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Stereotactic body radiation therapy for lung metastases from soft tissue sarcoma

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Abstract ***Purpose:*** To appraise the role of stereotactic body radiation therapy (SBRT) in patients with lung metastasis from primary soft tissue sarcoma.
Methods: Twenty-eight patients (51 lesions) were analysed. All patients were in good performance status (1–2 eastern cooperative oncology group (ECOG)), unsuitable for surgical resection, with controlled primary tumour and the number of lung metastases was ⩽4. In a risk adaptive scheme, the dose prescription was: 30 Gy/1 fr, 60 Gy/3 fr, 60 Gy/8 fr and 48 Gy/4 fr. Treatments were performed with Volumetric Modulated Arc Therapy. Clinical outcome was evaluated by thoracic and abdominal computed tomography (CT) scan before SBRT and than every 3 months. Toxicity was evaluated with Common Terminology Criteria for Adverse Events (CTCAE) scale version 4.0.
Results: Leiomyosarcoma (36%) and synovial sarcoma (25%) were the most common histologies. Five patients (18%) initially presented with pulmonary metastasis, whereas 23 (82%) developed them at a median time of 51 months (range 11–311 months) from the initial diagnosis. The median follow-up time from initial diagnosis was 65 months (5–139 months) and from SBRT was 21 months (2–80 months). No severe toxicity (grades III–IV) was recorded and no patients required hospitalisation. The actuarial 5-years local control rate (from SBRT treatment) was 96%. Overall survival at 2 and 5 years was 96.2% and 60.5%, respectively. At last follow-up 15 patients (54%) were alive. All other died because of distant progression.

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Conclusions: SBRT provides excellent local control of pulmonary metastasis from soft tissue sarcoma (STS) and may improve survival in selected patients. SBRT should be considered for all patients with pulmonary metastasis (PM) and evaluated in a multidisciplinary team.

1. Introduction

Soft tissue sarcomas (STSs) are malignancies of mesenchymal origin which represent about 1% of adult's tumours [1]. Despite adequate treatment, 25–50% of patients with localised disease develop distant metastases [2–4], most frequently in the lungs. Metastatic status at the time of first diagnosis is not uncommon [5]. Depending on the number of the metastases, the site and the disease free interval (DFI) surgery or chemotherapy may be offered [6] Patients with indolent diseases may benefit from repeated surgical resections [7]. Conversely, patients with bilateral, rapidly progressing lung metastases are usually managed with chemotherapy or investigational therapies.

Radiation therapy to the lung has been traditionally reserved to patients unfit for surgery. However, with the recent technological improvements, the indications for radiation therapy are broadening [3]. Stereotactic body radiation therapy (SBRT), which allows for accurate delivery of high dose radiation to the target, proved to be effective in the treatment of metastatic lesions to the lungs and liver [8]. Few reports of SBRT in lung metastases from STS are available [9–11], showing excellent local control with minimal toxicity.

In the effort to determine the role of SBRT in the treatment of patients with lung sarcoma metastases, we retrospectively review the medical records of the patients treated at our institution.

2. Methods and material

2.1. Patients and procedures

The present prospective observational study, approved by local ethical committee, includes patients with lung metastases from soft tissue sarcoma (STS). At the initial diagnosis of primary tumour, all patients undergone open-surgery resection, followed by radiotherapy and/or adjuvant chemotherapy. At the time of recurrence, they were evaluated for salvage treatment, which included surgical resection, stereotactic body radiation therapy (SBRT) and chemotherapy. After receiving study approval from the institutional review board, to define the appropriate patient therapeutic strategy, each patient was evaluated by a multidisciplinary board including a medical oncologist, a radiation oncologist and a thoracic surgeon. The patients' general condition (age, performance status, symptoms) and disease status (other site of metastases, number of lung metastases, time to progression) were considered. SBRT was performed in case of one or more of the following: (1) indolent behaviour disease, (2) controlled primary tumour, (3) metastatic lesion less than five such as the definition of oligometastatic patients (4) pulmonary ipsilateral or bilateral disease, (5) progressive disease after chemotherapy and/or surgical resection, (6) contraindication to surgical resection, (7) synchronous lung lesions up to four.

From February 2008 to May 2014, 28 consecutive patients referred at our institution for metastatic lung soft tissue sarcoma, for a total of 51 lung lesions eventually underwent SBRT and were included in the study. Of these patients, 16 (57%) were female and 12 (43%) male with a median age of 64 years (range 23–89 years). The most common primary tumour was leiomyosarcoma 10 (36%) and the most common primary site of disease was the extremities 13 (46%). Lung metastatic lesions were present at diagnosis in five (18%) patients, whereas they developed in 23 (82%) patients after primary tumour treatment. At the time of SBRT, 23 (82%) patients had only lung lesions and five (18%) had additional metastatic localisations, one patient had a stable residual retroperitoneal tumour and four one isolated bone metastases.

SBRT was performed as first treatment of lung metastases in six patients (no pathological confirmation was available for these patients), while in 22 patients it was performed at progression of lung lesions after chemotherapy and/or surgical resection of other metastases in the lungs. In 16 patients with single lung metastases, SBRT rather than surgery was performed for the following reasons: previous multiple surgical resection (8 pts), and/or advanced age and comorbidity (3 pts), and/or short Disease Free Interval (DFI) from diagnosis to appearance of lung metastases (3 pts), and/or site of occurrence (four patients with central lesions) and patient refusal (2 pts).

Patient's characteristics and treatment are shown in Table 1.

2.2. SBRT treatment

A 4D-CT scan was acquired for all patients before SBRT. The Clinical Target Volume (CTV, coincident in the study to the gross tumour volume GTV) was delineated on each 4D-CT phase to generate Internal Target Volume (ITV); the ITV was defined as the

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