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

In recent years, many hospitals and treatment centers have begun adopting multidisciplinary approaches for the treatment of bone metastases. 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. 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. 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...
Like other oncologists, we have created a multidisciplinary team centered on an orthopedic spine surgeon so that all patients who have initially been diagnosed at our hospital can be involved with all patients who have initially been diagnosed at our hospital enables the entire healthcare team to be involved with all patients who have initially been diagnosed at our hospital. 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. 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. Positions, radiologists, and physicians are in close contact.

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) 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.

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

| Location                                      | Score |
|-----------------------------------------------|-------|
| Junctional (occipit-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.

Table 1 shows the Spinal Instability Neoplastic Score (SINS)², which is a tool used to evaluate the stability of the vertebral body. The score is calculated based on various factors such as location, pain, bone lesion, radiographic spinal alignment, vertebral body collapse, and posterolateral involvement of spinal elements.

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 ≤ 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 ≤ 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.

Results

As presented in Fig. 2, most primary tumor sites were in the breast, lung, or prostate. The cancer types of the primary lesion are mostly breast cancer, lung cancer, and prostate cancer and have spread to all other carcinomas.

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 score³, Tomita classification⁴, Katagiri score⁵, and new Katagiri score⁶ to evaluate prognosis; (5) the SINS to evaluate the stability of the vertebral body⁷; (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) scale⁸. 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.

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(−))
Table 2. Baseline Characteristics.

|                      | SRE (+) | SRE (−) | P value |
|----------------------|---------|---------|---------|
|                      | (N=41)  | (N=704) |         |
| Age                  | 72      | 68      | 0.04    |
| Female sex-no. (%)   | 11 (42) | 318 (45)|         |
| SINS                 | 9.2     | 5.2     | <0.01   |
| Tomkashi score       | 7       | 8.8     | <0.01   |
| Tomita score         | 5.4     | 6.1     | <0.01   |
| Katagiri score       | 3.9     | 4       | 0.16    |
| New Katagiri score   | 4.8     | 5       | 0.75    |
| PS                   | 3.1     | 1.3     | <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. This will necessarily lead to an increase in the number patients

![Figure 3](image-url)
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. 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.

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. 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.

![Kaplan-Meier curve for Survival](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).)
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.

References

1. Cook RJ, Major P. Methodology for treatment evaluation in patients with cancer metastatic to bone. J Natl Cancer Inst. 2001;93 (7):534-8.
2. Saad F, Gleason DM, Murray R, et al. A randomized, placebo-controlled trial of zoledronic acid in patients with hormone-refractory metastatic prostate carcinoma. J Natl Cancer Inst. 2002; 94(19):1458-68.
3. Ibrahim T, Flamini E, Fabbri L, et al. Multidisciplinary approach to the treatment of bone metastases: Osteo-Oncology Center, a new organizational model. Tumori. 2009;95(3):291-7.
4. Howard LE, De Hoedt AM, Aronson WJ, et al. Do skeletal-related events predict overall survival in men with metastatic castration-resistant prostate cancer? Prostate Cancer Prostatic Dis. 2016;19 (4):380-4.
5. Plunkett TA, Rubens RD. The biology and management of bone metastases. Crit Rev Oncol Hematol. 1999;31(1):89-96.
6. Kimura T. Multidisciplinary approach for bone metastasis: A re-
view. Cancers (Basel). 2018;10(6):156.
7. Nakashiki K, Hasegawa T. The liaison service models of care for metastatic spine tumor patients. J Spine Res. 2017;9:1552-8.
8. Fisher CG, DiPaola CP, Ryken TC, et al. A novel classification system for spinal instability in neoplastic disease. Spine. 2012;35: 1221-9.
9. Tokuhashi Y, Matsuzaki H, Oda H, et al. A revised scoring system for preoperative evaluation of metastatic spine tumor prognosis. Spine (Phila Pa 1976). 2005;30(19):2186-91.
10. Tomita K, Kawahara N, Kobayashi T, et al. Surgical strategy for spinal metastases. Spine (Phila Pa 1976). 2001;26(3):298-306.
11. Katagiri H, Takahashi M, Wakai K, et al. Prognostic factors and a scoring system for patients with skeletal metastasis. J Bone Joint Surg Br. 2005;87(5):698-703.
12. Katagiri H, Okada R, Takagi T, et al. New prognostic factors and scoring system for patients with skeletal metastasis. Cancer Med. 2014;3(5):1359-67.
13. Oken MM, Creech RH, Tormey DC, et al. Toxicity and response criteria of the Eastern Cooperative Oncology Group. Am J Clin Oncol. 1982;5(6):649-55.
14. Prasad D, Schiff D. Malignant spinal-cord compression. Lancet Oncol. 2005;6(1):15-24.
15. Curtin M, Piggott RP, Murphy E, et al. Spinal metastatic disease: a review of the role of the multidisciplinary team. Orthop Surg. 2017;9(2):145-51.
16. Blum RH, Novetsky D, Shasha D, et al. The multidisciplinary approach to bone metastases. Oncology (Williston Park). 2003;17(6): 845-57; discussion 862-3, 867.
17. Uei H, Tokuhashi Y, Maseda M, et al. Clinical results of multidisciplinary therapy including palliative posterior spinal stabilization surgery and postoperative adjuvant therapy for metastatic spinal tumor. J Orthop Surg Res. 2018;13(1):30.
18. Laufer I, Sciubba DM, Madera M, et al. Surgical management of metastatic spinal tumors. Cancer Control. 2012;19(2):122-8.
19. Matamalas A, Valverde C, Benavente S, et al. Team approach: metastatic disease of the spine. JBJS Rev. 2018;6(5):6.
20. Loven D, Gornish M, Fenig GE, et al. Malignant epidural cord compression. Harefuah. 1996;131(11):457-62, 536.