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Clinical profile of long-term survivors of breast or thyroid cancer with metastatic spinal tumours

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Abstract Patients with breast or thyroid cancer with metastatic spinal tumours are expected to survive relatively longer than patients with other cancers with metastatic spinal tumours. The purpose of this study was to determine the clinical characteristics of long-term survivors of breast or thyroid cancer with metastatic spinal tumours. We studied the clinical profile of long-term survivors by comparing the characteristics of nine patients who had survived for at least 5 years after a spinal operation with the characteristics of 16 patients who had not. Our results showed that the longer the time from the diagnosis of the primary cancer to the spinal operation, the longer patients with breast or thyroid cancer and metastatic spinal tumours would survive. Six of the eight patients (75.0%) who had undergone the spinal operation at least 5 years after the diagnosis of the primary cancer survived especially long. In conclusion, the duration from the diagnosis of the primary cancer to the spinal operation is very useful for predicting a prognosis in patients with breast or thyroid cancer and metastatic spinal tumours.

Résumé Les patients présentant des métastases rachidiennes de cancer du sein ou de la thyroïde ont classiquement une survie plus longue qu'avec les autres cancers. Le but de cette étude est de déterminer les caractéristiques cliniques de ces longues survies. Nous avons comparé 9 patients qui avaient une survie d'au moins 5 ans après intervention rachidienne pour métastases avec 16 qui n'avaient pas cette longue survie. Les résultats montrent que plus le délai entre le diagnostic du cancer

primitif du sein ou de la thyroïde et l'intervention rachidienne est long plus la survie est longue. Six des huit patients (75%) qui avaient l'opération rachidienne au moins 5 ans après le diagnostic du cancer primitif avaient une survie particulièrement longue. En conclusion le délai entre le diagnostic du cancer primitif et l'opération du rachis est un bon élément prédictif du pronostic chez les patients atteint d'un cancer du sein ou de la thyroïde avec des métastases rachidiennes.

Introduction

Because bone metastasis occurs at an advanced stage of cancer, patients with metastatic spinal tumours generally have a poor prognosis. However, the prognosis for patients with metastatic spinal tumours is improving with the progress of chemotherapy, hormonal therapy, and radiotherapy in recent years [5, 6, 12]. In the field of spinal surgery, more stable and radical techniques have become available for patients with metastatic spinal tumours as new spinal implants are developed and operative techniques for the spine are improved [3, 4, 9]. Patients with breast or thyroid cancer with metastatic spinal tumours are expected to survive relatively longer than patients with other cancers with metastatic spinal tumours [2]. We studied the clinical profile of these long-term survivors by comparing the characteristics of those who survived for at least 5 years after a spinal operation with those who did not.

Subjects and methods

A total of 94 patients diagnosed with metastatic spinal tumours underwent spinal operations in our hospital from 1991–1998. Among them, 25 patients with breast ($n=13$) or thyroid cancer ($n=12$) as the primary cancer were the subjects of our study. These 7 men and 18 women had an average age of 60.6 years (range: 31–72 years) at the time they underwent operation for their paraparesis or acute pain. The operations involved cervical vertebrae in seven

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Table 1 Clinical data of all subjects

Case	Group	Primary cancer	Age	Gender	Surgical treatment	Operation	Alive or dead	Cause of death	Survival periods (years)	Ambulatory periods (years)
1	A	Breast	55	Female	Total spondylectomy	Scheduled	Alive	–	13	13
2	A	Breast	48	Female	Palliative surgery	Emergency	Alive	–	12	12
3	A	Breast	66	Female	Palliative surgery	Emergency	Dead	Died from cancer	7	7
4	A	Breast	52	Female	Palliative surgery	Emergency	Dead	Died from cancer	6	6
5	A	Thyroid	48	Male	Palliative surgery	Emergency	Dead	Died from cancer	9	9
6	A	Thyroid	66	Female	Palliative surgery	Emergency	Alive	–	8	6
7	A	Thyroid	55	Male	Palliative surgery	Emergency	Dead	Died from cancer	8	8
8	A	Thyroid	53	Female	Palliative surgery	Scheduled	Dead	Died from cancer	8	8
9	A	Thyroid	67	Female	Total spondylectomy	Scheduled	Dead	Died from cancer	7	7
10	B	Breast	31	Female	Palliative surgery	Emergency	Dead	Died from cancer	0.9	0.5
11	B	Breast	68	Female	Palliative surgery	Emergency	Dead	Died from cancer	0.8	0.8
12	B	Breast	55	Female	Palliative surgery	Emergency	Dead	Died from cancer	1	0
13	B	Breast	45	Female	Palliative surgery	Emergency	Dead	Died from cancer	1.2	1.2
14	B	Breast	63	Female	Palliative surgery	Scheduled	Dead	Cerebral hemorrhage	3.5	3
15	B	Breast	71	Female	Palliative surgery	Emergency	Dead	Died from cancer	4	3.5
16	B	Breast	55	Female	Palliative surgery	Emergency	Dead	Died from cancer	2	2
17	B	Breast	59	Female	Total spondylectomy	Scheduled	Dead	Died from cancer	3	3
18	B	Breast	66	Female	Palliative surgery	Emergency	Dead	Myocardial infarction	0.8	0.8
19	B	Thyroid	52	Female	Palliative surgery	Emergency	Dead	Died from cancer	0.5	0
20	B	Thyroid	58	Male	Palliative surgery	Emergency	Dead	Died from cancer	0.8	0.8
21	B	Thyroid	66	Male	Palliative surgery	Emergency	Dead	Died from cancer	3	2.5
22	B	Thyroid	59	Male	Palliative surgery	Emergency	Dead	Died from cancer	2.5	2.5
23	B	Thyroid	64	Male	Palliative surgery	Scheduled	Dead	Died from cancer	3	3
24	B	Thyroid	37	Female	Palliative surgery	Emergency	Dead	Died from cancer	1.5	0
25	B	Thyroid	72	Male	Total spondylectomy	Scheduled	Dead	Brain injury	2.5	2.5

patients, thoracic vertebrae in 15 patients, and lumbar vertebrae in three patients. Total spondylectomy for the complete removal of tumours was performed on four patients, and palliative surgery for spinal-cord decompression and reconstruction of the spine was performed on 21 patients. Spinal instrumentation was used in all patients. No patient underwent operation for the specific removal of bone metastases; however, bone metastases that existed in the spine before spinal operation were removed.

These 25 patients were divided into two groups (Table 1): group A, in which nine patients (four with breast cancer and five with thyroid cancer) survived for at least 5 years after the spinal operation, and group B, in which 16 patients (nine with breast cancer and seven with thyroid cancer) failed to survive for at least 5 years after the spinal operation. In group A, the nine patients were three men and six women with an average age of 59.7 years (range: 48–70 years) at the time of surgery. Total spondylectomy was performed in two patients and palliative surgery in seven patients; these procedures were performed as emergency operations in six patients and as scheduled operations in three patients. The mean survival period after the spinal operation was 8.7 ± 2.3 years (mean $\pm$ SD), and 6 of the 9 patients had died from cancer as of July 2005. Among the three surviving patients, one was disease-free and the other two had bone metastases involving the spine. The ambulatory period after the operation was $8.4 \pm$

2.5 years. In Group B, the 16 patients were 5 men and 11 women with an average age of 61.1 years (range: 31–72 years) at the time of surgery. Total spondylectomy was performed in two patients and palliative surgery in 14 patients; these procedures were performed as emergency operations in 12 patients and as scheduled operations in four patients. The mean survival period after the spinal operation was 1.9 ± 1.1 years, and 13 of the 16 patients died from cancer. The ambulatory period after the operation was 1.6 ± 1.2 years.

No significant difference was observed in age, gender, or operative technique between groups A and B. For chemotherapy with anticancer agents, all of the patients with breast cancer were treated with 5-FU, adriamycin, or cyclophosphamide before and after the operation for breast cancer, but they were not treated with anticancer drugs after the spinal operation. None of the patients with thyroid cancer were treated with anticancer drugs.

In our study, the following five items were compared between groups A and B: (1) whether radical treatment for the primary cancer was performed, (2) pathological findings of the primary cancer, (3) whether external radiotherapy and/or adjuvant therapy other than anticancer drugs were given after the spinal operation, (4) the times from the diagnosis of the primary cancer to the spinal operation, and (5) Tokuhashi's score [8]. Tokuhashi's score is a scoring system for the prognosis of patients with

Table 2 Summarized results

Case	Pathological findings	External irradiation	Adjuvant therapy	Duration from the diagnosis to the operation (years)
1	Papillary ductal carcinoma	None	Hormone therapy	10
2	Solid ductal carcinoma	40 Gy	Hormone therapy	8
3	Solid ductal carcinoma	30 Gy	Hormone therapy	5
4	Papillary ductal carcinoma	40 Gy	Hormone therapy	2.5
5	Follicular carcinoma	40 Gy	Internal irradiation	8
6	Follicular carcinoma	40 Gy	Internal irradiation	–
7	Papillary carcinoma	40 Gy	Internal irradiation	6
8	Papillary carcinoma	30 Gy	Internal irradiation	0.5
9	Follicular carcinoma	None	Internal irradiation	7
10	Papillary ductal carcinoma	40 Gy	Hormone therapy	1.2
11	Solid ductal carcinoma	40 Gy	Hormone therapy	1.5
12	Solid ductal carcinoma	40 Gy	Hormone therapy	5
13	Solid ductal carcinoma	40 Gy	Hormone therapy	0.5
14	Papillary ductal carcinoma	30 Gy	Hormone therapy	0.5
15	Scirrhous carcinoma	30 Gy	Hormone therapy	1
16	Papillary ductal carcinoma	40 Gy	Hormone therapy	2.5
17	Solid ductal carcinoma	40 Gy	Hormone therapy	1
18	Solid ductal carcinoma	30 Gy	Hormone therapy	2.5
19	Follicular carcinoma	None	None	1
20	Medullary carcinoma	30 Gy	Internal irradiation	1.5
21	Follicular carcinoma	30 Gy	Internal irradiation	–
22	Papillary carcinoma	40 Gy	Internal irradiation	6
23	Papillary carcinoma	40 Gy	Internal irradiation	0.5
24	Follicular carcinoma	None	None	2.5
25	Papillary carcinoma	30 Gy	Internal irradiation	3.5

metastatic spinal tumours based on the total score (maximum, 15 points) for six evaluation items: the systemic condition at the time of the spinal operation, the number of bone metastatic foci other than those in the spine, the number of spinal metastatic foci, the site of the primary cancer, the presence of metastases in major organ,; and the condition of paraparesis. To evaluate the systemic condition, a three-step scale was used in which each patient was regarded as good if “able to work on light duty,” as mildly deteriorated if “unable to work on light duty but not in bed for at least 50% of the daytime,” and as severely deteriorated if “in bed for at least 50% of the daytime.” In statistical analyses, the Student’s *t*-test and the chi-square test were used, and differences with $P < 0.05$ were regarded as significant.

Results

Of the nine patients in group A, eight with primary cancer confirmed by the time of the spinal operation had undergone radical surgery to remove the primary cancer. One patient did not have primary cancer confirmed by the time of the spinal operation; it was subsequently diagnosed and 4 weeks later the patient underwent radical surgery to remove it. Of the 16 patients in group B, 15 with primary cancer confirmed by the time of the spinal operation had undergone radical surgery to remove the primary cancer.

One patient did not have primary cancer confirmed by the time of the spinal operation; it was subsequently diagnosed and 3 weeks later the patient underwent radical surgery to remove it. Thus, in both groups, radical operations to remove the primary cancer were performed in all patients.

In group A, the pathological findings of the primary breast cancer were two cases of solid ductal carcinoma and two cases of papillary ductal carcinoma, while those of the primary thyroid cancer were three cases of follicular carcinoma and two cases of papillary carcinoma. In group B, the pathological findings of the primary breast cancer were five cases of solid ductal carcinoma, three cases of papillary ductal carcinoma, and one case of scirrhous carcinoma, while those of the primary thyroid cancer were three cases of follicular carcinoma, three cases of papillary carcinoma, and one case of medullary carcinoma. No clear difference was found between the groups in the pathological findings of the primary cancer (Table 2).

External irradiation at a dose of 30–40 Gy was performed after the spinal operation in 7 of the 9 patients in group A and in 14 of the 16 patients in Group B. Two patients in Group A did not receive external irradiation because their tumours were deemed to have been completely removed by total spondylectomy. Two patients in group B did not receive external irradiation because radiotherapy was considered to be insufficient treatment due to the patients’ complete paraplegia. For adjuvant

Table 3 Results of Tokuhashi’s score

Case	Total score	Systemic condition	Number of spinal metastatic foci	Number of bone metastatic foci	Metastases in major organs	Condition of paraparesis (Frankel’s classification)
1	15	Good	1	0	None	E
2	12	Mildly deteriorated	1	1	None	C
3	11	Severely deteriorated	2	0	None	C
4	10	Severely deteriorated	2	0	None	B
5	11	Severely deteriorated	1	0	None	
6	13	Mildly deteriorated	1	1	None	D
7	8	Severely deteriorated	2	0	Lung	B
8	13	Good	2	1	None	D
9	15	Good	1	0	None	E
10	9	Severely deteriorated	1	0	Lung	B
11	10	Mildly deteriorated	1	1	None	C
12	8	Severely deteriorated	3	2	None	A
13	12	Mildly deteriorated	2	0	None	C
14	13	Good	2	1	None	E
15	9	Severely deteriorated	2	1	None	B
16	13	Mildly deteriorated	1	0	None	D
17	14	Good	1	0	None	D
18	8	Severely deteriorated	2	0	Brain	B
19	7	Severely deteriorated	4	0	Lung	A
20	11	Severely deteriorated	1	0	None	B
21	12	Mildly deteriorated	1	2	None	D
22	7	Severely deteriorated	2	1	Lung	B
23	12	Good	2	1	None	D
24	11	Severely deteriorated	1	0	None	B
25	14	Good	1	1	None	E

therapy after the spinal operation, hormonal therapy was given to all patients with breast cancer, and internal irradiation with I^{131} was performed in all patients with thyroid cancer in group A. In group B, hormonal therapy was given to all patients with breast cancer while internal irradiation with I^{131} was performed in 14 thyroid cancer patients; internal irradiation was not performed in the two patients who had not neurologically improved after the operation due to pre-existing complete paraplegia. Thus there was no difference between the groups in postoperative external radiotherapy or adjuvant therapy (Table 2).

The time from the diagnosis of the primary cancer to the spinal operation was 5.9 ± 3.1 years in group A, excluding the one patient with primary cancer unconfirmed at the time of the spinal operation. The duration was 2.0 ± 1.7 years in group B, excluding the one patient with primary cancer unconfirmed at the time of the spinal operation. A significant difference ($P < 0.01$) was found between the groups (Table 2).

The average Tokuhashi's score was 12.0 ± 2.3 points in group A and 10.6 ± 2.4 points in group B (Table 3), suggesting a trend slightly favourable to group A without any significant difference between the groups. Additionally, no significant difference was found between the groups in relation to the systemic condition, the number of non-spinal bone metastatic foci, the number of spinal metastatic foci, the presence of metastases in major organs, or the severity of paraparesis.

Discussion

The prognosis for patients with metastatic spinal tumours is complex because it depends not only on the site of the primary cancer and the operative technique but also on the patient's sensitivity to radiotherapy and chemotherapy [1, 11]. However, a scoring system for the prognosis of patients with metastatic spinal tumours has been developed by Tokuhashi et al. [8] as described above, and has been reported to be useful. In addition, Tomita et al. [10] have recently proposed another scoring system for prognosis based on three criteria: the site of the primary cancer, the presence of metastases in major organs, and the number of metastatic foci in bone. We found that the Tomita score for our results was 3.1 ± 1.7 points in group A and 3.6 ± 1.8 points in group B, suggesting a trend slightly adverse to group A without any significant difference between the groups. Therefore, the Tokuhashi and Tomita scores were found to be less useful for the prognosis of patients with metastatic spinal tumours when breast or thyroid were the primary cancer.

Tatsui et al. [7] studied the time from diagnosis of the primary cancer to radioactive accumulation in bone scintigraphy, and reported that the average duration was 29.4 months in cases of breast cancer and 12.8 months in cases of prostate cancer, both of which were longer than the

average time of 3.6 months in cases of lung cancer and 6.9 months in cases of gastric cancer. This indicates that the time before spinal metastasis is longer in cancer types with better prognoses. Our results showed that the longer the time from the diagnosis of the primary cancer to the spinal operation, the longer patients with breast or thyroid metastatic spinal tumours would survive. Six of the eight patients (75.0%) who had undergone the spinal operation at least 5 years after the diagnosis of the primary cancer survived especially long. These findings suggest that in patients with breast or thyroid cancer, metastasis to the spine is less likely to occur with tumours growing slowly in metastatic foci ("very slowly growing tumours") if a longer time elapses from the diagnosis of the primary cancer to the spinal operation. Eighteen of 25 patients in our study underwent emergency spinal operations, often with insufficient time for a prior bone scintigram, magnetic resonance image, or computed tomogram. However, checking the time from the diagnosis of the primary cancer to the spinal operation is easy and will provide a prognosis very quickly. We hope to study this approach further with more subjects.

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