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Original Article

Intramedullary spinal cord metastasis and radiotherapy

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Abstract

Aim: Intramedullary spinal cord metastasis (ISCM) is a rare but a severe condition. We aimed to evaluate the clinical features, the effect of radiotherapy on the functional results, and the quality of life and survival in patients with ISCM.

Material andMethods: We retrospectively assessed the results of 15 patients. Patients underwent 3D conformal radiotherapy (3D-CRT). Patients were reviewed in terms of neurological deficits, the localization of primary tumors, the duration of symptoms, onset symptoms, the localization of ISCM,and the interval between diagnosis and spinal metastasis. Post-radiotherapy outcomes and factors influencing the survival and the quality of life were analyzed.

Results: The mean duration of symptoms before diagnosis was 14.93 days (range; 1-52 days).The most common presenting symptoms of patients were lower back and back pain. Neurological deficit was present in 9 patients. Of these patients, partial improvement was observed following the radiotherapy in four patients. After the radiotherapy, the need of painkillers and pain were decreased in 10 of the patients with pain at the outset (66.7%). An association was detected between the initiation of radiotherapy within 10 days from the onset of symptoms and the quality of life (p=0.026).The mean survival rate was 5.9 months after being diagnosed with ISCM.

Conclusions: Motor deficit and pain-related quality of life were corrupted in most of the patients with ISCM. Early diagnosis and suitable treatment might promote to the functional condition of the patient. It is important to initiate radiotherapy within a period of less than 10 days from the onset of symptoms.

Keywords: Intramedullary Tumor; Radiotherapy; Survival; Quality Of Life.

INTRODUCTION

Intramedullary spinal cord metastase (ISCM) is a rarely seen medical condition. It affects 0.1-0.4% of all cancer patients (1,2,3). The frequency of ISCM increases by means of the use of magnetic resonance imaging (MRI) and longer survival of cancer patients have been achieved throughout the past decade (4). It is observed in most of the cancer types and it is most common in lung and breast cancer (1,4). Pain and weakness are the common initial symptoms. Many patients develop neurological deficit and it progressed rapidly. Urinary and gaita incontinence might be present. ISCM can occur in any segment of spinal cord, and thoracic region is the most common site (5,6). The lesions are diagnosed primarily with MRI in the routine clinical practices, and MRI has a high sensitivity in identifying the spinal and leptomeningeal neoplasms1 (Figure 1). The MRI of the spinal cord and brain must be performed for the cancer patients developing neurological deficit. PET-CT might be considered in patients having contraindication to MRI (2,7,8). At the time of diagnosis of ISCM, 41-89% of the patients had brain metastasis (1,3,7) and 15-55% had leptomeningeal neoplasms (1,3). Prognosis is very poor with an overall survival time of 3 to 4 months following the diagnosis (5,9,10). A rapid assessment and treatment are required due to rapidly progressive motor deficit.

As the ISCM are rare, there is not a valid standard treatment. The treatment involves radiotherapy, surgical resection, chemotherapy and steroids. The concomitant use of external beam radiotherapy and steroid is reported as the most efficient treatment option to prevent developing paraplegia (5,11,12). The treatment is challenging despite of these developments. Treatments can provide functional recovery and improve survival. In the present study, we aimed to assess the clinical features of patients and the effect of radiotherapy (RT) on patients with ISCM.

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MATERIAL and METHODS

Study Design

We retrospectively reviewed the medical records of patients diagnosed with ISCM and received RT in our clinic between January 2010 and September 2017. MRI was performed on all patients. Patients with extradural metastasis, primary central nervous system (CNS), and hematologic malignity were excluded from the study. The study protocol was approved by ethics committee. This Study is based on the Helsinki Declaration Principles.

Radiotherapy

All patients underwent 3D conformal RT with 4-18 MV photon beam. 3D-CRT was delivered in one fraction per day and 5 days per week. Four patients received 3 Gray (Gy) in 10 fractions, nine patients received 2.5 Gy in 12 fractions and two patients received 2.5 Gy in 10 fractions. The radiotherapy was delivered by the lateral field in one patient, and by the anteroposterior / posteroanterior fields in others. RT sites were defined by including a lower and upper vertebra of the metastatic lesion. All patients were given corticosteroid therapy (16-24 mg) after admission to the hospital, and the dose was gradually reduced at the end of the treatment.

We made an assessment in terms of primary tumor site, the localization of lesions, the duration of symptoms, onset symptoms, the presence of neurological symptoms, and brain metastasis, the interval between spinal metastasis and diagnosis and post-RT response in our patients.

The reduction of pain and the need of steroid and painkillers, and the recovery of neurological deficit were accepted as improvement in the quality of life. During radiotherapy, all patients were evaluated weekly for treatment response and toxicities. Following RT, patients were followed up once a month for the first 3 months and then every 3 months for 2 years. At each follow-up, a complete history and a physical examination, including a neurological examination were performed. Imaging studies were performed according to clinical follow-up findings on examinations. Adverse effects were assessed in accordance with the Radiation Therapy Oncology Group (RTOG) criteria.

Statistical Analysis

Overall survival was defined as the time from the date of ISCM and to the date of death or final follow-up. For statistical analyses, SPSS (Statistical Package for Social Sciences) 13 statistical package was used. Overall survival was calculated according to the Kaplan-Meier analysis. Factors that may be associated with improvement in quality of life and neurological function were compared with the chi-square test. The significance of statistical analysis was established at $p<0.05$.

RESULTS

Of the 15 patients, six were male (40%) and nine were female (60%). The mean age of the patients was 50.33 years (range; 22-75 years). Six patients had lung cancer, six patients had breast cancer, one patient had parotid cancer, one patient had liver cancer and one patient had stomach cancer. Lesions were in the cervical cord (n=2), thoracic cord (n=3), lumber region (n=3) and whole spinal cord (n=7) in the patients. Five patients had single lesion. Of the patients, 12 (80%) had brain metastasis before or after the treatment. The onset symptoms were pain (n=8), urinary incontinence and weakness in the legs (n=1), paraplegia (n=3), incapability to walk (n=1), back pain and incapability to walk (n=2), and back pain and loss of power in the arm (n=1). Among the patients with neurological deficit, three had paraplegia, four had loss of lower-extremity motor, one had urinary incontinence and one had loss of upper extremity motor.

The mean duration of symptoms before diagnosis was 14.93 days (range; 1-52 days). Post-radiotherapy pain and need of painkillers were decreased in 10 of 11 patients with pain at the outset. An improvement was observed in the quality of life of 10 patients (66.7%). Nine patients (60%) had neurological deficit and improvement was observed in four of these patients (44.4%) at the post-RT period. The interval between diagnosis and development of spinal metastasis was 21.65 months (range; 2.96-94.26 months), and the mean follow-up period was 5.9 months (range; 0.59-17.35 months). Three patients (20%) were still alive at the end of follow-up period (Table 1 and 2) (Figure 2).

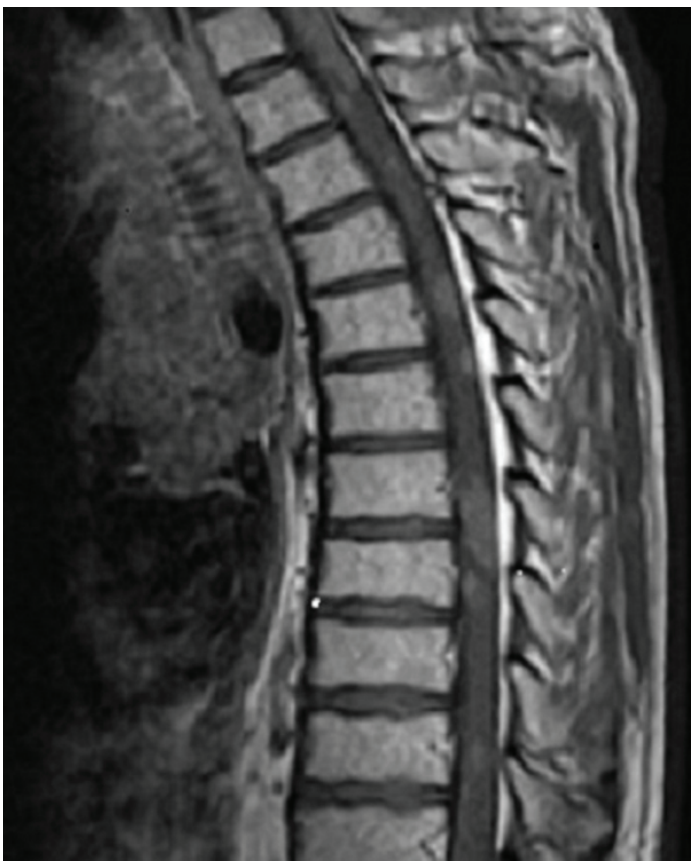

Figure 1. MRI images of intramedullary mass

Table1. Patient characteristics

	n(%)
Age (years)	
	22-75
	50.33(mean)
Gender	
Female	9(60%)
Male	6(40%)
KPS	
10-40	1(6.7%)
50-70	8(53.3%)
80-100	6(40%)
Primary tumor mass	
Breast	6(40%)
Lung	6(40%)
Liver	1(6.7%)
Parotis	1(6.7%)
Stomach lymphoma	1(6.7%)
Brain metastasis	
Absent	3(20%)
Present	12(80%)
Number of tumors	
Single	5(33.6%)
Multiple	10(66.7%)
Localization of tumor	
Cervical	2(13.3%)
Thoracic	3(20%)
Lumbosacral	3(20%)
Whole spinal	7(46.7%)
Neurological deficit	
Present	9(60%)
Absent	6(40%)
Post-RT neurological deficit	
Improvement	4(44.4%)
No improvement	5(55.6%)
RT dose	
300x10	4(26.7%)
250x12	9(60%)
250x10	2(13.3%)

KPS: Karnofsky Performance Status Scale

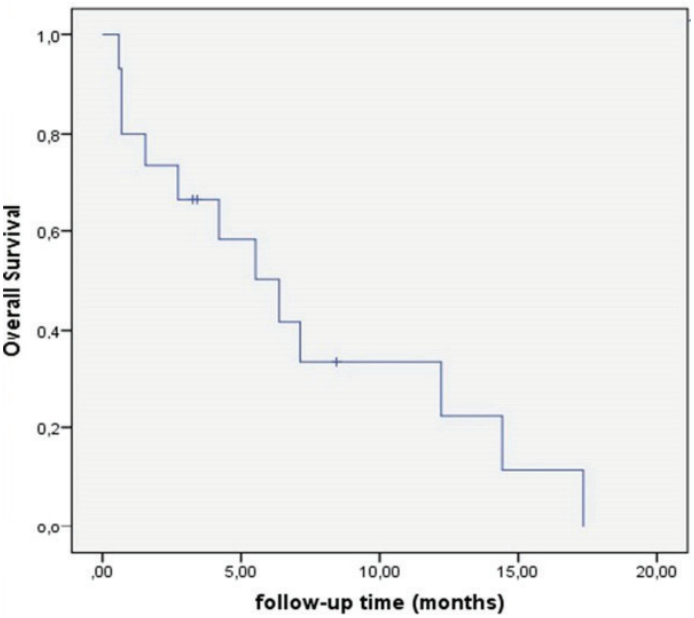

Figure 2. Overall survival rates

The most common adverse effects were hematological. Three patients had grade 2 neutropenia (20%), 2 had grade 3 thrombocytopenia (13.3%) and 1 had grade 2 anemia (6.7%). An association was detected between the initiation of radiotherapy within 10 days from the onset of symptoms and the quality of life (p=0.026). The development of neurological deficit, multiple metastasis and leptomeningeal neoplasms were determined as negative factors on the overall survival; however, a statistical significance was not detected.

Table 2. Patient results

No	Primary tumor	Age	Gender	Duration of symptoms (day)	Improvement in the quality of life	Neurological deficit	Post-RT improvement	Follow-up	Outcome
1	Breast	58	F	5	Present	Present	Present	1.54	Death
2	Breast	32	F	20	Present	Present	Present	14.42	Death
3	Breast	67	F	24	Absent	Present	Absent	0.69	Death
4	Breast	44	F	15	Present	Absent		2.73	Death
5	Breast	51	F	25	Absent	Present	Absent	12.22	Death
6	Breast	47	F	1	Present	Absent		3.42	Survival
7	Lung	48	F	1	Present	Present	Present	0.69	Death
8	Lung	56	M	1	Present	Absent		7.13	Death
9	Lung	55	M	5	Present	Absent		17.35	Death
10	Lung	42	M	24	Absent	Present	Absent	4.21	Death
11	Lung	61	M	15	Absent	Present	Absent	6.37	Death
12	Lung	42	M	25	Present	Present	Present	3.25	Survival
13	Liver	55	M	52	Absent	Present	Absent	0.59	Death
14	Parotis	75	F	5	Present	Absent		8.44	Survival
15	Stomach lymphoma	22	F	6	Present	Absent		5.52	Death

DISCUSSION

ISCM is a rare complication that might cause severe problems in the cancer patients. Although it has been reported more frequently in the lung and breast cancer, only a few reports have been published involving malign melanoma, kidney tumor, colorectal and ovarian metastasis in the literature (1,4,12,5,10,7). ISCM is generally seen in patients at the advanced stage. The interval from primary diagnosis to spinal metastasis was reported as 17-25 months (1,4,9). The initial symptoms are mostly pain, sensory loss, motor loss and incontinence (13). ISCM develop at every level of spinal cord and it is more frequently observed in the thoracic vertebra (5,6). Although it has been reported that the cervical cord is the most common site in the literature, there are studies reporting equal involvement of all sites (1,10) . In the present study is, mostly thoracic involvement was detected; however, 46.7% patients had ISCM effecting whole spinal cord.

As ISCM is a rare condition, there is not a common consensus in the treatment. RT, chemotherapy, steroids or surgery are performed in the treatment of ISCM. Treatment options are based on the experiences of retrospective clinical studies. The primary purpose is the prevention of paraplegia and pain. Patient's performance and demand should be also considered while deciding the treatment.

RT has been preferred in the treatment of ISCM for many years and accepted as a golden standard (3). RT with concomitant steroids has been accepted as the most effective treatment method in ISCM (3,5,9,11). However, it might not be effective on RT-resistant tumors. RT provides neurological recovery and pain palliation in most of the patients. While Hasshii et al. reported improvement in the neurological deficits or relief of pain in the 56% of patients after the RT, they did not detect any difference in the 44% of the patients (11). RT usually reduces tumor growth and it might prevent further neurological deficit (2,4,9). RT should be performed as early as possible for more successful outcomes.

Steroids can be used together with other treatment options. Steroid therapy offered no additional benefit when combined with RT (14). Steroids might usually decrease pain and cause temporal improvement in the neurological condition.

Surgical resection can be preferred in selected patients, especially in patients having single lesion, controlled systemic disease, good performance and not having leptomeningeal neoplasia. Improvement was observed in the overall survival and quality of life of patients who underwent surgery (1,4,5,15). Kalayci et al. reported that surgical resection had been performed in 34% of the patients. In patients who received conservative therapy; 50% improved, 28% showed no change, and 22% deteriorated. In patients who underwent surgical resection, improvement was detected in 77% and no change was reported in 23% of the patients. As the overall survival was 9.4 months in surgically treated patients, it was 5 months in conservatively treated patients (1). This condition might be related to the good performance and controlled systemic diseases of the selected patients. Surgery is becoming a more frequent option due to advanced microsurgical techniques and improvement in the image quality. However, there is lack of a prospective study comparing the surgery and RT, and showing the superiority of the one option to other. Therefore, patients must be evaluated individually while deciding the treatment option.

Chemotherapy is occasionally used as a single treatment option. It is not adequately efficient due to blood-spinal cord barrier and low drug permeability. However, it might be preferred in chemotherapy sensitive tumors, such as lymphoma or small cell carcinoma.

ISCM has poor prognosis despite of treatments. The mortality ratios were reported as 80% within 3-4 months after the onset of the first symptom (1,10). The median survival is published as 3-4 months (9,11,14). In the present study, the median survival was detected as 5.9 months. In accordance with the study outcomes of Kalaycı et al., the survival rate was two times longer in surgically treated patients in comparison to conventionally treated patients. Lee et al. reported the overall survival as 1 month and 5.5 months in patients having primary lung cancer and breast cancer, respectively. They showed that ISCM patients arising from breast cancer had better prognosis; however, the overall survival was 3.9 months (5). Histological grade and type of tumor are among the major factors determining the survival. Survival was shorter in patients with poor differentiated carcinoma than in those with adenocarcinoma (3). The clinical factors effecting the prognosis could not been detected clearly due to the limited number of studies. Dam-Hieu et al. showed the effect of neurological condition, the presence of CNS metastasis and primary tumor type on overall survival but they could not find a statistically significant result (4). In our study, we found that the development of neurological deficit, the presence of multiple metastasis and leptomeningeal metastasis had a negative effect on survival, but we could not detect a statistically significant result.

CONCLUSION

Mortality rate is extremely high in patients with ISCM despite of all treatment options. The treatment should be initiated as early as possible and patient's demand, performance and the presence of a systemic disease should be considered while deciding the treatment method. RT is still accepted as a golden standard even though other treatment options.

Competing interests: The authors declare that they have no competing interest.
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