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Research Article

Radiotherapy for spinal metastases from breast cancer with emphasis on local disease control and pain response using repeated MRI

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ABSTRACT

Aims: To evaluate metastatic lesions within the radiation field using repeated magnetic resonance imaging (MRI) and to compare the imaging findings with pain response following radiotherapy (RT) in patients with spinal metastases (SM) from breast cancer.
Material and methods: 32 Patients with SM from breast cancer admitted for fractionated RT were included in this study. MRI examinations of the spine were scored for the extent of bone metastases, epidural disease and the presence and severity of vertebral fractures. Clinical response was defined according to the updated international consensus on palliative RT endpoints.
Results: At 2 and 6 months after RT, 38% and 44% of the patients were classified as responders. None of the patients developed motor deficits. Importantly, a decrease in the intraspinal tumor volume after RT was reported in all patients. Only 6% of the patients showed bone metastases progression within the RT field, whereas 60% of the patients showed disease progression outside the RT portals. 5 Patients developed new fractures after RT, and fracture progression was observed in 21 of the 38 lesions (55%). The pain response to RT did not correlate with the presence of vertebral body fracture before RT, fracture progression or other recorded MRI features of metastatic lesions.
Conclusion: RT provided excellent local tumor control in patients with SM. Most patients benefit from RT even in cases of progressive vertebral fracture. Pain response was not associated with imaging findings and MRI cannot be used to select patients at risk of not responding to RT.

1. Introduction

External beam radiotherapy (RT) is a well-established and efficacious method of palliating painful bone metastases [1,2]. Patients with bone metastases are at high risk for skeletal-related events such as pathologic fractures or spinal cord compression [3]. This may affect the pain response following RT and lower the quality of life in these patients [4]. However, limited data exist on the local disease control and the incidence of fractures after conventional fractionated RT to the spine [2,4–8]. Furthermore, the impact of fractures on pain response is essentially unknown.

Magnetic resonance imaging (MRI) is the modality of choice for the diagnosis and follow-up of cancer patients with spinal metastases (SM). Only a few studies have evaluated pain response and imaging features after RT in patients with SM, and the findings have been inconsistent [9–11]. Hence, it is important to determine to what extent the RT response rate in SM is correlated with the presence of skeletal complications such as fractures or compression syndromes. Thus, the aim of this study was to evaluate the irradiated metastatic lesions and the rate of local tumor control using repeated MRI and to compare the imaging findings with pain response after RT in patients with SM from breast cancer.

2. Material and methods

2.1. Patients

All consecutive patients with symptomatic SM who were admitted to our institution in 2007 and 2008 were considered for inclusion in a prospective clinical study [12]. The current paper

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is a retrospective analysis of 32 patients (30 women and 2 men) with SM from breast cancer who were part of the aforementioned clinical study [12]. The inclusion criteria for the present study were as follows: first-time admittance for RT for SM from breast cancer, no motor deficit prior to RT, survival for more than 6 months after RT, available pre- and post-treatment MRI of the vertebral column, age greater than 18 years and signed informed consent. Post-treatment MRIs were conducted to evaluate local disease progression and as a part of routine follow-up for systemic disease status. All patients completed an MRI exam prior to RT and an MRI exam after such treatment. Pretreatment MRIs were performed within 2 months prior to RT. Post-treatment MRIs were performed within 2–6 months of the RT. Patients with paravertebral metastases with direct extension into vertebral bodies and patients with leptomeningeal or intramedullary metastases were not eligible.

All patients were interviewed prior to and at 2 and 6 months after RT using a validated Norwegian version of the Brief Pain Inventory form [12,13]. The worst, average and least pain experiences during the previous 24 h and the current pain level were recorded using a 10-point scale. The worst pain experience was used as the principal outcome measure. Details on opioid consumption during the previous 24 h, including the drug name, daily dose and administration route, were recorded. All opioids were converted into the oral morphine-equivalent dose (OMED).

Clinical response to treatment was defined according to the updated International Bone Metastases Consensus Working Party palliative RT endpoints [1]. A complete response (CR) was defined as a pain score of 0 with no increase in the OMED. A partial response (PR) was defined either as a pain reduction of 2 or more points measured on a 10-point scale or an OMED reduction of 25% or more. Pain progression (PP) was defined as a pain increase of 2 or more points or an increase in the OMED of 25% or more. Patients not classified as having CR, PR or PP were defined as having an indeterminate response (IR). Patients with either CR or PR were defined as responders, whereas patients with either IR or PP were defined as non-responders [1].

2.2. MRI studies

64 MRI studies were performed in 32 patients. Entire spine MRI examinations were available in all but 2 patients. All images were retrospectively reviewed by one radiologist (MDS) who was blinded to the clinical records. Bone metastases were categorized as either diffuse infiltration of the bone marrow or focal lesions [14,15]. The metastasis with the largest diameter or that was most suitable to measure was recorded as the target lesion. To avoid partial volume artifacts, only lesions with a diameter equal to or greater than 8 mm were considered measurable ($2 \times$ slice thickness) [15].

Other recorded features included tumor-conditioned spinal canal stenosis (SCS), compression of the spinal cord, cauda equina and nerve roots. SCS was defined as a narrowing of the cross-sectional area of the spinal canal by a soft tissue tumor extension, bone fragments or both. Compression of the spinal cord was defined as a deviation or indentation of the spinal cord by an epidural tumor or bone fragments. Compression of the cauda equina was defined as an obliteration of the cerebrospinal fluid in the dural sac at the affected level. Nerve root compression was defined as contact between the tumor masses or bone fragments and the spinal nerves in the recess or intervertebral foramen [16].

Vertebral body fractures were recorded both prior to and after RT. A difference of ≥ 2 mm ($2 \times$ pixel spacing) between the pre- and post-treatment vertebral height was recorded as fracture progression. Additional studied features included the level of the fractures, the percentage of vertebral height loss, and the percentage of metastatic vertebral body involvement.

The appearance of new lesions, a change in the metastatic pattern from focal to diffuse or at least a 20% increase in the largest diameter of the target lesions after RT was defined as progression. The disappearance of lesions or a reduction at least 30% in the diameters of the target lesions was defined as a response [14,15]. The radiological response of spinal lesions was evaluated both inside and outside the RT portals. To assess the epidural tumor volume, a cross-sectional area of the spinal canal was measured at the affected level and compared with the cross-sectional area at the same level on post-treatment images.

2.3. Statistical analyses

Data were analyzed using IBM SPSSc Statistics version 21 (IBM, New York, NY, USA). Descriptive statistics including frequency distributions and percentages were used to describe the patient population. Chi-squared tests were used to compare proportions. All reported p values were based on 2-sided tests; $p < 0.05$ was considered statistically significant.

2.4. Ethics

This study was approved by the Regional Ethics Committee, and written informed consent was obtained from all patients.

3. Results

3.1. Patients

The mean patient age at the start of treatment was 58 years (range 82–35). All patients received a radiation dose of 30 Gy delivered in 10 fractions within 2 weeks. RT was given in combination with ongoing chemotherapy (4 patients), hormone treatment (22 patients), bisphosphonates (7 patients) or corticosteroids (7 patients). Importantly, none of the patients developed neurological symptoms at the 2- or 6-month follow-up. All patients were ambulatory prior to and at 2 months after RT; at 6 months after RT, 1 of the 32 patients was non-ambulatory due to poor performance status related to general disease progression.

The mean pain scores were 4.3, 3.9 and 3.7 at baseline, 2 months and 6 months after RT, respectively. The corresponding mean OMED values were 100, 96 and 145 mg, respectively. At 2 and 6 months after RT, 12 patients (38%) and 14 patients (44%) were classified as responders. Age, ongoing chemotherapy, hormone therapy and the use of bisphosphonates were not associated with the pain response; however, patients younger than 65 years of age showed a better response than did the older patients (11 vs. 1 responder at 2 months).

3.2. MRI findings

Pretreatment MRIs were obtained within 1–47 days (mean 16 days) prior to RT. Post-treatment MRIs were obtained within 61–180 days (mean 103 days) after the completion of RT. The recorded MRI findings are presented in Table 1.

On the pretreatment MRIs, 23 patients had focal bony metastases and 9 patients had diffuse metastatic bone marrow infiltration. SCS was noted in 21 patients. For all but 1 patient, SCS was caused by both the epidural tumor and fracture. Compression of the spinal cord/cauda equina was present in 8 patients. Fractures were noted in 22 patients (13 patients at a single spinal level and in 9 patients at multiple levels). In total, 38 fractures were evaluated in 22 patients. All fractures were pathological, tumor-induced fractures.