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Original research

Performance status versus anatomical recovery in metastatic disease: The role of palliative radiation treatment

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ABSTRACT

Metastatic disease is a common complication of the most advanced malignancies. It may compromise the patients' quality of life, often posing a greater risk than the primary disease itself. Currently, several different therapeutic approaches are available to palliate or cure (single metastasis with primary neoplasm under control – radical surgery) secondary disease. In particular, radiation therapy is widely used, as it often leads to full or at least partial functional recovery, depending on the number and location of metastases. The aim of our study was to evaluate whether clinical improvement subsequent to radiation therapy may be related to anatomical recovery of the site of metastasis in cancer patients with metastatic disease. Given the heterogeneity of the diseases considered and the general complex conditions of the patients, a single method could not be used to evaluate the response to radiation treatment and its correlation with the performance status (PS). Thus, depending on the specific disease being assessed, we divided the patients into different groups. Patients in the same group were followed up with the same methods. This correlation was noted in a very high percentage of patients, predominantly in patients with vertebral and brain metastases. Moreover, we investigated the use of magnetic resonance imaging (MRI)-diffusion weighted imaging (DWI) in the study of spinal metastases. We propose its use in the local evaluation of vertebral secondary lesions, both in the diagnostic phase and during the assessment of treatment efficacy.

1. Introduction

Metastatic disease is a common complication occurring in the most advanced malignancies. It may compromise the patients' quality of life, often more adverse than the primary disease itself. The unique features of secondary diseases are their location and number. The number of secondary deposits is relatively important, because a single metastasis is often more clinically relevant than multiple metastases, even with several organs being involved. Some primary neoplasms tend to diffuse to specific organs [1,2]. Thus, in some cases, the presence of metastases is suspected even before their clinical evidence. Then a preventive treatment can be prescribed to prevent the growth of the metastases (e.g., whole-brain radiation treatment for small cell lung cancer (SCLC)) [3–6,9].

Currently, several different therapeutic approaches are available to palliate or cure (single metastasis with primary neoplasm under control – radical surgery) secondary disease. Radiation therapy is predominantly used in this respect, as it often allows full or at least partial functional recovery, depending on the number and location of metastases.

As radiation treatment of secondary disease is palliative in almost all cases, we extended our study not just to patients with

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one or more secondary deposits but also to patients requiring palliative treatment because of severe complications resulting from direct extension/invasion of the primary neoplasm to the neighbouring organs [7–13].

Our concept of treatment considers not just patients with neoplastic disease and their staging but the mere presence of symptoms as well, which require a specific treatment.

In our study, we assessed various radiation treatments performed in our institution for patients with advanced and symptomatic neoplastic disease [14]. As these patients were followed up with clinical and imaging evaluation, we were able to reveal the correlation between the efficacy of the radiation treatment and the recovery of the disease-free organ. This recovery in turn contributes significantly to the patient's performance status (PS).

2. Materials and methods

We selected patients diagnosed with symptomatic lesions in various organs between January 2011 and May 2015; they were followed up in the early and mid-term. Their PS was clinically assessed. Further, on comparing their pre- and post-treatment scans, we found a significant correlation between treatment efficacy, functional recovery of the patient and anatomical recovery of the irradiated organ. Each treatment was performed with LINAC Siemens Mevatron 6 Megavolt.

A total of 267 patients were enrolled in our study, 92 of whom presented with vertebral metastases, arising from the lung (33.89%), breasts (24.21%), prostate (16.21%) and less frequent malignancies (25.78%) (Table 1).

As we explained in detail in another study, we only enrolled patients with vertebral cervical, dorsal and lumbar secondary deposits treated with standard dose fractionation of 3 Gy in 10 daily sessions (62 patients, 35M, 27F). The lesions were examined before radiation therapy, and 30 and 60 days after treatment via magnetic resonance imaging (MRI)-diffusion weighted imaging (DWI).

The remaining 30 patients who presented with vertebral metastases and received different dose fractionation schemes were excluded. This was done to make the examined population uniform and to avoid stressing patients with an already poor initial PS. As explained in detail subsequently, only 58 of the 62 patients were followed up completely over time.

A total of 138 patients were instead treated for brain metastases (47 of whom were diagnosed with a single metastasis and 91 with multiple lesions). Among these patients, 127 patients (71M, 56F) who received standard radiation treatment (whole-brain 3-Gys treatment in 10 daily sessions, with a total of 30 Gy). The lesions were mostly due to secondary disease, more frequently due to pulmonary (62.21%, SCLC cases included), breast (16.53%) and skin primary neoplasms (melanoma, 3.15%) (Table 2). Of the 127 enrolled patients, 103 were followed up over time with brain MRI scanning between the 40th and the 60th day after the end of radiotherapy.

Twenty-three patients (17M, 6F) underwent radiotherapy for mediastinal syndrome or clinical syndromes primarily with respiratory symptoms (dyspnoea and cyanosis) and dyspepsia (due to oesophageal compression). Some of these patients also showed signs of stasis in the superior caval system (oedema) and heart failure, resulting in expansion (and compression) of primary tumours arising from the lungs (78.26%), thymus (8.69%) and pleura (8.69%) to mediastinal structures (Table 3). The most appropriate dose fractionation was selected based on the clinical conditions of patients during the first evaluation instead of the underlying aetiology of the mediastinal syndrome. In particular, six patients in compromised clinical conditions (26.08%) were treated with 5 Gy each in four daily fractions for a total of 20 Gy. Alternatively, three patients (13.04%) with severe symptoms especially involving the upper gastrointestinal tract were treated with 4 Gy each in five daily fractions for a total of 20 Gy. For 10 patients with better lung compliance (43.47%), a standard fractionation scheme of 3 Gy for 10 sessions was used, Two patients were treated with 2 Gy in 25 daily fractions, which was the most widely used scheme. Our target volumes also included the right hilum in one patient and the right pulmonary apex in the other, who were treated simultaneously with the mediastinal region, always as palliative therapy. Finally, one patient was treated with 2 Gy in 23 sessions, extending the target volume to a lung lobe. Another underwent a 2.5-Gy radiotherapy in 16 fractions. Given the heterogeneity of the treatments for patients with mediastinal syndrome, the inhomogeneous clinical and anatomical results and the suboptimal clinical conditions of this patient population, only 10 patients treated with 3 Gy in 10 fractions were included in this study, particularly those treated and periodically assessed in our hospital. All 10 were assessed with a contrast-enhanced chest computed tomography (CT) scan, 30–40 days after the end of the radiation therapy.

Finally, we also included 14 patients (12M, 2F) presenting with 'haemorrhagic bladder'. This was due to invasion by advanced-stage prostate adenocarcinoma (pT3a sec. TNM 7th ed.) in two patients (14.28%) and directly due to bladder cancer in nine patients. In particular, five of the latter (35.71%) showed local

Table 1
Primary neoplasms causing vertebral metastases.

	N° patients (%)
Lung	21 (33.89%)
Breast	15 (24.21%)
Prostate	10 (16.12%)
Kidney	4 (6.45%)
Unknown	3 (4.83%)
Larynx	2 (3.22%)
Colorectal	2 (3.22%)
Stomach	1 (1.61%)
Bladder	1 (1.61%)
Leiomyosarcoma	1 (1.61%)
Sarcoma	1 (1.61%)

Table 2
Primary neoplasms causing brain mets.

	N° patients (%)
Lung	79 (62.21%)
Breast	21 (16.53%)
Melanoma	4 (3.15%)
Intestinal	3 (2.36%)
Prostate	3 (2.36%)
Kidney	3 (2.36%)
Stomach	2 (1.57%)
Bladder	2 (1.57%)
Thymus	1 (0.79%)
Ovaries	1 (0.79%)
Uterus	1 (0.79%)
Unknown	6 (4.72%)

Table 3
Neoplasms causing Mediastinal Syndrome.

	N° patients (%)
Lung	18 (78.26%)
Thymus	2 (8.69%)
Pleura	1 (4.34%)
Epithelioid of unknown origin	1 (4.34%)
Bladder	1 (4.34%)