Radiation Therapy Alone Provides Excellent Outcomes for Spinal Cord Compression from Vertebral Lymphoma

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Abstract. *Aim: Malignant spinal cord compression (SCC) is treated with radiotherapy (RT). Additional neurosurgery has become more widely used since a trial showed a benefit for selected patients. Although lymphomas were excluded from that trial, neurosurgery is also increasingly being performed in these patients. This study investigated whether neurosurgery is actually required for this group. Patients and Methods: Twenty-nine patients receiving RT alone for SCC from vertebral lymphoma were analyzed for motor function, walking ability, in-field recurrence and survival. Results: Overall response was 100% (72% improvement, 28% stable). At 1, 6 and 12 months after RT, 83%, 100% and 100% of patients were able to walk; 64%, 100%, and 100% of non-ambulatory patients regained their walking ability. Freedom from in-field recurrence was 100% at 6 and 12 months. Survival rates at 6 and 12 months were 79% and 75%. Conclusion: RT alone resulted in excellent outcomes for SCC from lymphoma. These patients may not require surgery.*

Patients with spinal cord compression (SCC) from lymphoma represent 1-2% of all patients with SCC (1). However, this group deserves special consideration because lymphomas are very radiosensitive. SCC from malignant disease is treated with radiation therapy (RT) alone or decompressive neurosurgery plus RT. Ten years ago, a randomized trial showed that combined treatment was superior to RT alone with respect to walking ability and survival in carefully selected patients (2). Since then, neurosurgery plus RT has become more widely used for SCC. Despite the fact that patients with lymphomas were excluded from that randomized study, some surgeons perform decompressive surgery in these patients. This study evaluated RT alone for SCC from lymphoma to address the question as to whether neurosurgery is actually required for these patients.

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Patients and Methods

Twenty-nine patients treated with RT alone for SCC from vertebral lymphoma between 1999 and 2014 were included in our retrospective study. RT was delivered with 6 to 18 MeV photon beams from a linear accelerator, and target volumes encompassed affected vertebral bodies plus one adjacent vertebra on either side. Patients were analyzed for the effect of RT on motor dysfunction of the legs, walking ability, need for treatment of symptomatic in-field recurrence of SCC, and survival. In addition for the whole cohort, seven factors were evaluated: age at RT (≤65 *versus* >65 years), gender, lymphoma grade (low *versus* high), dynamic of motor dysfunction (fast: ≤7 days *versus* slow: >7 days), pre-RT ambulation function (able *versus* not able to walk), number of affected vertebral bodies (1-2 *versus* ≥3) and fractionation (5×4 Gy *versus* long-course RT=10×3 Gy/15×2.5 Gy/20×2 Gy). To avoid redundancy, performance status was not investigated: Ambulatory patients had an Eastern Cooperative Oncology Group score of 1-2, and patients unable to walk a score of 3-4.

Improvement of motor dysfunction was defined as change of at least one category on a scale modified according to Tomita *et al.*: 0=normal strength; 1=ambulatory without aid; 2=ambulatory with aid; 3=not ambulatory (3). Accordingly, deterioration of motor dysfunction was rated as change of at least one category. Overall response was defined as improvement or no further worsening of motor weakness. Associations between the effects of RT on motor dysfunction and the seven factors were analyzed with a logistic regression analysis. Need for treatment of an in-field recurrence and survival were calculated from the last RT fraction. Univariate analyses were carried out with Kaplan–Meier analyses supplemented by log-rank tests. Significant factors were included in a Cox regression analysis.

Table I. *Associations between the potentially determining factors and the effect of radiotherapy (RT) on motor dysfunction. The p-values were derived from the logistic regression analysis.*

Factor	Improvement (%)	No progression (%)	Deterioration (%)	*p*-Value
Age at RT				
≤65 Years (n=16)	63	38	0	
>65 Years (n=13)	85	15	0	0.20
Gender				
Female (n=10)	70	30	0	
Male (n=19)	74	26	0	0.83
Lymphoma grade				
Low (n=15)	80	20	0	
High (n=14)	64	36	0	0.35
Pre-RT dynamic of motor dysfunction				
Fast (≤7 days) (n=10)	40	60	0	
Slow (>7 days) (n=19)	89	11	0	**0.010**
Pre-RT ambulatory function				
Able to walk (n=15)	80	20	0	
Not able to walk (n=14)	64	36	0	0.35
Number of affected vertebral bodies				
1-2 (n=14)	93	7	0	
≥3 (n=15)	53	47	0	**0.036**
Fractionation schedule				
5×4 Gy (n=4)	25	75	0	
Long-course (n=25)	80	20	0	**0.048**
Whole series (n=29)	72	28	0	

Statistically significant values are shown in bold.

Results

The overall response at 1 month was 100% (72% improvement plus 28% stable). Results according to the seven factors are presented in Table I. In the logistic regression analysis, improvement of motor dysfunction was associated with slow development of motor dysfunction (p=0.010), only 1-2 vertebral bodies affected (p=0.036), and long-course RT (p=0.048). Of those 21 patients assessable at 6 months, 88% showed improvement and 12% were stable. Of those 15 patients assessable at 12 months, 87% showed improvement and 13% were stable, respectively. At 1, 6 and 12 months after RT, 83% (24/29 patients), 100% (24/24) and 100% (15/15) were able to walk, respectively. At each follow-up time, all ambulatory patients maintained their ability to walk, and 64% (9/14), 100% (9/9), and 100% (4/4), respectively, of non-ambulatory patients regained their walking ability.

The rate of freedom from treatment for an in-field recurrence was 100% at 6 and 12 months. Therefore, analyses of the individual factors for associations with in-field recurrences were not performed. Survival rates at 6 and 12 months were 79% and 75%, respectively. On univariate analyses (Table II), survival was positively correlated with slow development of motor dysfunction (p<0.001), pre-RT ability to walk (p=0.022), only 1-2 vertebral bodies affected (p=0.032), and long-course RT (p=0.003). In the Cox regression analysis, dynamic of motor dysfunction (risk ratio=5.06, 95% confidence interval=1.44-33.78; p=0.010), ambulation (risk ratio 12.11, 95% confidence interval=1.23-416.67; p=0.031), and number of affected vertebral bodies (risk ratio=3.99, 95% confidence interval=1.11-27.40; p=0.033) were significant, in contrast to the fractionation schedule (risk ratio=1.54, 95% confidence interval=0.21-14.29; p=0.67).

Discussion

SCC from malignant disease is an emergency. For decades, the vast majority of patients received RT alone. Since 2005, the situation has changed. In a randomized trial of patients with relatively favorable survival prognoses and Karnofsky performance scores ≥70, post-treatment ambulation rates were 84% after neurosurgery plus RT and 57% after RT alone, respectively (p=0.001) (2). Of non-ambulatory patients, 62% (10/16) and 19% (3/16), respectively, regained their walking ability (p=0.01). Patients maintained ambulation for a median of 4.1 and 0.5 months, respectively (p=0.003). Median survival times were 4.2 and 3.3 months, respectively (p=0.033). The effect of RT for malignant SCC varies considerably with respect to the primary tumor type (4-6). The effect is most favorable for highly radiosensitive tumors such as lymphomas (7, 8).

Table II. *Associations between the potentially determining factors and survival (univariate analysis).*

Factor	Survival at 6 months (%)	Survival at 12 months (%)	*p*-Value
Age at RT			
≤65 years (n=16)	75	75	
>65 years (n=13)	85	76	0.83
Gender			
Female (n=10)	80	80	
Male (n=19)	79	72	0.68
Lymphoma grade			
Low (n=15)	93	87	
High (n=14)	64	64	0.13
Pre-RT dynamic of motor dysfunction			
Fast (≤7 days) (n=10)	50	38	
Slow (>7 days) (n=19)	95	95	**<0.001**
Pre-RT ambulatory function			
Able to walk (n=15)	93	93	
Not able to walk (n=14)	64	56	**0.022**
Number of affected vertebral bodies			
1-2 (n=14)	100	92	
≥3 (n=15)	60	60	**0.032**
Fractionation schedule			
5×4 Gy (n=4)	25	n.a.	
Long-course (n=25)	88	84	**0.003**
Whole series (n=29)	79	75	

n.a.: Not available, RT: radiotherapy. Bold *p*-values: significantly different.

Due to the results of the trial of Patchell *et al*., SCC treatment has changed (2). Meanwhile, in some Institutions, more patients receive combined treatment than RT alone, including those with highly radiosensitive tumors such as lymphomas. However, it is not clear whether the latter patients benefit from neurosurgery, which can be associated with severe complications (2, 9, 10).

According to this study, RT alone is very effective for SCC from lymphoma. The overall response rate was 100%, and 72% of patients improved; 83% of patients were ambulatory after RT, and 64% of non-ambulatory patients could walk after RT. These favorable results persisted: at 1 year, all patients were able to walk, regardless of their pre-RT ambulatory status. At 1 year, no patient needed treatment for an in-field recurrence of SCC. The results of RT alone in this study were at least as favorable as those reported in the combined modality group of the randomized trial. Furthermore, survival was excellent in the present study, with a 1-year survival rate of 75%. When interpreting this study, the relatively small number of patients and retrospective design should be considered. Ideally, the results should be confirmed in a larger prospective series. However, since SCC from lymphoma is rare, a new study cannot be expected soon.

In conclusion, RT alone provides excellent outcomes for patients with SCC from lymphoma in terms of response, ambulatory function, need for treatment of an in-field recurrence and survival. Thus, neurosurgery should be omitted in these patients.

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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