Liaison Treatment for Metastatic Spinal Tumors

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Abstract:

Introduction: The cancer board system employed at many hospitals and treatment centers involves multidisciplinary healthcare teams, including physicians, and the timing of treatment generally follows that of a consultation model. Thus, it is difficult to detect spinal metastases using the current implementation of the cancer board system, which can lead to delays in treatment. A new multidisciplinary treatment strategy for patients with metastatic spinal tumors was designed, and 745 patients were treated based on this strategy.

Methods: In the first 5 years using the liaison treatment approach, 745 patients were diagnosed with metastatic spinal tumor. Tumors were discovered before a skeletal-related event (SRE) in 704 patients and after an SRE in 41 patients. We conducted our analysis in two patient groups: those with and without an SRE at the time of treatment initiation.

Results: In most patients, the average spinal instability neoplastic score was 5.2, which indicates that we were able to detect the spinal tumor before a significant breakdown of the spinal support system. Ninety-five percent of patients were classified according to the Frankel grade classification during their initial diagnosis, and many patients initially underwent treatment before the onset of paralysis. Of patients with an SRE, 33% were Frankel grade E, indicating that approximately half were paralyzed at initial diagnosis. The median survival duration was prolonged by approximately 9 months in patients without an SRE compared with those with an SRE.

Conclusions: Orthopedic spine surgeons are responsible for maintaining activities of daily living, improving quality of life, and prolonging life expectancy in patients with metastatic spinal tumors. The results of this study revealed that the liaison treatment system for metastatic spinal tumors has made it possible to successfully prevent SREs without neurological deficits and to prolong survival.

Keywords:

multidisciplinary treatment, a SRE, metastatic spinal tumor, liaison treatment

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Introduction

Cancer treatments have changed dramatically in the past decade. Advances in treatment modalities, such as chemotherapy, molecularly targeted therapy, bisphosphonates (zoledronic acid), and radiotherapy, have helped in increasing the life expectancy of patients with cancer. However, a concomitant increase in the number of patients with bone metastases can be expected. Metastatic spinal tumors differ from other types of bone metastases in that the occurrence of skeletal-related events (SRE)[1,2] can result in significantly reduced activities of daily living (ADLs) and quality of life (QOL). Reduced ADLs can lead to contraindications for certain anticancer agents or radiotherapy, resulting in a shortened life expectancy[3,4].

In recent years, many hospitals and treatment centers have begun adopting multidisciplinary approaches for the treatment of bone metastases[3]. The management of patients with bone metastases requires close cooperation within treatment teams consisting of specialists in fields such as oncology, palliative care, radiation therapy, orthopedics, nuclear medicine, and radiology[5]. Treatment strategies for bone metastases secondary to a variety of primary cancers should be comprehensively planned, taking into consideration the status of the primary cancer and the patient's prognosis and social background[6]. This approach to patient care is important to improve outcomes and QOL. Although the cancer board system employed at many hospitals and treatment centers involves multidisciplinary healthcare teams, including physicians, the timing of treatment generally follows

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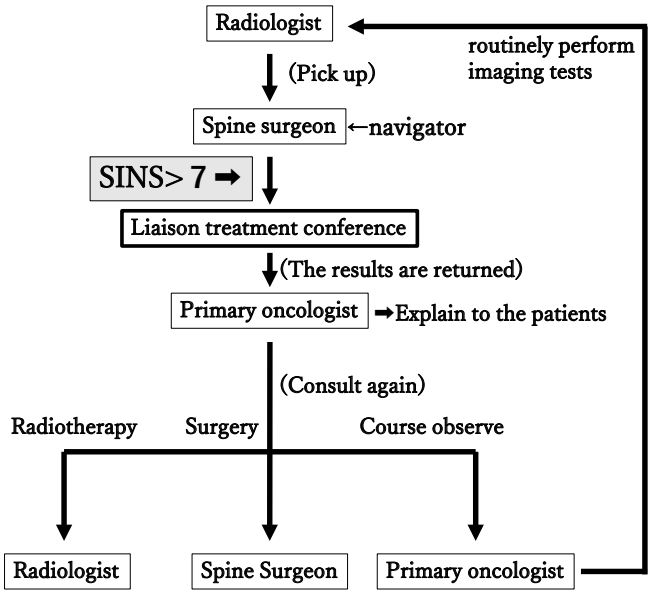

Figure 1. Liaison treatment.
All patients initially diagnosed with metastatic spinal tumors using computed tomography (CT), magnetic resonance imaging (MRI), positron emission tomography-CT (PET-CT), or bone scintigraphy are reviewed monthly by radiologists. Similarly, all images used for diagnosis are also reviewed by spine surgeons. The instability of the spine is evaluated using the spinal instability neoplastic score (SINS) of the metastasized vertebra. For each of the patients reviewed on a monthly basis, those with a SINS>7 (imminent instability) are reviewed during the liaison conference call to discuss possible treatments. Spine surgeons, radiologists, and physicians are in close contact.

that of a consultation model. In other words, the primary oncologist only discusses problematic patients with the multidisciplinary team at his or her discretion. However, they sometimes overlook signs of serious SRE, such as pain, motor dysfunction, and sensory disturbance, if these signs are not severe or if patients have more serious symptoms that are unrelated to SRE[6]. In this system, it is essential for the primary oncologist to monitor all patients with metastatic spinal tumors and to coordinate with multiple departments. If this is not feasible, treatment procedures are unfortunately subject to "doctor's delay." Thus, detecting spinal metastases using the current implementation of the cancer board system is difficult, and this can lead to delays in treatment.

In cases of metastatic spinal tumor, an orthopedic spine surgeon should play a leading role. The liaison model employed at our hospital enables the entire healthcare team to be involved with all patients who have initially been diagnosed with metastatic spinal tumors by radiologists[7]. We have created a multidisciplinary team centered on an orthopedic spine surgeon and are practicing a new approach to patient care known as liaison treatment.

The present paper aims to inform the scientific community about a new organizational treatment model specifically designed for patients with metastatic spinal tumors.

Materials and Methods

Liaison treatment (Fig. 1)

All patients initially diagnosed with metastatic spinal tumors using computed tomography (CT), magnetic resonance imaging (MRI), positron emission tomography-CT (PET-CT), or bone scintigraphy are reviewed monthly by radiologists. Similarly, all images used for diagnosis are also reviewed by spine surgeons. The instability of the spine is evaluated using the spinal instability neoplastic score (SINS[8]) of the metastasized vertebra. Spinal instability neoplastic score (SINS) use a combined score of six variables, including lesion location, pain, and degree of vertebral body destruction. A score of less than 6 of a possible 18 points indicates stability, whereas scores of 7 to 12 and more than 13 indicate imminent instability and instability, respectively (Table 1).

For each of the patients reviewed on a monthly basis, those with a SINS > 7 (imminent instability) are reviewed during the liaison conference call to discuss possible treatments.

During these conference calls, the primary oncologists regularly review images of patients who do not require immediate surgery or radiotherapy, prioritized based on risk factors. In this way, the radiologist's interpretation of each image is reviewed by the orthopedic spine surgeon on a regular basis, and metastatic progression can be detected early. The sequence of events wherein the spine surgeon reviews patient images selected by the radiologist is an important aspect of this treatment method. In addition, spine surgeons, radiologists, and physicians are in close contact to prevent serious SREs in advance, a process that is very important and effective.

Treatment strategy at our hospital

Our treatment approach combines the expert opinions of the primary oncologist and each specialist and takes into consideration each patient's conditions and life expectancy. Our first-line treatment for patients with pain but not paralysis is radiotherapy. However, for patients with a SINS > 13, we actively consider surgery as a treatment option.

For patients with a SINS between 7 and 12, we actively consider surgery for those (1) whose primary lesion is in the thoracic spine, (2) who have osteolytic destruction of the posterior wall of the vertebral body or pedicle, or (3) who have evidence of vertebral body destruction.

However, if patients do not want surgery, have a poor general condition, and have metastases in almost all vertebrae, surgery is not recommended. In addition, in principle, surgery is performed in patients where the primary site is under control or who still have treatment options.

A clear surgical indication that impacts life expectancy has yet to be identified due to the recent transitions in treatment modalities. Conventional surgeries are only indicated for patients with a life expectancy of more than 6 months;

Table 1. The Spinal Instability Neoplastic Score (SINS)[2].

SINS Component	Score
Location	
Junctional (occiput-C2, C7-T2, T11-L1, L5-S1)	3
Mobile spine (C3-6, L2-4)	2
Semirigid (T3-T10)	1
Rigid (S2-5)	0
Pain*	
Yes	3
Occasional pain but not mechanical	1
Pain-free lesion	0
Bone lesion	
Lytic	2
Mixed (lytic/blastic)	1
Blastic	0
Radiographic spinal alignment	
Subluxation/translation present	4
De novo deformity (kyphosis/scoliosis)	2
Normal alignment	0
Vertebral body collapse	
>50% collapse	3
<50% collapse	2
No collapse with >50% body involved	1
None of the above	0
Posterolateral involvement of spinal elements**	
Bilateral	3
Unilateral	1
None of the above	0
Less than 6: stability	
7 to 12: imminent instability	
More than 13: instability	

*Pain relief with recumbency and/or pain with movement/loading of spine.
**Facet, pedicle, or costovertebral joint fracture or replacement with tumor.

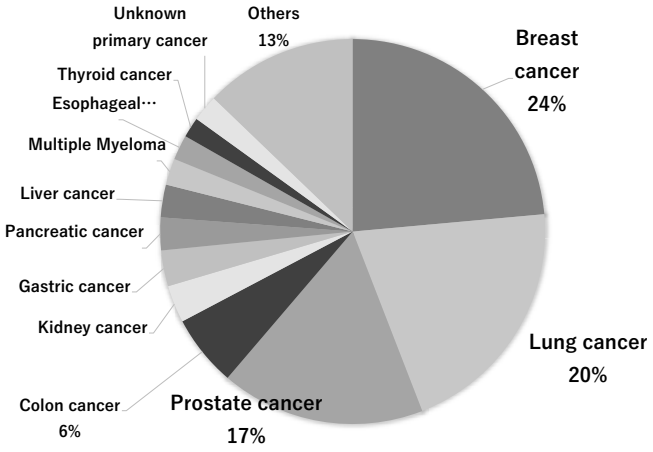

Figure 2. Primary tumor site.
The cancer types of the primary lesion are mostly breast cancer, lung cancer, and prostate cancer and have spread to all other carcinomas.

however, the efficacies of minimally invasive surgeries have been demonstrated in numerous studies[5-7]. Thus, surgery has become an option for patients with a life expectancy shorter than 6 months, especially if minimally invasive surgery leads to earlier ambulation or discharge. Furthermore, minimally invasive surgery does not make patients ineligible for postoperative adjuvant radio- or chemotherapy, enabling earlier transitions to such treatments.

Patients

A total of 1064 patients were diagnosed with metastatic spinal tumors at our hospital from April 2012 to December 2018. In the first 5 years using the liaison treatment approach, 745 were diagnosed with metastatic spinal tumor between December 2013 and December 2018. Tumors were discovered before an SRE in 704 patients and after an SRE in 41 patients. Of the latter 41 patients, 38 were diagnosed because of an SRE or were referred from other hospitals after an SRE. We conducted our analysis in two patient groups: those with (SRE(+)) and without an SRE (SRE(−)) at the time of treatment initiation.

Outcome-related factors

The correlation of outcome with the following items was evaluated: (1) age; (2) gender; (3) cancer type of primary lesion; (4) the Tokuhashi score[9], Tomita classification[10], Katagiri score[11], and new Katagiri score[12] to evaluate prognosis; (5) the SINS to evaluate the stability of the vertebral body[8]; (6) the Frankel grade classification to assess the degree of spinal cord injury; and (7) performance status (PS) to evaluate QOL. PS was evaluated using the Eastern Cooperative Oncology Group PS (ECOG PS) scale[13]. Survival time was calculated from the date of enrollment to the date of death using the Kaplan-Meier method. Statistical analyses were conducted using the SPSS software, version 23.0 (IBM Japan Business Services Co., Ltd., Tokyo, Japan), with a significance level of 5%. Between-group differences in baseline characteristics and clinical outcomes were assessed using the Mann-Whitney U test.

Results

As presented in Fig. 2, most primary tumor sites were in the breast, lung, or prostate.

The average age did not differ significantly between patients with and without an SRE (Table 2). In terms of prognosis evaluation, only the Tokuhashi score differed significantly between the two groups ($P \leq 0.01$). In most patients without an SRE, the average SINS was 5.2, indicating that we were able to detect the spinal tumor before a significant breakdown of the spinal support system. On the other hand, the average SINS was 9.2 in patients with an SRE, indicating that these patients began treatment in the imminently unstable state ($P \leq 0.01$). Moreover, as presented in Table 3, many patients in the group without an SRE initially underwent treatment at less than 6 points, thereby indicating stability according to SINS classification.

Table 2. Baseline Characteristics.

	SRE (+) (N=41)	SRE (−) (N=704)	P value
Age	72	68	0.04
Female sex-no. (%)	11 (42)	318 (45)	
SINS	9.2	5.2	P<0.01
Tokuhashi score	7	8.8	P<0.01
Tomita score	5.4	6.1	P<0.01
Katagiri score	3.9	4	0.16
New Katagiri score	4.8	5	0.75
PS	3.1	1.3	P<0.01

SRE: skeletal-related events
SINS: the spinal instability neoplastic score
PS: performance status
PS was evaluated using the Eastern Cooperative Oncology Group Performance status (ECOG PS) scale.

Table 3. Classification of SINS.

SINS	SRE (+)	SRE (−)
6≥ (stability)	8 (20%)	514 (73%)
7~12 (imminent instability)	28 (68%)	182 (26%)
13≤ (instability)	5 (12%)	8 (1%)
total	41	704

Ninety-five percent of patients were classified according to the Frankel grade classification during their initial diagnosis, and as presented in Fig. 3, many patients initially underwent treatment before the onset of paralysis. Of patients with an SRE, 33% were Frankel grade E, indicating that approximately half were paralyzed at initial diagnosis.

As presented in Table 4, in the group without an SRE, there were few cases requiring surgery.

Table 5 presents the classification of procedure. In the group without an SRE, many surgeries with MISt were performed. The drugs bisphosphonate and denosumab were administered in nearly half of both groups (Table 4).

PS at the initial diagnosis was significantly lower in patients with an SRE (score, 3.1) compared with those without an SRE (score, 1.3) (P ≤ 0.01). The patients without an SRE performed better than those with an SRE (Table 2). Patient QOL was compromised by the occurrence of SRE.

The median survival duration for the patients without an SRE was longer than those with an SRE by approximately 9 months (21.0 months, 95% confidence interval (CI) 18.0-23.9) compared with those with an SRE (12.0 months, 95% CI 0-28.7) (P ≤ 0.05) (Fig. 4).

Discussion

Advances in the diagnosis and treatment of cancer patients have prolonged life expectancy, and the number of cancer patients is expected to increase in the future[14]. This will necessarily lead to an increase in the number patients

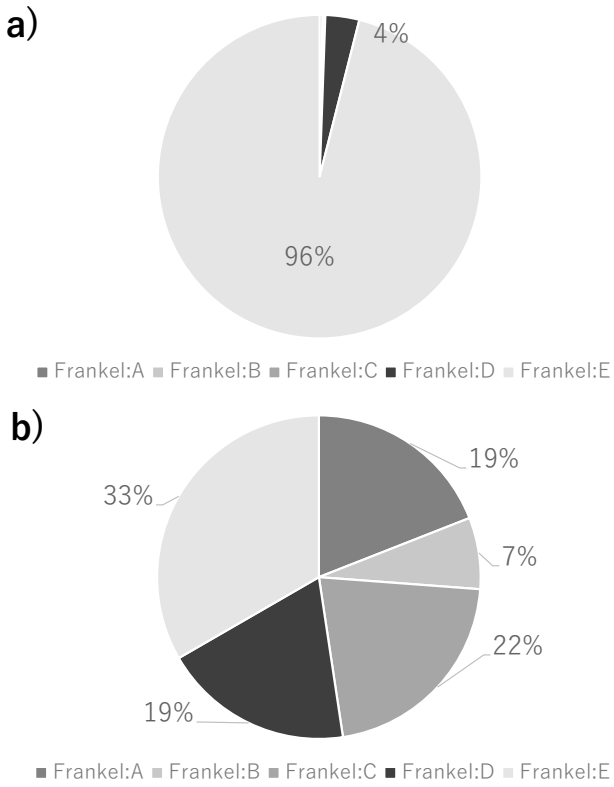

Figure 3. The occurrence situation of paralysis.
Tumors were discovered before an SRE in 704 patients and after an SRE in 41 patients.
a) The percentage of Frankel E at the time of the therapeutic intervention was 96% before an SRE occurred.
b) In patients who intervened after the onset of SRE, Frankel E (normal) defect was observed only in 33% of patients, and approximately 50% of patients were paralyzed at the initial diagnosis.

Table 4. Cancer Treatments.

	RT		OPE		Bisphosphonates & Denosumab	
	(+)	(−)	(+)	(−)	(+)	(−)
SRE (+) (N=41)	28 (68%)	13	15 (34%)	26	26 (63%)	11
SRE (-) (N=704)	204 (29%)	500	35 (5%)	669	366 (52%)	338

SRE: skeletal-related events
RT: radiotherapy

Table 5. Classification of Operation.

Procedure	pts SRE (+)	pts SRE (-)
Decompression surgery alone	5	0
Decompression surgery with posterior approach	6	4
Posterior approach alone (conventional)	0	1
Posterior approach alone (MISt)	3	26
BKP	1	4

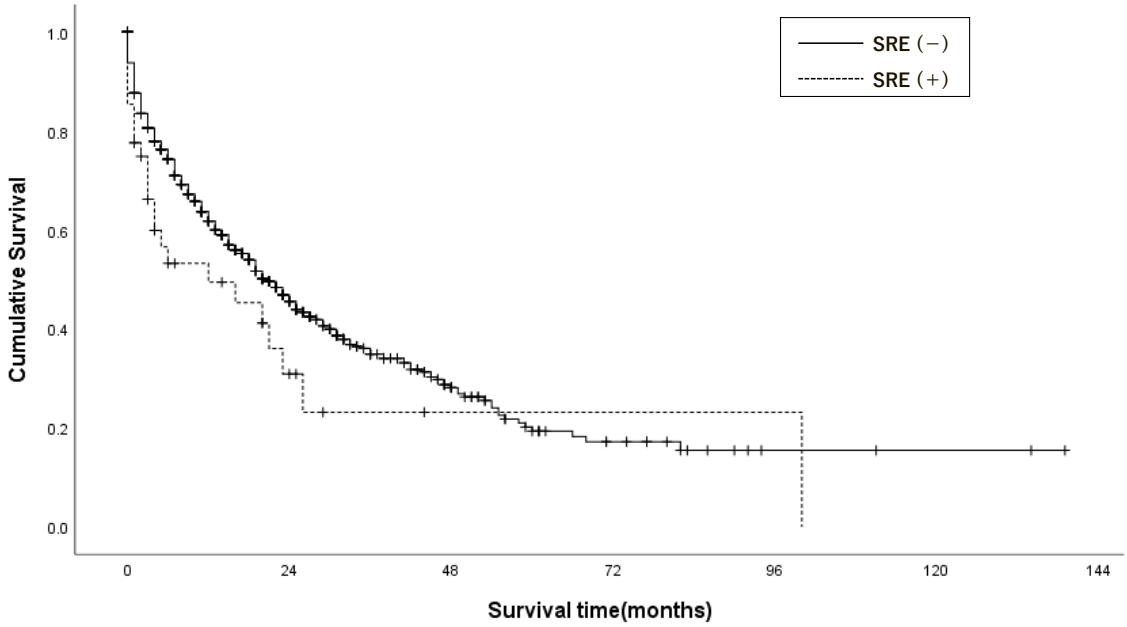

Figure 4. Kaplan-Meier curve for Survival.
The median survival duration was 21.0 months (95% confidence interval (CI) 18.0-23.9) for patients without an SRE and 12.0 months (95% CI 0.0-28.7) for patients with an SRE. Prognosis was prolonged for approximately 9 months in patients without an SRE (P≤0.05).

with spinal metastases. Metastasis to the spine and spinal cord compression in SRE are oncologic emergencies that reduce patient survival and QOL. Spine surgeons are charged with ensuring that ADLs can be maintained, QOL can be improved, and life expectancy can be prolonged in patients with metastatic spinal tumors.

In recent years, multidisciplinary treatment for metastatic spinal tumors has gained much attention[3,5,6,15-19]. Therapeutic strategies that take into account patient prognosis and background, as well as the status of the primary cancer, are important to improve outcome and QOL. Evidence is accumulating on the efficacy of cancer boards and the prevention of SRE applying multidisciplinary treatment methods, and a dramatic decrease in emergency surgeries has been demonstrated[3,6,17].

While cancer boards and multidisciplinary teams are effective, their meetings are often held only biweekly or monthly, and it is therefore sometimes difficult to manage patients with a serious impending SRE in a timely manner. Coordination and rapidly scheduled meetings between spine surgeons, radiologists, and primary oncologists are important, and if these cannot be achieved, treatment procedures may be delayed[6,20]. Therefore, there is a need for a more organized approach involving a dedicated team of specialists who follow these patients.

Our goal was to detect spinal metastasis in all patients with cancer at our hospital. To this end, we formed a multidisciplinary working group centered on an orthopedic spine surgeon and began using the liaison treatment approach in December 2013. This system relies on the initial diagnosis of metastatic spinal tumors by a radiologist, which allows our hospital to monitor all patients with these tumors. Radiologists must make sure that they do not miss spinal anomalies that appear not only at the primary site but also at the edge of the image. Subsequently, an expert spine surgeon evaluates the stability of the spine. Although evaluation methods, such as SINS, exist, a spine surgeon can diagnose signs of an imminent SRE and design an appropriate treatment plan. Thus, a spine surgeon should oversee the entire system owing to his or her expertise regarding the spine.

Coordination of medical care provided by each expert healthcare professional, including the spine surgeon, is important. In contrast to the conventional, reactive treatment approach of waiting until after an SRE, the spine surgeon must proactively provide treatment for patients with spinal metastasis. Spine surgeons should not hesitate to address metastatic spine tumor cases. This enables collaboration between the primary oncologist, radiologist, and spine surgeon, leading to early detection and treatment. Our results revealed that this treatment approach reduced SRE rates and led to median survival gains of approximately 9 months.

This system has limitations in its current form. Although it makes it possible to monitor patients who start treatment before an SRE, it does not allow for early treatment of patients who are referred after experiencing an SRE or those who are initially diagnosed with spinal metastasis. For patients who are paralyzed or have reduced PS when treatment is initiated, the results are poor. Future studies should include further collaborations with other hospitals in the region.

Conclusions

Advances in cancer treatments are expected to increase the number of patients living with cancer, and also, therefore, the number of those with spinal metastases. Orthopedic spine surgeons are responsible for maintaining ADLs, improving QOL, and prolonging life expectancy in patients with metastatic spinal tumors. The results of this study revealed that the liaison treatment system for metastatic spinal tumors has made it possible to successfully prevent SREs without neurological deficits and to prolong survival. With the predicted survival outcome, appropriate choices for not only evaluation but also treatment can be made by multidisciplinary professionals.

Conflicts of Interest: The authors declare that there are no relevant conflicts of interest.

Author Contributions: KN wrote and prepared the manuscript, and all the authors participated in the study design. All authors have read, reviewed, and approved the article.

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