typical radiographic appearance and to determine the sensitivity of the various radiologic examinations. The lesions were identified antemortem by either myelography, CT, MR, and/or intraoperative spinal sonography (IOSS). Final diagnosis was based on biopsy material from either the spinal cord lesion, another metastatic site, and/or the primary tumor. Ten patients had primary tumors located outside the central nervous system, while only two patients had primary brain tumors. Metrizamide myelography and CT demonstrated a definite intramedullary mass in nine of 11 patients. In five patients the mass was relatively small, well-defined, single, and resembled a primary spinal cord neoplasm. In the other four patients, longer and sometimes several segments of the cord were involved. These appeared irregular and nodular and were often associated with intradural lesions at separate sites. MR detected not only enlargement and abnormal signal in the cord but also clinically unsuspected brain lesions. IOSS localized lesions for biopsy and monitored tumor resection. These various imaging procedures showed that cord metastases were often more extensive than anticipated clinically. Spread of tumor into the spinal and intracranial subarachnoid space was common. Imaging of the entire spinal canal and brain, preferably with MR, is therefore recommended to aid in diagnosis, prognosis, and treatment.

While metastatic disease to the osseous spine with secondary epidural extension and cord compression has often been described, metastases to the spinal cord of nonneurogenic origin have seldom been reported [1–7]. In contrast to those of CNS origin [8], intramedullary metastases arising from primary tumors outside the CNS are believed to be rare, often found only at autopsy [9–20]. Recent experience with 12 patients with spinal cord metastases, 10 of whom had non-CNS primary tumors and all of whom had diagnoses established antemortem, has led us to believe that these intramedullary lesions may occur more often than previously thought and that the availability of newer imaging techniques such as water-soluble myelography with CT, MR, and intraoperative spinal sonography (IOSS) may make them more easily detectable before death. The sensitivity of these procedures in the detection of spinal neoplasms in general has been described [5, 21–25]; however, a detailed analysis of the appearance of spinal cord metastases (whether of extra- or intra-CNS origin) on all these newer imaging studies has not, to our knowledge, been published. Our object is to report our experience in imaging these frequently elusive intramedullary neoplasms and to determine which was the most sensitive test in detecting this tumor.

Materials and Methods

The clinical records, surgical data, pathologic material, and radiologic studies of 12 patients with spinal cord metastases were reviewed retrospectively. Diagnosis was established by cord biopsy in seven and by biopsy of other metastatic sites in three. In the other two patients, both with biopsy-proven primary tumors and intramedullary spinal lesions shown
radiographically, there was CT evidence of brain metastases that responded to radiation therapy.

The imaging procedures reviewed and compared for diagnostic value and sensitivity included myelography (10 with metrizamide, one with Pantopaque), CT, MR, and IOSS. Spinal CT studies were performed after instillation of metrizamide with 5-mm-thick sections and included nine immediate and four delayed metrizamide CT studies. MR of the spine and brain was performed on mid-field-strength systems (0.35–0.6 T) with spin-echo (SE) techniques with both T1- and T2-weighted imaging. Routinely, the spine was imaged in the sagittal view and occasionally also in axial and coronal projections. A surface coil was used when the cervical cord was evaluated. The brain was studied in the axial view, supplemented by coronal and sagittal projections. Pulse sequences for the spine included repetition times (TR) of 0.3–2.8 sec and echo times (TE) of 26–80 msec. For the brain, the TR was 0.3–2.3 sec and the TE 26–80 msec. IOSS was performed with an ATL NeuroSector scanner using a 7.5-MHz in-line transducer.

Results

Clinical

The patients were six women and six men aged 23–73 years. Primary tumors were lung (four), melanoma (three), brain (two), and lymphoma (one). One patient had two simultaneous primary tumors (lung and breast). The primary was unknown in another patient, but was postulated as arising from the breast. There was surgical proof of the primary tumor in nine patients; the other three patients had biopsy-proven metastases.

In 10 patients symptoms consisted of progressive weakness and/or pain, accompanied in eight by numbness and/or bladder or bowel dysfunction. In one patient there was progressive leg numbness and lightening sensations, and in another numbness of the buttocks and urinary incontinence. Symptom duration was usually short: 1–3 weeks in six patients; 1–2 months in four, and 7 months in one. One patient, however, had symptoms for 13 months.

The clinical diagnosis of metastatic disease was strongly entertained in four patients (those with other known metastases at the time of initial evaluation for cord compression). In the other eight patients, the diagnosis was not as obvious because, before myelography, there was no known primary in four patients, no known metastases in three, and the clinical picture was more suggestive of a cord infarct in one patient despite known metastatic disease. In addition, laboratory studies were nonspecific. CSF, examined in eight patients, showed an elevated protein in all, of 47–1490 mg/dl. Blood cell counts were either normal or minimally elevated. Cytology was done in two patients and was negative. Because of the uncertainty of diagnosis, the cord lesions were biopsied in seven patients (Table 1). Partial or gross total tumor removal was accomplished in six.

Treatment consisted of surgery and radiation therapy in seven patients, radiation therapy alone in three, and radiation therapy and intrathecal methotrexate in one. One patient died before radiation therapy was begun. Prognosis was poor. Six patients had progressive neurologic deterioration and died within 2 weeks to 6 months of initial presentation. Two patients had initial improvement after surgery and/or radiation therapy but developed new sites of spinal metastases 3–6 months later. Of the other four patients, two were lost to follow-up and two were diagnosed only recently.

Imaging Studies

Table 2 summarizes the sites of spinal involvement found during radiologic evaluation. No patient had metastatic involvement of the osseous spine.

Myelograms were obtained initially in 11 patients. The 12th patient did not have a myelogram because of the presence of brain metastases, which made spinal puncture potentially unsafe. Myelography was unequivocally positive in nine of the 11 patients, showing an intramedullary mass lesion. In five patients (all of whom had primaries outside the CNS) the mass was focal, small (extending over only one spinal level), well marginated, and mimicked a primary spinal cord neoplasia (Fig. 1A). Four of these five discrete lesions were located in the conus. In the other four patients (two of whom had CNS primary tumors), longer segments of the spinal cord were involved, causing partial or total obstruction in three and associated with multiple segments of spinal cord involvement in one. Intradural lesions separate from the cord mass were present in three patients (one with and two without a CNS primary) (Fig. 2). In the other two patients (both with primaries of nonneurogenic origin), the spinal cord was at the upper limits of normal in size in one and showed equivocal cord enlargement, only on retrospective review, in the other.

<table>
<thead>
<tr>
<th>Spinal Cord Histology</th>
<th>Site of Primary</th>
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<tbody>
<tr>
<td>Small-cell undifferentiated carcinoma</td>
<td>Lung (biopsy proven)</td>
</tr>
<tr>
<td>Poorly differentiated carcinoma</td>
<td>Lung (biopsy proven)</td>
</tr>
<tr>
<td>Papillary adenocarcinoma</td>
<td>Lung (biopsy proven)</td>
</tr>
<tr>
<td>Anaplastic small-cell carcinoma</td>
<td>Brain (biopsy proven)</td>
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<tr>
<td>Melanoma</td>
<td>Unknown</td>
</tr>
<tr>
<td>Primitive neuroectodermal tumor</td>
<td>Brain (unbiopsied cerebellar lesion seen on MR)</td>
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<tr>
<td>Poorly differentiated adenocarcinoma</td>
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<table>
<thead>
<tr>
<th>Site</th>
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</tr>
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<tbody>
<tr>
<td>Cervical cord</td>
<td>2</td>
</tr>
<tr>
<td>Distal cervical–upper thoracic cord</td>
<td>1</td>
</tr>
<tr>
<td>Middle or lower thoracic cord</td>
<td>2</td>
</tr>
<tr>
<td>Conus medullaris</td>
<td>4</td>
</tr>
<tr>
<td>Lower thoracic cord and lumbar intradural lesions</td>
<td>2</td>
</tr>
<tr>
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<td>1</td>
</tr>
<tr>
<td>Total</td>
<td>12</td>
</tr>
</tbody>
</table>
Fig. 1.—73-year-old woman with small-cell lung carcinoma.

A and B, Smooth enlargement of conus (arrows) on metrizamide myelogram (A) and CT scan (B).

C and D, MR shows widened cord and its well-defined margins (arrows) and excludes other sites of cord involvement on coronal (SE 300/45) (C) and sagittal (SE 300/30) (D) views.
Metrizamide CT was performed in 10 of the 11 patients who had myelography. In the three patients having both immediate and delayed scans, the findings were best seen on the immediate CT scans because of sharper delineation of the spinal cord. In the one patient who had only a delayed CT study, however, abnormal contrast uptake was seen in the cord just above and below the point of maximal cord enlargement. The metrizamide CT scans delineated the spinal cord mass and the intradural lesions better than myelography. In two of the three patients with spinal obstruction, CT showed metrizamide beyond the area of myelographic block. Metrizamide CT was also used to guide the percutaneous biopsy of two of the patients with lumbar intradural lesions. However, in these particular cases the biopsies were not diagnostic.

MR of the spine, performed in six patients, was positive on initial evaluation, showing cord enlargement and abnormal signal. MR was crucial to the diagnosis of a spinal cord lesion in the one patient in whom myelography was deemed dangerous and not done, and in the two patients with equivocal myelograms. One of these latter patients was a 36-year-old woman with a history of progressive leg weakness and pain but no known primary tumor; MR was the study that established the presence of a spinal cord mass (Figs. 3A and 3B) and prompted cord biopsy in the operating room under sonographic control (Fig. 3C), which revealed metastatic glioblastoma.

Follow-up MR of the spine was performed in three patients and showed new areas of spinal involvement in two. In one of these patients the new site of metastasis was shown as an area of high-intensity signal in the cervical cord without associated cord enlargement. Follow-up MR in both these patients mitigated against the need for further myelography. In the third patient, however, myelography and CT were needed (Figs. 3D and 3E).

MR of the brain was performed in three patients. In one patient both IV enhanced CT and MR demonstrated a parenchymal metastasis. In another patient MR was positive when single-dose contrast CT was negative. It showed a sizable lesion in the cerebellum that was unsuspected clinically. However, follow-up MR did not demonstrate well subarachnoid seeding that was shown nicely on contrast-enhanced CT. In the third patient both CT and MR showed multiple nodules in the subarachnoid cisterns from the tumor seeding, but CT (Fig. 3F) showed the lesions to better advantage. The borders of the lesions were easier to discriminate because of the contrast enhancement on the CT scan.
Fig. 3.—Cord lesion was undiagnosed initially on metrizamide myelogram (not shown).

A and B, Sagittal MR shows mildly enlarged cervical cord on SE 500/28 (A, arrows) with abnormal high-intensity signal on SE 2000/56 (B).

C, Intraoperative sonogram identified most echogenic portion (black arrow) of hyperechoic tumor and localized it for biopsy. Notice increased echoes and shadowing caused by needle marker (white arrow) above intact dura. After radiation therapy 4 months later, follow-up MR from C1 to T3 (not shown) failed to show tumor recurrence, despite neurologic deterioration.

D and E, Metrizamide myelogram from above (D) and CT (E), however, revealed complete block at T7 secondary to irregular cord lesion at T3–T4 level (arrows), just below level of original tumor and surgical site.

F, Contrast-enhanced CT 2 weeks later shows multiple enhancing nodules in CSF pathways (arrows). The patient died of widespread metastases a short time later.
IOSS was performed in six of the seven patients who underwent cord biopsy, and it proved critical to the surgical procedure, confirming the intramedullary location of the lesions and showing them mainly as echogenic masses within the cord that were bulging the dura and causing significant obliteration of the cord’s central echo. IOSS differentiated cord enlargement secondary to tumor from edema because the edematous cord appeared diffusely hypoechoic and the tumor hypechoic, as illustrated in Figure 4. In the five other cases IOSS also localized the best site for biopsy and confirmed the accuracy of the biopsy. IOSS determined tumor resectability by demonstrating well-defined margins in one patient and poorly defined margins in five patients. Two of the latter five patients were also seen to have exophytic growth of tumor into the subarachnoid spaces.

Neoplastic involvement of the brain was common. Parenchymal, dural, and/or subarachnoid tumor was present in eight of the 12 patients as shown on MR and/or CT and confirmed at surgery in two. In two the lesions represented the primary neoplasm (a glioblastoma in one and a primitive neuroectodermal tumor in the other). In the other six patients the lesions were metastatic and developed before or simultaneously with the cord metastases in five patients.

Discussion

Intramedullary spinal cord metastases are an unusual complication of malignancies arising outside the CNS [1-7, 9-20]. Of 1096 carcinoma patients studied prospectively at autopsy by Chason et al. [15], metastases to the CNS were found in 200. Only 10% of these 200 patients had intramedullary spinal cord metastases. If one considers their entire patient population, less than 1% of their cancer patients developed metastases to the spinal cord. Similar results were reported by Costigan and Winkelman [10]. Intramedullary spinal metastases represented 2.1% of cases in their clinico-pathologic study of 627 patients with systemic cancer. In the study by Edelson et al. [1], intramedullary spinal cord metastases were found in six (3.4%) of 175 metastatic spinal canal lesions, an incidence the authors believed was higher than that reported in most large series. In a review of the English-language literature since 1960, Grem et al. [16] found only 50 reported cases of intramedullary spinal cord metastases of nonneurogenic origin, to which they added five of their own. This low incidence of intramedullary spinal cord metastases of nonneurogenic origin contrasts with the high incidence of bony and epidural metastases in patients with systemic cancer [3, 20].

Of the tumors of nonneurogenic origin metastasizing to the spinal cord, carcinoma of the lung is the most common [1, 4, 5, 7, 12, 14], accounting in some series for 50% or more of the cases [1, 7, 15, 16]. Both small-cell and non-small-cell bronchogenic carcinomas have been reported [4, 11, 16], and in one review were found to be equally represented [16]. The high association of small-cell bronchogenic carcinoma with brain metastases is, of course, well known [4, 11]. In the study of Grem et al. [16], breast carcinoma was found to be the second most common. Lymphoma, melanoma, colorectal carcinoma, Hodgkin’s disease, head and neck carcinoma, and leukemia are other reported primaries [1, 3, 12, 16]. It is interesting to note that lymphomas and melanomas metastasize with greater regularity to the spinal cord than to the epidural space [1]. In less than 2% of cases, the site of the primary tumor has been unknown [16].

The thoracic cord is the most common site of intramedullary metastases of non-CNS origin, followed by the cervical cord [16]. At autopsy the spinal cord grossly appears firm and swollen, frequently in a fusiform manner [16]. Multiple segments are often affected. Microscopically, in the area of cord enlargement the spinal cord may be completely replaced by metastatic tumor [16]. Infarction and necrosis are common, and cone-shaped central softening can be seen [12, 16, 18]. Leptomeningeal and intradural involvement can be found in conjunction with the intramedullary tumor [1, 4, 6, 7, 10, 11, 26]. Osseous metastases, however, are distinctly uncommon [12].

Most spinal cord tumors of non-CSF origin are believed to develop from hematogenous arterial dissemination of tumor emboli and less often from the vertebral venous plexus or from direct extension from the nerve roots or CSF [16, 19]. This is in direct contrast to tumors of CNS origin. It is well known that certain intracranial neoplasms, including medul-
loblastomas, ependymomas, and gliomas, commonly spread into the CSF pathways and that this leptomeningeal involvement sometimes leads to direct invasion of the spinal cord [8, 20, 27-33]. Spinal cord metastases from medulloblastomas were reported in 12.5% of cases in one series [29] and in 43% in another series [28]. Gross evidence of spinal metastases was found in one-third of cases when the spinal cord was resected in patients with cerebral glioma [8]. This different mechanism of spread to the spinal cord may account for some differences in appearance between intramedullary lesions of CNS origin and those of non-CNS origin.

In those patients with primary CNS tumors that seed to the CSF and spinal cord, multiple dorsal nodular implants of varying sizes on the spinal cord and nerve roots have typically been found in association with thickened leptomeninges [8]. While this appearance has also been seen in intramedullary metastases of nonneurogenic origin from secondary tumor spread into the CSF from the spinal cord, single tumors causing fusiform expansion of the cord have been reported most often [1, 4, 16, 19, 20].

Patients with spinal cord metastases arising from primary tumors outside the CNS typically present with symptoms of short duration, usually of 1–5 weeks [1, 7, 10, 12]. Pain and weakness, often accompanied by bladder and bowel dysfunction and sensory loss, are the most common presenting complaints [1, 4, 7, 12, 16]. Survival is short, often under 2 months, due to rapid neurologic deterioration and to the presence of widespread metastases, including those to the brain [4, 9, 10, 12, 16]. Clinical diagnosis is often difficult, especially when there is no known primary or known metastasis. Neither the clinical picture nor the CSF findings help to distinguish intramedullary metastasis from epidural metastasis, leptomeningeal carcinomatosis, paraneoplastic necrotizing myelopathy, radiation myelopathy, ruptured arteriovenous malformation, or other lesions causing an acute myelopathy [1, 7, 9, 12, 16].

Radiologic studies can aid diagnosis. In the past, myelography has been the most important diagnostic procedure in detecting intramedullary metastases of nonneurogenic origin [1, 5, 16, 19, 20]. While plain films have usually been negative, myelograms, routinely obtained with Pantopaque, have been reported to show intramedullary mass lesions, sometimes totally obstructing the flow of contrast material [1, 4, 12, 16, 19, 20]. These lesions have usually involved short segments of the cord and have produced symmetric and fusiform enlargement, often without cord displacement [1, 4, 16, 19, 20]. Irregularity of these focal lesions has been noted [19, 20]. With superficial cord infiltration, a less common occurrence, lobular excrescences protruding eccentrically from the widened spinal cord have been seen [19, 20]. Extensive single-cord lesions sometimes associated with multiple separate intradural nodules and multiple separate intramedullary lesions have also been described [6, 19]. Myelography has been helpful in differentiating intramedullary metastases from leptomeningeal carcinomatosis since the latter usually appears as multiple nodules bead the cauda equina [6]. Myelography has also been helpful in differentiating extramedullary metastases, although there have been exceptions to this, especially when the lesions were fungating and irregular [1]. In cases of single intramedullary lesions, difficulty has also been encountered in distinguishing intramedullary metastasis from primary neoplasm and from syringomyelia [4]. In these cases, however, the clinical history has usually allowed a distinction to be made.

Despite the value of myelography, limitations to this procedure have been described. Myelograms have been reported to be negative in as many as 40–42% of intramedullary metastases of nonneurogenic origin [1, 4, 5, 7, 10, 12, 16]. Because of the drawbacks of myelography, CT has been suggested to aid in detection. CT has shown hyperdensities in the spinal cord on both plain and IV contrast-enhanced studies [4, 5]. Plain and IV-enhanced CT scans, however, have not been used extensively in patients with this disease. While the potential value of intrathecal metrizamide has been mentioned [5], the use of metrizamide CT scans has not been reported. The diagnosis of spinal cord metastases of nonneurogenic origin has often been made only postmortem [9–12].

While the results of our study agree with the reported in the literature for patients with spinal metastases of non-CNS origin with regard to their clinical history, clinical course, tumor type, lack of concurrent bony and epidural involvement, and frequent neoplastic involvement of the brain, they differ with regard to the sensitivity of radiologic studies. Spinal cord lesions were detected radiographically in every patient in our series. We believe this high rate of positive radiologic studies is directly related to the application of newer imaging techniques. The use of metrizamide for myelography, for example, allowed us to diagnose intramedullary mass lesions in most patients. CT scans after myelography aided in diagnosis also. By clearly demonstrating irregularity and nodularity to the spinal cord lesion and by showing more distinctly than myelography multiple intradural lesions, metrizamide CT scans made metastatic disease the most likely diagnosis. They also were seen to be potentially useful in obtaining tissue diagnosis through the percutaneous biopsies of associated lumbar intradural lesions [34]. IOSS documented the presence of intramedullary lesions at surgery and guided their biopsy. This procedure proved critical in those cases where spinal cord enlargement was not diagnosed myelographically and where difficulty with prior biopsy had been encountered at an outside institution. IOSS differentiated cord edema from intramedullary metastasis, a distinction that probably cannot be made by MR at this time (Fig. 4).

MR has only recently been used in the detection of spinal cord lesions [23–25]. The value of this imaging device in diagnosing spinal cord disease noninvasively was confirmed by our study also. While we do not know the false-negative rate of this procedure since we did not use autopsy material to select our cases, MR appeared to be very sensitive in detecting intramedullary metastases of both nonneurogenic and CNS origin. The initial studies in all six patients examined with MR showed cord enlargement, even when it was subtle. Widening of the spinal cord was best seen on T1-weighted SE images in the sagittal view and gave the first indication of an intramedullary lesion. T2-weighted SE images showed high-intensity signal within the cord and documented intrinsic
cord disease, even in the one patient whose follow-up MR study showed no cord enlargement at the site of a new cord metastasis. MR detected disease that could not be seen on myelography since it demonstrated areas between myelographic blocks. It also provided an easy and noninvasive means of imaging the entire spinal canal and brain, which allowed for the detection of clinically silent abnormalities both initially and at follow-up. While one disadvantage of MR was that it was nonspecific, other limitations were restricted to those that could be potentially overcome in the future, namely, the limited resolution of the thoracic cord with the body coil and difficulty in detecting meningeal metastases in the spine and brain. The use of surface coils and paramagnetic contrast agents may help eliminate these diagnostic problems.

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