

Malignant Spinal Cord Compression: Clinical Presentation, Treatment Outcome and Prognostic Factors

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Background: Malignant spinal cord compression (MSCC) is an emergency condition in oncology, which immediately needs appropriate treatment. Additionally, MSCC has high morbidity. The aim of the present study is to evaluate clinical presentation, treatment outcome and to determine prognostic factors in MSCC patients.

Materials and Methods: A retrospective study was conducted and enrolled 71 adult patients with newly diagnosed of MSCC by using Magnetic Resonance Imaging (MRI) or myelogram in Srinagarind University Hospital, Khon Kean, Thailand from January 1st, 2000 to December 31st, 2010. Clinical and survival data were evaluated by uni- and stepwise multivariate analysis.

Results: 71 patients with MSCC were enrolled; 46 male (65%) and 25 female (35%), with an average age of 51 years old. The highest incidence age of MSCC was 41 to 60 years old. The most common primary malignant site was unknown primary origin (39.5%) followed by lung cancer (11.3%), lymphoma (7.0%), prostate cancer (5.6%), cholangiocarcinoma (5.6%) and hepatocellular carcinoma (5.6%). The most common presenting symptom was weakness (88.7%) and grade 0 of motor function was commonly found compared to the others. The modalities of treatment were surgery, radiation, chemotherapy, and steroid therapy. The most common treatment was radiation plus steroid. Only 14 patients (20%) received chemotherapy. These patients were diagnosed with hematologic malignancy (42.8%) particularly lymphoma and acute leukemia. The overall survival time of patients was about 6.8 months (95% confidence interval, CI: 5.8 to 7.7). Patients with age less than 40 years old, receiving either steroid treatment or chemotherapy tended to have longer survival time. Only chemotherapy treatment was a significantly good prognostic factor (Hazard ratio was 0.84; 95% CI: 0.73 to 0.96).

Conclusion: MSCC is the important disease that causes disability, decreased quality of life and high mortality. Early diagnosis and treatment might improve survival time in patients particularly who receiving chemotherapy and having chemo-sensitive tumor with good performance.

Keywords: Malignant spinal cord compression; MSCC; Clinical presentations; Treatment outcome; Prognostic factor

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Malignant spinal cord compression (MSCC) is defined as spinal cord or cauda equina compression by direct pressure, vertebral collapse or instability by metastatic spread or direct extension of malignancy, which causes neurological disability⁽¹⁾. MSCC occurs approximately 5% of all patients with cancer and causes morbidity⁽²⁾. Approximately 85% of MSCC cases result from a consequence of metastasis of a primary tumor. The common primary sites of cancer are lung, prostate and breast cancer^(1,3,4). Other cancers frequently associate

with MSCC including lymphoma, renal cancer, multiple myeloma, melanoma and sarcoma^(4,5). Thoracic spine is affected more than 70% of all MSCC cases followed by lumbosacral region (20%) and cervical region (10%). However, multiple site involvement could be found about 20 to 25% of all MSCC cases^(3,5). The most common site of vertebrae, which are frequently affected, is the vertebral body resulting in the anterior compression of the spinal cord (85 to 90%). Paravertebral mass growing through the foramina are less frequent found (10 to 15%)^(1,3,6).

Signs and symptoms of malignant spinal cord compression are pain (88 to 96%), motor weakness (76 to 78%), autonomic dysfunction (40 to 64%) and sensory loss (51 to 80%). Some patients (8 to 37%) with MSCC also have asymptomatic presentation with involvement of other vertebral bodies^(1,3,6,7). Pain is usually the earliest presenting symptom and has often presented for several weeks before MSCC is diagnosed. The distinct characteristic of pain is localized or radicular pain with typically increasing pain intensity over several weeks^(3,4,6). Approximately 60 to 85% of patients have motor weakness at the first time of

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diagnosis. Pretreatment neurological status of patients is the most important predictor factor to indicate the motor function after the complete course of treatment. Sensory deficit is slightly less common clinical presentation compared to motor weakness; however, it is still detectable in patients about 40 to 90%. The spinal sensory deficit is usually presented 1 to 5 segments below the anatomic levels of cord compression and patients may occasionally present with bowel and bladder dysfunction or gait ataxia^(1-4,6,7).

Median survival of patients was 3 months after the primary diagnosis of MSCC and it is found in treated patients whereas un-treated patients have only 1 month of median survival. Pretreatment ambulatory status is the most important predictor factor of patient ambulation after treatment and of improved survival. Median survival after spinal cord compression depends on the number of metastases, the type of tumor, and the patient's functional status⁽⁸⁾. The aim of the present study is to evaluate clinical presentation, treatment outcome and to determine prognostic factors in MSCC patients.

Materials and Methods

A retrospective study was conducted in MSCC patients, who received treatment in Srinagarind Hospital, Khon Kaen University (a 1,000-bed university hospital), Khon Kaen, Thailand, during January 1st, 2000 to December 31st, 2011. The present study was reviewed and approved by the institutional review board (HE561261).

Patients were definite diagnosed as MSCC by Magnetic Resonance Imaging (MRI) or myelogram findings, which was confirmed by the radiologist. The enrolled patients had the age more than 15 years and were newly diagnosed MSCC. The patients who had spinal cord compression from other causes such as epidural abscess, compression fracture or no definite diagnosis of MSCC by MRI or myelogram e.g., diagnosis by clinical features of patients or patients' history of brain tumor, brain metastasis or other major neurologic diseases, which may also cause motor dysfunction, were excluded.

Demographic data of patients including sex, age, types of cancer, first clinical presentation were recorded. Motor power of patients were evaluated both before and after treatment of MSCC. The most severe grading of motor power from each part in patients was recorded both before and after the treatment. Motor power is classified into 6 levels (grade 0 to 5). The definition of grade 0 is no muscle movement. Grade 1 is visible muscle movement but no movement at the joint. Grade 2 is movement at the joint but not against gravity. Grade 3 is movement against gravity but not against added resistance. Grade 4 is movement against resistance but less than normal strength. Grade 5 is normal strength of muscle. After treatment, patients were followed-

up for 3 months or before they were dead to evaluate the grading of motor power. Improvement and deterioration of motor function were defined as a change of at least one level of motor function.

The treatment modalities of MSCC patients were surgery, radiation, chemotherapy, and steroid treatment. The procedure of surgery for MSCC patients was decompressive laminectomy. If patients had surgical condition, the surgical procedure was done as soon as possible after definite diagnosis of MSCC by MRI or myelogram. However, some patients, who had paraplegic condition without residual motor function for more than 24 hours, were not offered a laminectomy for the first choice of treatment. Basically, patients normally had additional radiation after surgery. Patients, who were treated with single treatment of radiotherapy, were received the first dose of radiation once the definite diagnosis of MSCC by imaging was made. A single posterior field of radiation was given to the patients to target the affected part of the spines including at least one adjacent vertebra above and below the epidural block. The average cumulative doses radiation was 300 cGy. Corticosteroid was commonly used in many patients and the dosage used was various. The administration form of corticosteroid was either intravenous dexamethasone or oral dexamethasone/prednisolone and the dose of steroid was gradually tapering off as soon as possible based on the clinical evaluation and drug adverse effects. Additionally, a small proportion of patients did not receive any specific treatment because these patients accepted the prognosis of disease and required the palliative approach.

Statistical analysis

The objectives of the present study were to evaluate the clinical outcomes and to determine prognostic factors of MSCC patients. The survival time was defined as the duration from the date of MSCC diagnosis to the death date of patients, which were resulted from any causes. Patients' characteristics and cancer data were summarized as mean and percentage.

The cumulative survival rates were analyzed using the Kaplan-Meier method. The differences of the Kaplan-Meier curves were calculated using the log-rank test. Many variable factors were analyzed for prognostic factors including sex, age, the first clinical presentation, the degree of motor function before and after treatment, receiving surgery, radiotherapy, chemotherapy, and corticosteroid treatment. Univariate analysis was performed using the Chi-squared test. A stepwise multivariate analysis was performed using the Cox proportional hazard model. To achieve the overall statistically significant results, the p-value must be less than 0.05 and the 95% confidence interval (CI) are used to evaluate the adjust confidence. The statistical analyses

were performed by using Stata software version 11. The data were complete for analysis on September 30th, 2014.

Results

Demographic data and clinical presentation

Seventy-one MSCC patients were enrolled in this study. The patients' characteristics are presented in Table 1. There was higher proportion of male participants compared to female. The most common age group of MSCC patients was 41 to 60 years old.

The most common primary site of tumor was unknown primary. Additionally, the primary tumor sites, which were able to identify, were lungs, lymphoma, prostate, bile duct and hepatocellular carcinoma (HCC). Prostate and lungs were the most common primary tumor sites, which were found in male patients while the most common primary tumor sites in female were breast, bile duct and lungs.

The most common presenting symptom of patients was weakness followed by paresthesia, back pain, and bowel and bladder involvement, respectively. The first and second most common severities of motor function before treatment was grade 0 (55%) and grade II (20%), respectively. Only one patient had clinical presenting symptom without neurological deficit.

Most patients received both radiation and corticosteroid treatment followed by tri-modality treatment including surgery, radiation, and corticosteroid. Only two patients of all had no specific treatment. Twenty-two percentages of all patients had improved motor function after treatment. For the patients, who well responded to treatment, the deficit motor function was one level improved better than the motor function level prior to treatment.

Prognostic factors of MSCC patients

The median overall survival time of all patients was 6.8 months (95% CI, ranging 5.8 to 7.7 months) (Figure 1). Six months and 1-year survival rate were 39.4% and 19.4%, respectively. Univariate analysis showed that prognostic factors; age, receiving corticosteroid treatment and receiving chemotherapy, were associated with overall survival of MSCC patients. In addition, only receiving chemotherapy factor was a significant prognostic factor via multivariate analysis. Whilst, sex, clinical presentation, degree of motor function before and after treatment, receiving surgery and radiotherapy did not significantly associate with prognostic factors (Table 2).

Discussion

The results of the present study showed that MSCC was found in male as higher proportion compared to female cancer patients. The median age of MSCC patients was 51 years. It was explained that the high incidence of cancer was

Table 1. Demographic data and clinical presentation of 71 malignant spinal cord compression patients

Variables	n (%)
Sex	
Male	46 (64.7)
Female	25 (35.2)
Age	
≤40	19 (26.7)
>40	52 (73.2)
Primary site of tumor	
Unknown primary	22 (30.9)
Lung cancer	8 (11.2)
Lymphoma	5 (7.0)
Prostate cancer	4 (5.6)
Thyroid cancer	4 (5.6)
Bile duct cancer	4 (5.6)
Hepatocellular carcinoma	4 (5.6)
Breast cancer	3 (5.6)
Leukemia	3 (5.6)
Others	15 (5.6)
First clinical presentation	
Motor weakness	62 (88.5)
Numbness	54 (77.1)
Back pain	48 (68.5)
Bowel and bladder involvement	30 (42.8)
Motor power at presentation	
Grade 0	39 (54.9)
Grade 1	4 (5.6)
Grade 2	14 (19.7)
Grade 3	7 (9.8)
Grade 4	6 (8.4)
Grade 5	1 (1.4)
Motor power after treatment	
Grade 0	35 (49.2)
Grade 1	9 (12.6)
Grade 2	12 (16.9)
Grade 3	6 (8.4)
Grade 4	9 (12.6)
Grade 5	0
Treatment	
Surgery	34 (48.5)
Radiotherapy	42 (60.0)
Chemotherapy	14 (20.0)
Corticosteroid	47 (67.1)

commonly found in male compared to female and the older age group was found cancer at higher proportion compared to the younger age group. Therefore, oncologic emergency, especially malignant cord compression, was found at high incidence in that population. These results were comparable to the previous study^(4,9).

The present study also revealed that the etiology of

MSCC is unknown. It was suggested that when the patients were diagnosed as cancer and know their prognosis, they usually accepted it and would not like to know about the primary site of the disease. However, lungs, lymphoma, prostate and breast cancer were the most common primary sites in patients, who had known the primary disease and this was consistent with the previous reports^(1,3-6,9). The present study also showed that both CCA and HCC were the most common cause of MSCC compared to the previous

studies because this region is the epidemic area and had high incidence of these cancers. Liver flukes play a major role in bile duct cancer carcinogenesis. *Opisthorchis viverrini* infection is a common risk factor for CCA in Thailand whereas viral hepatitis B infection is an important risk factor for HCC⁽¹⁰⁾.

Previous studies proposed that back pain was the most common clinical presentation of MSCC patients followed by motor weakness, autonomic dysfunction and sensory loss^(1,3,6,11). However, the present study showed that motor weakness was the most common clinical presentation followed by numbness. In addition, weakness was very severe resulting in disability and the most common motor function was grade 0. It was described that the patients did not seriously concern about back pain or might ignore this symptom because the back pain is a very common problem resulting from working. Consequently, this delayed the time for these patients to see the doctor for appropriate diagnosis and treatment. Therefore, these patients usually had the late stage of disease.

The present study showed that 22% of patients with impaired motor function were improved after treatment. Previous report showed that six percentage of MSCC patients

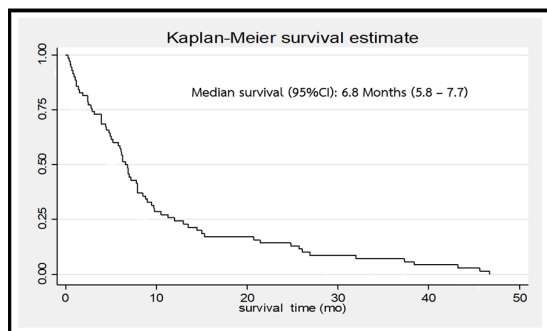


Figure 1. Kaplan-Meier survival curve for the overall survival time of 71 patients with malignant spinal cord compression.

Table 2. Prognostic factors of 71 malignant spinal cord compression patients

Variable	Univariate			Multivariate		
	MS (months)	95% CI	p-value	HR	95% CI	p-value
Age			0.003	1.02	0.55 to 1.89	0.938
≤40 years	8.8	1.5 to 29.1				
≥41 years	8.5	5.3 to 11.6				
Underwent surgery			0.227			
Yes	6.3	5.2 to 7.3				
No	8.5	3.7 to 13.2				
Receiving radiotherapy			0.620			
Yes	8.5	5.4 to 11.6				
No	6.3	4.5 to 8.0				
Receiving chemotherapy			0.020	0.84	0.73 to 0.96	0.020
Yes	7.2	6.0 to 8.3				
No	3.9	1.5 to 6.2				
Receiving steroid			0.054	1.13	0.92 to 1.39	0.205
Yes	9.5	5.1 to 13.8				
No	5.8	4.0 to 7.5				
Motor power at presentation			0.452			
Grade 0	9.7	2.3 to 17.0				
Grade 1 to 5	7.9	4.9 to 10.8				
Motor power after treatment			0.141			
Grade 0	5.0	3.3 to 6.6				
Grade 1	6.8	5.3 to 8.2				
Grade 2	7.9	6.2 to 9.5				
Grade 3	2.4	2.0 to 6.8				
Grade 4	10.5	8.1 to 12.8				

had improved motor function and were able to ambulate. Patients, who were treated with laminectomy followed by radiotherapy, had response of treatment better than those treated with either radiotherapy or laminectomy⁽⁷⁾.

The overall survival time of MSCC patients in the present study was 6.8 months after diagnosis of MSCC. Previous study investigating in patients with malignant spinal metastasis demonstrated that estimated average survival time of patients with MSCC approximately ranged between 3 and 7 months and 36% of patients possibly had survival time up to 12 months⁽¹²⁾. The results presented that patients, who had survival time more than 12 months, were 19.4%, which was lower than the results of the previous reports. This is possibly because the patients included in the present study had severe clinical presentation and patients did not want to have an aggressive treatment. The present study also showed that the patients, who received both surgery and steroid treatment, had the longest survival time compared to the others. Previous report studying breast cancer patients with metastasis and developing malignant spinal cord compression, showed that single treatment of radiation was comparative effective treatment in those patients⁽¹³⁾. Additionally, some other studies presented that stereotactic radiosurgery, which is the treatment for patients with spinal axis tumors, had no different clinical outcome compared to patients, who received surgery followed by radiation⁽¹⁴⁾.

The prognostic factors, which were analysed by univariate analysis, showed that patients, who had age less than 40 years old, steroid treatment or chemotherapy, had survival time longer than the others. However, chemotherapy was the only one prognostic factor, which is significant, analysed by multivariate analysis. The author described that patient who had good performance status with good motor function usually received chemotherapy treatment. In addition, most patients, who received chemotherapy, was hematologic malignancy (42.8%) such as lymphoma and acute leukemia which had good response to chemotherapy. However, previous study demonstrated that patients with spinal cord compression from myeloma presented that age of patients had no influence on survival time of patients⁽²⁾.

The limitation of the present study was small numbers of sample size because patients, who were included in the present study, must have the definite diagnosis by MRI or myelogram. Many patients, who had a clinical presentation of malignant spinal cord compression, but MRI or myelogram was not performed, were diagnosed as MSCC by plain films. The plain films usually showed osteolytic lesion and compression fracture. Additionally, many patients from the secondary care of hospitals were transferred to Srinagarind Hospital for radiation but these patients did not have the investigation of MRI or myelogram. Consequently,

all these patients were not included in the present study. Other limitation of the present study was pathology for definite diagnosis of cancer. The authors showed most common of MSCC was unknown primary origin (39.5%). After diagnosis, many patients were treated by radiation and palliative care. The authors denied tissue biopsy for definite diagnosis. In addition, the medical records of many patients were not completely recorded, therefore, these patients were also excluded from the present study.

For future study, the authors would like to further study about defining an appropriate time since patients develop abnormal motor function at the first presentation until patients receive an appropriate treatment for evaluating the golden period.

Conclusion

MSCC is the important disease that causes disability, decreased quality of life and high mortality. Early diagnosis and treatment possibly improve survival time, particularly patients with chemo-sensitive tumor and good performance, who receive chemotherapy.

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What is already known on this topic?

Malignant spinal cord compression (MSCC) is an emergency condition in oncology, which immediately needs appropriate treatment. Additionally, MSCC has high morbidity.

What this study adds?

The results of this study revealed that early diagnosis and treatment might improve survival time in patients particularly who receiving chemotherapy and having chemo-sensitive tumor with good performance.

Conflicts of interest

The authors declare no conflict of interest.

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