The Radiation Therapy for Spinal Cord Compression in Hematologic Malignancy

In Ah Kim, M.D., Ihl Bohng Choi, M.D., Su Mi Chung, M.D., Ki Mun Kang, M.D.
Chul Seong Kay, M.D., Byung Ok Choi, M.D., Ji Young Jang, M.D.
Kyung Sub Shinn, M.D., Chun Choo Kim, M.D.*

Department of Therapeutic Radiology and Internal Medicine, Catholic University Medical College, St. Mary's Hospital, Seoul, Korea*

=Abstract=

Spinal cord compression, an oncologic emergency, is a rare complication of hematologic malignancy. Our experience was obtained with a series 32 patients following retrospective analysis for assessing the role of radiation therapy and identifying the prognostic factors affecting on treatment outcome.

Diagnosis was usually made by means of radiologic study such as myelography or computerized tomography (CT) or magnetic resonance imaging (MRI) and neurologic examination. Five cases were diagnosed by subjective symptom only with high index of suspicion.

In 31 cases, the treatment consisted in radiation therapy alone and the remained one patient had laminectomy before radiation therapy because of diagnostic doubts. Total treatment doses ranged from 800 cGy to 4000 cGy with median of 2000 cGy. Initially large fraction size more than 250 cGy were used in 13 patients with rapidly progressed neurologic deficit.

The clinical parameters considered in evaluating the response to treatment were backache, motor-sensory performance and sphincter function. Half of all patients showed good response. Partial response and no response were noted in 37.5% and 12.5%, respectively. Our results showed higher response rate than those of other solid tumor series.

The degree of neurologic deficit at that time of diagnosis was the most important predictor of treatment outcome. The elapsed time from development of symptoms to start of treatment was significantly affected on the outcome. But histology of primary tumor, total dose and use of initial large fraction size were not significantly affect on the outcome. These results confirmed the value of early diagnosis and treatment especially in radiosensitive hematologic malignancy.

Key Words : Spinal cord compression, Hematologic malignancy, Radiation therapy

INTRODUCTION

Spinal cord compression is rare but serious complication in patients with hematologic malignancy. As advances in the treatment of hematologic malignancy lead to further prolongation of life span, secondary involvement of the nervous system becomes increasingly important[1]. Especially spinal cord or cauda equina compression is

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oncologic emergency because delay in treatment often results in irreversible paralysis and loss of sphincter control. Prompt diagnosis and treatment are necessary if permanent neurologic sequale were to be avoided[2].

There are many reports for spinal cord compression due to various tumors. But few studies reviewed the patients with spinal cord compression due to hematologic malignancy seperated from solid tumors. In this study, we analyzed the response rate and identified the predictors of outcome for spinal cord compression in hematologic malignancy.

MATERIALS AND METHODS

From October 1988 to May 1993, 32 patients with hematologic malignancy received emergency radiation therapy due to spinal cord compression at St. Mary's hospital. The hospital records of 32 patients were analyzed retrospectively.

At diagnosis, nineteen were leukemia, four were lymphocytic lymphoma, nine were multiple myeloma. Of nineteen leukemic patients, seven were acute lymphocytic leukemia (ALL), seven were acute myelocytic leukemia (AML) and five were chronic myelocytic leukemia (CML) (Table 1).

Eighteen patients were male and eight were female. Age ranged from 3 to 72 years old with median of 32.

The diagnosis of spinal cord compression was

Table 1. Classification accoding to Histologic Type

histologic diagnosis	Number of patients(%)
Leukemia	19 (59.4%)
ALL	7 (21.9%)
AML	7 (21.9%)
CML	5 (15.6%)
Lymphocytic lymphoma	4 (12.5%)
Multiple myeloma	9 (28.1%)
Total	32 (100%)

Table 2. Diagnostic Method of Cord Compression

Diagnostic methods	Number of patients(%)
Subjective symptom only	5 (15.6%)
Neurologic examination	8 (25.0%)
Radiologic examination	19 (59.4%)
Total	32 (100)%

based on radiologic study (myelography, spinal CT, MRI) or obvious neurologic manifestations or subjective symptoms only with high index of suspicion (Table 2). Examination of spinal fluid was done in eleven cases. Seven were ALL and four were lymphocytic lymphoma.

Radiation therapy was given with 6 MV linear accelerator (SAD 100 cm) through posterior one portal which included one or two vertebral bodies above and below the lesion to provide a margin of safety. Occasionally bilateral 2 opposed ports were used in patients with cervical spinal cord lesion in order to avoid radiation esophagitis. All patients received medium to high doses of steroid depending on the degree of neurologic deficit. Decompressive laminectomy preceded radiation therapy in one case because of diagnostic doubts.

For objective measurement, treatment response were classified into three categories as follows[3]:

A. Good response; patient return to normal function or experienced only slight neurologic dysfunction.

B. Partial response; moderate degree of neurologic impairment persisted.

C. No response ; pain or initial neurologic deficit persisted.

Response rate was statistically analyzed in relation to histology, treatment dose, grade of neurologic deficit and elapsed days after onset of symptoms. Fisher's exact test was performed.

RESULTS

Pain was most frequent clinical manifestation

(81.3%). Sensory impairment and motor weakness were noted in 46.9% and 43.8%, respectively. Six patients experienced sphincter dysfunction(Table 3).

The frequency of spinal column levels involved was shown in Table 4. The commonly compressed segments are in the lumbar and thoracic area. Of 32 patients encountered 14 were in the lumbar area, 13 were in the thoracic area, 5 were in the sacral area and 3 were cervical area. Cornus medullaris and cauda eqinal involvement were noted in three patients. They showed selective autonomic dysfunction without definite evidence of motor and sensory discrepancy. Diffuse meningeal involvement was noted in five patients. One of these patients had initial CNS presentation(Table 4).

Fig. 1 showed overall response rate. The half of all patients showed good response. Partial response were noted in twelve of 32 patients. Four patients were not responded to radiation therapy.

Table 5 showed the response rate according to histologic type. There was no statistically significant differences in 3 histologic type by Fisher's exact test($P>0.05$). In the leukemic patients group, good response was 57.9% and partial response was 10.5%. There was no significant differences in the response rate among the leukemic subgroup. In the multiple myeloma group, good response was 55.6% and partial response was 33.3%. Three of 4 lymphoma patients showed partial response and remained one patient showed no response.

The degree of neurologic deficit[3] at that time of diagnosis was significant impact on the treatment outcome. All of 11 cases with grade 1 neurologic deficit had good response. Three of 8

Table 3. Clinical Manifestations

Symptoms & Signs	Number of patients(%)
Back pain	20 (62.5%)
Motor weakness	14 (43.8%)
paresis	8
paralysis	6
Sensory impairment	15 (46.9%)
Sphincter dysfunction	6 (18.8%)

Table 4. Involved Segment of Spinal Cord

Involved segment	Number of patients(%)
Cervical	3 (9.4%)
Thoracic	13 (40.6%)
Lumbar	14 (43.8%)
Sacral	5 (15.6%)
Cauda equina	3 (9.4%)
More than one segment	8 (25.0%)
Diffuse meningeal involvement	5 (15.5%)

Table 5. Response Rate according to Pathologic Type(%)

Respose pathology	Good Response	Partial Response	No Response	Total
Leukemia	11(57.9)	6(31.6)	2(10.5)	19
ALL	5	2	–	7
AML	3	3	1	7
CML	3	1	1	5
Lymphoma	0(0)	3(75.0)	1(25.0)	4
Myeloma	5(55.6)	3(33.3)	1(11.1)	9
Total	16	12	4	32

Table 6. Response Rate according to Grade of Neurologic Deficit(%)

Response Grade*	Good Response	Partial Response	No Response	Total
I	5(100)	–	–	5(100)
II	9(75.0)	3(25.0)	–	12(100)
III	2(28.6)	4(57.1)	1(14.3)	7(100)
IV	–	5(62.5)	3(37.5)	8(100)
Total	16	12	4	32

*Grading system of neurologic deficit[3]
Grade
I : back pain only without clinical neurologic sign
II : slight neurologic dysfunction such as muscular weakness, sensory deficit or abnormal reflex
III : paraparesis &/or loss of sphinter control
IV : complete paralysis

Table 7. Response Rate according to Elapsed Time from Development of Symptom to Start of Treatment(%)

Response Days	Good Response	Partial Response	No Response	Total
1-2	5(83.3)	1(16.7)	-	6(100)
3-7	9(60.0)	5(33.3)	1(6.7)	15(100)
8-14	2(33.3)	2(33.3)	2(33.3)	6(100)
> 14	-	4(80.0)	1(20.0)	5(100)
Total	16	12	4	32

Table 8. Response Rate according to Total Dose(%)

Response Dose(cGy)	Good Response	Partial Response	No Response	Total
<2500	7(21.9)	2(6.3)	1(3.1)	10(31.3)
>2500	9(28.1)	10(31.3)	3(9.3)	22(68.7)
Total	16(50.0)	12(37.6)	4(12.4)	32(100)

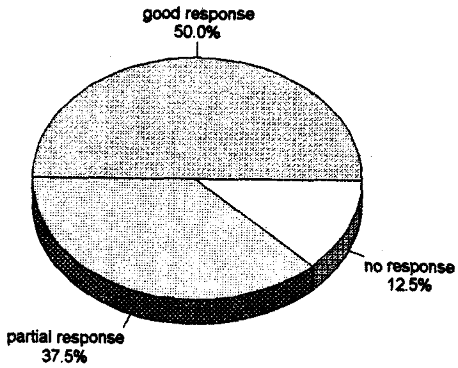

Fig. 1. Overall response rate

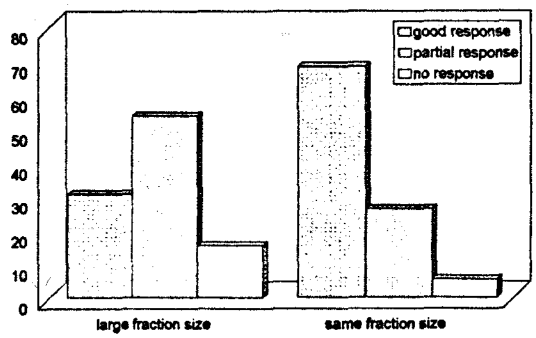

Fig. 2. Response rate according to intial fraction size

cases with grade 4 neurologic deficit showed no response. The difference of response rate in relation to this factor was statistically significant (P=0.0001) (Table 6).

Table 7 showed response rate according to elapsed time from development of symptoms to start of treatment. Treatment outcome significantly dependent on this factor (P=0.014). The patients whose radiation therapy was given within 2 days after development of cord compression symptoms, had the good response in five of 6 patients and partial response in one patient. None of six patients who was treated more than 14 days after development of symptoms, had good response.

Table 8 showed response rate in relation to total radiation dose. The total doses were converted to equivalent dose by TDF (time, dose, fractionation) factor corresponding to 200 cGy. There was no significant differences among the each dose group (P>0.05). Initially, large fraction size more than 250 cGy were used in 13 patients with rapidly progressive neurologic symptoms. The response rate of these 13 cases were compared with response rate of 19 cases who treated with fraction size less than 250 cGy. There was no significant differences in response rate according to these factor (P>0.05) (Fig. 2).

DISCUSSIONS

Epidural cord compression remains an urgent therapeutic problem. About 7% of spinal cord compression is due to hematologic malignancy[4]. The review of recent literature shows continued interest in the controversy over the optimum management of patients with epidural metastatic neoplasia. Because the patients presenting with this syndrome have a variety of primary neoplasm, each with different growth characteristics. Precise and complete neurological assessment at that time of initiation of therapy is often lacking, making evaluation of therapeutic results difficult. Also few studies review sufficient numbers of patients to allow statistical evaluation of therapeutic outcome[4-5].

Radiobiologically, human tumors have different intrinsic radiosensitivity according to various histologic type. Malaise and Fertil reported that hematologic tumors had smaller surviving fraction after irradiation of 2 Gy than other solid tumors[6,7]. They also showed that hematologic tumors usually have smaller doubling time and larger growth fraction than those of solid tumors[8]. The review of current literature indicate that radiation therapy alone is successful in approximately 40 to 50% of patients with spinal cord compression due to various tumors[3,4,5,9]. But few studies reviewed sufficient number of patients with spinal cord compression due to hematologic malignancy separated from solid tumors. Ikehara et al analyzed eleven patients with spinal cord compression due to metastatic tumors. Regardless of the pretreatment neurologic status and type of treatment given, the functional prognosis in this small series of patients appears to be favorable for radiosensitive tumors such as malignant lymphoma and multiple myeloma[10]. Friedman et al reported the results of spinal cord compression due to malignant lymphoma. The major response rate was 75%(good response in 55% and partial response in 20%) [3]. Kristian et al analyzed 28 patients with spinal cord compression due to epidural malignant lymphoma. Major response rate were 91% in Hodgkin's disease and 87% in non-Hodgkin's lymphoma[11]. Ten spinal cord compression due to leukemia were analyzed by Kim et al. The response to radiation therapy was excellent in 8 patients[12]. Delauche et al reviewed the data for eight patients with solitary plasmacytoma who presented with cord compression. Neurologic deficits were reversed in every patients after radiation therapy[13]. In our series, the major response rate was 87.5%(good response was 50% and partial response was 37.5%).

The treatment results seem to be dependent on the degree of neurologic deficits at the time of treatment was initiated. Friedman et al indicated that the percentage of good response decreased from 70% in non-neurological deficit group to 10% in grade IV neurologic deficit group [3]. Kristian et al reported that fifteen of 16 patients with mild to moderate motor loss achieved good response. But five of 10 patients had good response in the group with severe motor loss[11]. In our series, fourteen of 17 patients in grade I and II group achieved good response. None of 8 patients with grade IV neurologic deficit showed good response. When there are minor or no neurologic deficits, the chances of controlling the compression are high and the results become poorer in more advanced neurologic symptoms.

The clinical presentation of cord compression is often divided into two stages. The prodromal stage occurs in most patients and consist of back pain and radicular pain or paresthesias. Prodromal symptoms may occur days to months before radiologic diagnosis. At this stage, spine radiographs may show no abnormality or may reveal bony lesions or paravertebral mass. The stage of cord compression usually follows the prodromal back pain but can be presented from the onset. It consists of motor followed by sensory impairment, with sphincter loss being the last impairment to occur[9].

The treatment result was significantly dependent on the elapsed time from development of symptoms to start of treatment. Five of 6 patients whose treatment had been started within 2 days after development of symptoms showed good response. Friedman et al reported that radiation therapy, when initiated in the early phase of compression and in an adequate dose, may reverse the neurologic deficit and locally control the disease. They suggested that a minimal dose of 2500 cGy seems to be necessary[3]. Lyons et al also recommended at least 2500 cGy[14]. But total doses were not significant impact on treatment outcome in our series.

Kristian et al compared the response between high dose, short-term treatment (500 cGy, 5 to 6 times) group and long-term treatment (200 cGy, 18 to 20 times) group. Both schedules exhibited similar TDF values and were found to be equally effective[11]. In our series, the large fraction size more than 250 cGy were applied in initial 3 or 4 fractions for patients with rapidly progressed neurologic deficits. The difference of response rate according to fraction size was not found. High proportion of poor prognostic patients who had rapid neurologic progression might be contribute in this result.

Though tumor type and other pretreatment factors, as well as advances in cancer therapy influence the outcome in some patients with epidural spinal cord compression, overall prognosis has changed little in 20 years[15]. Our results showed higher response rate than those of other solid tumor series, but similar to those of other hematologic tumor series reported in the literature. Our results also confirmed the findings of many previous series in demonstrating that severe neurologic deficit on presentation was associated with a less frequent response to treatment and poor outlook. The best hope for favorable outcome, therefore, lies in early and accurate diagnosis of epidural tumor in patients with back pain and minimal or no neurologic deficit with high index of suspicion[16-17]. It is especially important for radiosensitive hematologic malignancy.

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국문초록＝

혈액암에서 발생한 척추압박증상의 방사선 치료

가톨릭대학교 의과대학 성모병원 치료방사선과, 내과학교실*

김인아 · 최일봉 · 정수미 · 강기문 · 계철승
최 병 옥 · 장 지 영 · 신 경 섭 · 김 춘 추*

최근 혈액암에 있어서 적극적인 복합항암요법및 골수이식등으로 장기 생존자의 수가 증가함에따라 과거에 흔하지 않았던 합병증, 특히 척추 신경의 침범으로 인한 압박증상을 보이는 환자들의 수가 점차 증가하고 있다. 혈액종양과 고형종양간에 방사선 감수성의 현저한 차이가 있음 에도 불구하고, 척수압박증상에 관한 대부분의 보고들이 혈액종양을 따 로 구분하여 분석하지 않았으며, 충분한 수의 혈액종양환자를 대상으로 한 보고가 드문 실정이다. 이에 저자들은 1988년부터 1993까지 척수압박으로인해 응급 방사선치료를 받은 32명의 혈액종양 환자를 대상으로 후향적 분석을 시행하여 치료결과 및 예후인자를 알아보고자하였다. 신경학적 진찰이나 방사선학적 검사 (척수조영술, 전산화단층촬영, 자기공명영상촬영) 로 진단된 경우가 27례 이었고, 환자가 호소하는 증상 을 중심으로 'high index of suspicion'으로 진단한 5례를 포함하였다.

발병당시 조직학적 진단이 없어 수술을 시행한 1례를 제외한 모든 환자가 방사선 단독으로 치료받았으며, 조사량의 범위는 800 cGy 에서 4000 cGy로 중앙값은 2000 cGy 이었다. 혈액종양의 방사선 감수성을 고려하여 200 cGy이하의 분할조사량이 사용되었으며, 신경학적 증상의 진행속도가 빠른 13례에 있어서는 치료초기 2회 내지 3회에 걸쳐 250 cGy 이상의 고분할선량이 사용되었다. 전체환자의 50%에서 좋은 반응을 보였고, 37.5%에서 부분반응을 보였으며, 12.5%는 치료에 반응이 없었다. 이러한 반응율은 문헌에 보고된 고형암에 비해 높았으며, 혈액종양만을 대상으로한 다른 보고들과 유사하였다. 진단당시 신경학적증상의 정도가 치료결과에 영향을 미치는 가장 중요한 예후인자였고, 증상의 출현에서 치료시작까지 소요된 기간도 치료결과에 유의한 영향을 미치는 것으로 나타났다. 반면에 조직학적 진단의 종류, 총방사선량, 초기고분할선량의 사용여부등에 따른 치료결과의 차이는 관찰되지 않았다.