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Epidural Spinal Cord Compression as the Presenting Manifestation of Tumor of Unknown Origin

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Epidural spinal cord compression is a common complication of malignancy. In the majority of cases, the primary site is known at diagnosis or is evident following limited investigation. During the period January 1975 to December 1987 we encountered seven cases of tumor of unknown origin presenting as cord compression. Myelography detected the site of cord involvement in six cases, and computed tomography of the spine was utilized in one case. All seven patients underwent laminectomy. Histologic diagnosis was adenocarcinoma in four cases, squamous in one case, and large cell undifferentiated carcinoma in two cases. Evaluation for a primary site was unrewarding. Prognosis was poor, with a median survival of 10 weeks. Only one patient had a satisfactory response to treatment.

Key words: cancer, occult primary

INTRODUCTION

Epidural spinal cord compression is a common neurologic complication in patients with cancer [1]. The most common tumors to produce this problem include lung cancer, breast cancer, lymphoma, sarcoma, multiple myeloma, and carcinoma of the prostate, kidney, and gastrointestinal tract [2–4]. In several studies of epidural cord compression secondary to metastatic cancer, tumors of unknown origin (TUO) accounted for 0 to 38% of the cases [5–14]. However, the clinical characteristics and course of such patients with TUO has not been described. We report seven patients with epidural cord compression as the presenting manifestation of TUO.

MATERIALS AND METHODS

The pathological records of all cases of epidural spinal cord tumors seen at the University of Missouri-Columbia and the Veterans Administration Hospital between January 1975 and December 1987 were retrospectively reviewed. Of sixty-nine cases diagnosed during this period, seven had TUO. Detailed information for these seven patients was obtained from the tumor registry and from a review of the patients' medical records. Specifically noted were age at diagnosis, methods of evaluation, presenting symptoms and signs, treatment, response to therapy, and survival from the date of diagnosis of the spinal cord compression. In addition, review of each histologic specimen was performed.

RESULTS

Patient characteristics are shown in Table I. There were four women and three men with a median age of 54 years (range, 39–95). Back pain and weakness were the most frequent presenting complaints. Localized nonradicular back pain occurred in two patients, and radicular pain occurred in one patient. Lower extremity weakness and/or paralysis occurred in five patients, two of whom also had back pain. One patient presented with urinary incontinence. Symptoms had been present for 3 days to 4 months.

Aside from the neurologic examination, the physical findings, including normal breast and prostate examination, were unremarkable. Bilateral lower extremity paresis was evident in two patients, and five patients had lower extremity weakness. Sensory level deficits were detected in six patients. A spinal cord level of anesthesia was present in four cases. Bowel and bladder dysfunction was evident in one case.

Normocytic, normochromic anemia was noted in one

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TABLE 1. Clinical Characteristics for Seven Patients With Epidural Cord Compression and Tumor of Unknown Origin*

Patient	Age (years)	Sex	Presenting symptoms and signs	Radiographic procedure to diagnose epidural cord compression	Level of cord compression	Histological features of epidural tumor	Therapy of epidural compression	Survival (weeks)
1	95	F	Back pain	CT scan	L4–L5	Squamous carcinoma	Laminectomy	5
2	59	F	Lower extremity weakness	Myelogram	T3–T5	Adenocarcinoma	Laminectomy radiation	12
3	54	F	Paralysis of lower extremity; urinary incontinence	Myelogram	T3–T4; T6–T7	Adenocarcinoma	Laminectomy	6
4	39	F	Numbness and weakness of lower extremities	Myelogram	T5	Large cell carcinoma	Laminectomy radiation	22
5	53	M	Back pain	Myelogram	T10–T12	Large cell carcinoma	Laminectomy radiation	10
6	54	M	Back pain; paralysis of lower extremities	Myelogram	T2–T4	Adenocarcinoma	Laminectomy	2
7	52	M	Back pain; weakness of lower extremities	Myelogram	L4–L5	Adenocarcinoma	Laminectomy radiation	40+

*CT = computed tomography; L = lumbar spine; T = thoracic spine.

patient; three patients had an elevated alkaline phosphatase; and hypercalcemia was present in one patient. Prostatic acid phosphatase was normal in each male patient.

Extent of radiographic evaluation varied from case to case. Chest radiograph did not reveal a lung mass in any patient. In one case, however, there were osteolytic lesions in the scapula and clavicle. Mammography was normal in each female. Intravenous pyelogram, performed in one case, was normal. Bone scan was consistent with metastatic disease to the spine in six cases, and X-ray correlation was noted in most cases including lytic lesions, vertebral compression, and erosion of the pedicles. In one patient, additional metastatic foci were observed on bone scan in the clavicle, scapula, and pelvis. Myelogram was abnormal in six patients, four of whom had a complete epidural block and two of whom had a partial block. One patient had computed tomography of the spine that showed cortical disruption of a vertebral body with tumor invasion into the epidural space. Each patient underwent therapeutic and diagnostic laminectomy to establish histologic diagnosis. Adenocarcinoma was found in four cases, squamous carcinoma in one case, and an undifferentiated large cell carcinoma in two cases. Subsequent to laminectomy, four patients received palliative radiotherapy.

Median survival from the time of diagnosis of spinal cord compression was 10 weeks (range, 2 to >40 weeks). One patient was alive at >40 weeks with evidence of an enlarging cerebral mass and has subsequently been lost to follow-up. Although this patient had significant clinical improvement in his lower extremity weakness after laminectomy and radiation, none of the remaining six patients had improvement in their clinical status. Subsequent follow-up did not reveal the primary site in any case. However, one patient developed multiple lung metastases, and another patient developed several bone lesions. These two patients expired with systemic disease, while the remaining four succumbed to local complications and/or infection. Postmortem examinations were not done in any patient.

DISCUSSION

Tumor of unknown origin (TUO) is a common manifestation of malignancy, and represents 3% to 10% of cancers [4,15,16]. The most common presentation of TUO is lymph node metastases, followed in descending order by liver, bone, brain, lung, skin, and pericardial metastasis [15]. Epidural spinal cord compression, as the initial manifestation of TUO, is quite infrequent, and the precise incidence is not known. During a 13 year period we only encountered seven patients with this diagnosis. Of 69 cases of biopsy-proven epidural cord compression due to cancer, TUO accounted for only 10% of the cases.

The clinical features of our seven cases of epidural TUO are similar to the cardinal manifestations of other epidural spinal tumors [1–3,11,12]. Unlike epidural tumor of known origin, laminectomy is required for both diagnostic and therapeutic reasons. Similar to other presentations of TUO, radiographic search for an occult primary is unrewarding in our hands [17,18] and others [4,16]. Consequently we recommend that radiographic procedures be limited to chest X-ray, bone scan, and mammography in females. Serum protein electrophoresis should also be performed. Myelography and/or CT of

the spine [13] and nuclear magnetic resonance imaging [14] are necessary to detect the level of cord compression.

Since the most frequent histologic cell type in our series was adenocarcinoma, electron microscopy [19] may be useful to identify poorly differentiated tumors that are adenocarcinomas. Immunochemistry [20] for prostate-specific antigen and estrogen receptors may be of benefit in establishing a diagnosis of prostate or breast cancer, as these tumors may respond to hormone manipulation.

The prognosis of our patients was poor, with a median survival of 10 weeks. Moreover, only one patient who received post-operative radiotherapy had a satisfactory response to treatment. Because of the small number of cases and poor quality of life of the remaining six patients, the exact role of radiation therapy cannot be defined in this population of patients. Although laminectomy was necessary for the diagnosis in each case, the advent of fine needle aspiration biopsies may obviate laminectomy in some cases in the future, making radiotherapy the primary modality of treatment. Last, in selected cases, hormone therapy or chemotherapy may be of benefit if the diagnosis of a hormonally responsive tumor is established.

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REFERENCES

1. Gilbert MR, Grossman SA: Incidence and nature of neurologic problems in patients with solid tumors. Am J Med 81:951–954, 1986.
2. Rodriguez M, Dinapoli RP: Spinal cord compression with special reference to metastatic epidural tumors. Mayo Clin Proc 55:442–448, 1980.
3. Bruckman VE, Bloomer WD: Management of spinal cord compression. Semin Oncol 5:135–140, 1978.
4. Nissenblatt MV: The CUP syndrome (carcinoma unknown primary). Cancer Treat Rev 8:211–224, 1981.
5. Torma T: Malignant tumors of the spine and the spinal extradural space. A study based on 250 histologically verified cases. Acta Chir Scand [Suppl] 225:1–138, 1957.
6. Wright RL: Malignant tumors in the spinal extradural space: Results of surgical treatment. Ann Surg 157:227–231, 1963.
7. Hall AL, Mackay NNS: The results of laminectomy for compression of the cord and cauda equina by extradural malignant tumor. J Bone Joint Surg [Br] 55:497–505, 1973.
8. White WA, Patterson RH, Bergland RM: Role of surgery in the treatment of spinal cord compression by metastatic neoplasm. Cancer 27:558–561, 1971.
9. Brice J, McKissock W: Surgical treatment of malignant extradural spinal tumors. Br Med J [Clin Res] 2:1341–1344, 1965.
10. Bernat JL, Greenberg ER, Barrett J: Suspected epidural compression of the spinal cord and cauda equina by metastatic carcinoma. Clinical diagnosis and survival. Cancer 51:1953–1957, 1983.
11. Gilbert TW, Kim JH, Posner JB: Epidural spinal cord compression from metastatic tumor: Diagnosis and treatment. Ann Neurol 3:40–51, 1978.
12. Rodichok LD, Harper GR, Ruckdeschel VC, Price A, Roberson G, Barron KD, Horton J: Early diagnosis of spinal epidural metastases. Am J Med 70:1181–1188, 1981.
13. Weissman DE, Gilbert M, Wang H, Grossman SA: The use of computed tomography of the spine to identify patients at high risk for epidural metastases. J Clin Oncol 3:1541–1544, 1985.
14. Sarpel S, Sarpel G, Yu E, Hyder S, Kaufman B, Hindo W, Ezdinli E: Early diagnosis of spinal-epidural metastasis by magnetic resonance imaging. Cancer 59:1112–1116, 1987.
15. Ringenberg QS: Tumors of unknown origin. Med Pediatr Oncol 13:301–306, 1985.
16. Haskell CM, Cohran AV, Barsky SH, Steckel RJ: Metastasis of unknown origin. Curr Probl Cancer 12:1–58, 1988.
17. Ringenberg QS, Doll DC, Yarbro JW, Perry MC: Tumors of unknown origin in the bone marrow. Arch Intern Med 146: 2027–2028, 1986.
18. Ringenberg QS, Doll DC, Loy TS, Yarbro JW: Malignant ascites of unknown origin. Cancer 64:753–755, 1989.
19. Mackay B, Ordonez NG: The role of the pathologist in the evaluation of poorly differentiated tumors. Semin Oncol 9:396–415, 1982.
20. DeLellis RA, Dayal Y: The role of immunohistochemistry in the diagnosis of poorly differentiated malignant neoplasms. Semin Oncol 14:173–192, 1987.