

Outcomes After Irradiation of Epidural Spinal Cord Compression Due to Metastatic Thyroid Cancer

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Abstract. Aim: Epidural spinal cord compression (ESCC) from thyroid cancer is uncommon. This study aimed to contribute to the identification of the most appropriate treatment for these patients. Patients and Methods: Fourteen patients receiving irradiation alone were retrospectively evaluated. Results: Improvement of motor deficits occurred in 36% of patients, further progression was prevented in another 43% (overall response=79%). One of six non-ambulatory patients (17%) became ambulatory. The 12-month rate of freedom from in-field recurrence was 85%; long-course irradiation was superior to short-course irradiation (100% vs. 67%, $p=0.11$). The 12-month survival rate was 41%. Age <70 years ($p=0.007$), no other metastases ($p=0.007$), differentiated cancer ($p<0.001$), ability to walk ($p=0.015$), affection of 1-3 vertebrae ($p<0.001$) and better performance score ($p=0.007$) were associated with survival. Conclusion: Irradiation resulted in a good response. Neurosurgery appears required for non-ambulatory patients to restore walking ability. Long-course irradiation resulted in excellent long-term freedom from in-field recurrence and appears preferable for patients with favorable survival prognoses.

Epidural spinal cord compression (ESCC) due to metastasis of vertebral bodies is not uncommon and may occur, depending on the primary tumor type, in almost every tenth adult cancer patient during their lifetime (1, 2). In patients developing ESCC, those with thyroid cancer represent a minority accounting for less than 1%. Therefore, uncertainty exists regarding the best possible treatment. Particularly, two major

questions need to be addressed. The first question is whether patients with ESCC from metastatic thyroid cancer should be treated with irradiation alone or with neurosurgical decompression followed by irradiation. The second question is determining the optimal dose-fractionation regimen if irradiation alone is administered. The current study aimed to help answer these questions by evaluating the outcome of patients with ESCC from thyroid cancer after irradiation alone.

Patients and Methods

The data of 14 patients with malignant ESCC from metastatic thyroid cancer treated with irradiation alone were included in this retrospective study. Investigated end-points included improvement of motor deficits, ambulatory status, freedom from an in-field recurrence within the irradiated spine and survival. In addition to the results of the entire series, the effects of ten characteristics on patient outcomes were analyzed. The ten characteristics were: age (<70 vs. ≥ 70 years, median age=69.5 years), time between initial diagnosis of thyroid cancer and ESCC (≤ 12 vs. >12 months, median time=12.5 months), presence of other distant metastases (no vs. yes), histology of thyroid cancer (differentiated vs. anaplastic), gender (female vs. male), dynamic of developing motor deficits (fast=within one week vs. slow=within more than one week), ability to walk before start of irradiation (not able to walk vs. able to walk), number of vertebrae affected by ESCC (1-3 vs. ≥ 4), Eastern Cooperative Oncology Group (ECOG) performance score (1-2 vs. 3-4) and type of irradiation (short-course=1x8 Gy/5x4 Gy in one week vs. long-course=12x2.5 Gy in three or 20x2 Gy in four weeks). The distributions of these characteristics are summarized in Table I.

For evaluation of motor function, a simplified scale was used including four grades: grade 0 (normal strength), grade 1 (able to walk without aid), grade 2 (able to walk with aid) and grade 3 (not able to walk) (3). Improvement of motor deficits meant an improvement of at least one grade. For the analyses of freedom from an in-field recurrence and survival, the Kaplan-Meier method was applied (4). Univariate analyses were performed with the log-rank test.

Results

Median follow-up was 6.5 months (range=1-55 months) in all patients and 13 months (range=3-19 months) in those patients being alive at last follow-up. In the entire series, the

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Table I. *Patients' characteristics.*

| Characteristic | N (%) |
|---|---------|
| Age | |
| <70 years | 7 (50) |
| ≥70 years | 7 (50) |
| Time between diagnosis of thyroid cancer and ESCC | |
| ≤12 months | 7 (50) |
| >12 months | 7 (50) |
| Other distant metastases | |
| No | 6 (43) |
| Yes | 8 (57) |
| Histology of thyroid cancer | |
| Differentiated cancer | 10 (71) |
| Anaplastic cancer | 4 (29) |
| Gender | |
| Female | 10 (71) |
| Male | 4 (29) |
| Dynamic of developing motor deficits | |
| Fast (within one week) | 7 (50) |
| Slow (within more than one week) | 7 (50) |
| Ability to walk before irradiation | |
| Not able to walk | 6 (43) |
| Able to walk | 8 (57) |
| Number of vertebrae affected by ESCC | |
| 1-3 | 7 (50) |
| ≥4 | 7 (50) |
| ECOG performance score | |
| 1-2 | 7 (50) |
| 3-4 | 7 (50) |
| Type of irradiation | |
| Short-course irradiation | 7 (50) |
| Long-course irradiation | 7 (50) |

ESCC, Epidural spinal cord compression; ECOG, Eastern Cooperative Oncology Group.

Table II. *The effect of irradiation on motor function (overall response).*

| | Overall response (%) | p-Value |
|---|----------------------|---------|
| Age | | |
| <70 years | 86 | |
| ≥70 years | 71 | 0.95 |
| Time between diagnosis of thyroid cancer and ESCC | | |
| ≤12 months | 86 | |
| >12 months | 71 | 0.95 |
| Other distant metastases | | |
| No | 83 | |
| Yes | 75 | 0.97 |
| Histology of thyroid cancer | | |
| Differentiated cancer | 80 | |
| Anaplastic cancer | 75 | 0.99 |
| Gender | | |
| Female | 70 | |
| Male | 100 | 0.91 |
| Dynamic of developing motor deficits | | |
| Fast (within one week) | 71 | |
| Slow (within more than one week) | 86 | 0.95 |
| Ability to walk before irradiation | | |
| Not able to walk | 67 | |
| Able to walk | 87 | 0.93 |
| Number of vertebrae affected by ESCC | | |
| 1-3 | 86 | |
| ≥4 | 71 | 0.95 |
| ECOG performance score | | |
| 1-2 | 86 | |
| 3-4 | 71 | 0.95 |
| Type of irradiation | | |
| Short-course irradiation | 71 | |
| Long-course irradiation | 86 | 0.95 |

ESCC, Epidural spinal cord compression; ECOG, Eastern Cooperative Oncology Group.

overall response rate was 79%. Improvement of motor deficits occurred in 36% (5/14) of patients, and further progression was prevented in another 43% (6/14) of patients. None of the 10 investigated characteristics showed a significant association with overall response (Table II) and improvement of motor dysfunction (Table III). Following irradiation, eight patients (57%) were able to walk. Of the six patients who could not walk before irradiation, only one patient (17%) regained this ability.

In the entire series, the rates of freedom from an in-field recurrence were 85% and 85%, respectively, at 6 months and 12 months after irradiation. For none of the investigated characteristics, a significant association with freedom from an in-field recurrence was found (Table IV). However, long-course irradiation showed a trend towards improved freedom from a recurrence when compared to short-course irradiation ($p=0.11$).

Survival rates for all patients were 57% at 6 months and 41% at 12 months, respectively. Age <70 years ($p=0.007$), absence of other distant metastases ($p=0.007$), differentiated

thyroid cancer ($p<0.001$), ability to walk at the start of irradiation ($p=0.015$), affection of only 1-3 vertebrae by ESCC ($p<0.001$) and an ECOG performance score of 1-2 ($p=0.007$) were positively associated with survival (Table V).

Discussion

For cancer patients with distant metastases, personalized treatment regimens have become more important (5-7). This also applies to metastatic thyroid cancer. Both differentiated and anaplastic thyroid cancers have gained attention in anticancer research during recent years (8-10). Several experimental and clinical studies are available including studies investigating the efficacy of new drugs (11-14). In case of metastatic thyroid cancer, bone is a common metastatic site. When vertebral bodies are affected, the metastases may destroy the posterior edge of the vertebral body and lead to

Table III. *Improvement of motor function after irradiation.*

| | Improvement of motor function (%) | p-Value |
|---|-----------------------------------|---------|
| Age | | |
| <70 years | 43 | 0.95 |
| ≥70 years | 29 | |
| Time between diagnosis of thyroid cancer and ESCC | | |
| ≤12 months | 43 | 0.95 |
| >12 months | 29 | |
| Other distant metastases | | |
| No | 50 | 0.71 |
| Yes | 25 | |
| Histology of thyroid cancer | | |
| Differentiated cancer | 40 | 0.96 |
| Anaplastic cancer | 25 | |
| Gender | | |
| Female | 40 | 0.96 |
| Male | 25 | |
| Dynamic of developing motor deficits | | |
| Fast (within one week) | 29 | 0.95 |
| Slow (within more than one week) | 43 | |
| Ability to walk before irradiation | | |
| Not able to walk | 33 | 0.99 |
| Able to walk | 38 | |
| Number of vertebrae affected by ESCC | | |
| 1-3 | 57 | 0.37 |
| ≥4 | 14 | |
| ECOG performance score | | |
| 1-2 | 43 | 0.95 |
| 3-4 | 29 | |
| Type of irradiation | | |
| Short-course irradiation | 29 | 0.95 |
| Long-course irradiation | 43 | |

ESCC, Epidural spinal cord compression; ECOG, Eastern Cooperative Oncology Group.

Table IV. *Freedom from an in-field recurrence at 6 and 12 months after irradiation.*

| | At 6 months | At 12 months | p-Value |
|---|-------------|--------------|---------|
| Age | | | |
| <70 years | 86 | 86 | 0.91 |
| ≥70 years | 83 | 83 | |
| Time between diagnosis of thyroid cancer and ESCC | | | |
| ≤12 months | 83 | 83 | 0.61 |
| >12 months | 86 | 86 | |
| Other distant metastases | | | |
| No | 83 | 83 | 0.91 |
| Yes | 86 | 86 | |
| Histology of thyroid cancer | | | |
| Differentiated cancer | 80 | 80 | 0.42 |
| Anaplastic cancer | n/a | n/a | |
| Gender | | | |
| Female | 78 | 78 | 0.32 |
| Male | 100 | 100 | |
| Dynamic of developing motor deficits | | | |
| Fast (within one week) | 83 | 83 | 0.61 |
| Slow (within more than one week) | 86 | 86 | |
| Ability to walk before irradiation | | | |
| Not able to walk | 100 | 100 | 0.24 |
| Able to walk | 75 | 75 | |
| Number of vertebrae affected by ESCC | | | |
| 1-3 | 86 | 86 | 0.91 |
| ≥4 | 83 | 83 | |
| ECOG performance score | | | |
| 1-2 | 86 | 86 | 0.91 |
| 3-4 | 83 | 83 | |
| Type of irradiation | | | |
| Short-course irradiation | 67 | 67 | 0.11 |
| Long-course irradiation | 100 | 100 | |

ESCC, Epidural spinal cord compression; ECOG, Eastern Cooperative Oncology Group.

ESCC (1, 2). Since ESCC originating from vertebral body metastases of thyroid cancer is relatively rare, very little is known on the best available treatment for these patients. The vast majority of cancer patients with ESCC receive irradiation alone (1, 2). Selected patients including those with less radiosensitive or less favorable histology may have improved functional outcomes if irradiation is supplemented by upfront neurosurgery (15). However, spinal neurosurgery is associated with serious complications in more than 10% of the patients (15-17). In the present study, the overall response rate with respect to motor dysfunction (improvement or at least no progression) was quite favorable in the entire series. However, of those patients who were not able to walk prior to irradiation only 17% regained ambulatory status following treatment. In a previous randomized trial of patients with ESCC from different solid cancers, the post-treatment ambulatory rates were 84% after neurosurgery plus irradiation

and 57% after irradiation alone ($p=0.001$) (15). Furthermore, more patients in the neurosurgery group regained their walking ability (62% vs. 19%, $p=0.01$). Thus, patients with ESCC from thyroid cancer, who could not walk appear to benefit from upfront neurosurgery with respect to post-treatment ambulatory function.

If irradiation is administered alone, several dose-fractionation regimens are available, generally grouped as short-course (overall treatment time=up to one week) and long-course (overall treatment time=two to four weeks) (2). Previous studies of patients with ESCC from different primary tumors have shown that the commonly used dose-fractionation regimens have a similar effect on motor deficits (18-20). However, long-course regimens resulted in higher rates of freedom from an in-field recurrence of ESCC, particularly in patients with a more favorable survival

Table V. Survival at 6 and 12 months after irradiation.

| | At 6 months | At 12 months | p-Value |
|---|-------------|--------------|------------------|
| Age | | | |
| <70 years | 100 | 67 | 0.007 |
| ≥70 years | 14 | 14 | |
| Time between diagnosis of thyroid cancer and ESCC | | | |
| ≤12 months | 29 | 29 | 0.34 |
| >12 months | 86 | 51 | |
| Other distant metastases | | | |
| No | 100 | 80 | 0.007 |
| Yes | 25 | 13 | |
| Histology of thyroid cancer | | | |
| Differentiated cancer | 80 | 57 | <0.001 |
| Anaplastic cancer | 0 | 0 | |
| Gender | | | |
| Female | 40 | 40 | 0.35 |
| Male | 100 | 50 | |
| Dynamic of developing motor deficits | | | |
| Fast (within one week) | 57 | 57 | 0.51 |
| Slow (within more than one week) | 57 | 29 | |
| Ability to walk before irradiation | | | |
| Not able to walk | 17 | 17 | 0.015 |
| Able to walk | 88 | 88 | |
| Number of vertebrae affected by ESCC | | | |
| 1-3 | 100 | 83 | <0.001 |
| ≥4 | 14 | 0 | |
| ECOG performance score | | | |
| 1-2 | 100 | 67 | 0.007 |
| 3-4 | 14 | 14 | |
| Type of irradiation | | | |
| Short-course irradiation | 71 | 54 | 0.33 |
| Long-course irradiation | 43 | 29 | |

ESCC, Epidural spinal cord compression; ECOG, Eastern Cooperative Oncology Group. Values in bold are significant.

prognosis (21, 22). One has to be aware that the risk of an in-field recurrence increases with lifetime. In the current study of ESCC from thyroid cancer, long-course irradiation resulted in excellent long-term freedom from an in-field recurrence (100% at 12 months) and provided better results than short-course irradiation. Although significance was not achieved, patients with more favorable survival prognoses appear more appropriately treated with long-course, rather than short-course irradiation. This recommendation is in accordance with previous studies of ESCC from other solid tumors (21, 22). The survival prognosis of patients with ESCC from thyroid cancer can be estimated with the help of the characteristics significantly associated with survival in this study (Table V).

In conclusion, irradiation alone resulted in a good overall response with respect to its effect on motor dysfunction. However, neurosurgery appears required for non-ambulatory

patients to restore the ability to walk. Long-course irradiation resulted in excellent long-term freedom from in-field recurrence and appears preferable for patients with a more favorable survival prognosis.

Conflicts of Interest

On behalf of all Authors, the corresponding Author states that there are no conflicts of interest related to this study.

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