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Short communication

Focalized external radiotherapy for resected solitary brain metastasis: does the dogma stand?

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Abstract

Purpose: To investigate whether whole brain irradiation might be replaced by focalized irradiation after resection of a single brain metastasis in patients where extracranial tumor control is deemed to be obtained.

Patients and methods: Twelve patients were introduced in a phase I/II prospective study of conformal postoperative external irradiation after resection of a solitary brain metastasis. The radiation treatment consisted of 50.4 Gy (1.8 Gy per fraction, five fractions per week). The planning target volume consisted of the tumor bed and a 2 cm safety margin. All treatments were optimized with head immobilization, dedicated tomodensitometry and computer assisted three-dimensional treatment planning.

Results: The median survival was 7.2 months (range 2.4–50.4 months). Eleven of the 12 patients died. Eight of the 12 patients presented intracranial recurrence and seven died as a consequence of intracranial tumor progression.

Conclusions: Focalized external irradiation cannot serve as a reasonable alternative to whole brain radiotherapy (WBRT) even for patients with apparently one single resected brain metastasis. The dogma of 'one metastasis = multiple metastases' seems to be confirmed. © 1998 Elsevier Science Ireland Ltd.

Keywords: Focalized external irradiation; Resected solitary brain metastasis; Dogma

1. Introduction

The optimal treatment for a single brain metastasis remains to be established [1,9]. Local control and survival were reported to be higher if surgery was combined with radiotherapy as compared to radiotherapy alone in two randomized studies [2,3] and retrospectives series [5]. Survival after resection has been questioned and irradiation for a single brain metastasis is potentially of long duration. Therefore, the dogma of whole brain irradiation after resection should be questioned, especially when considering the potential risk of late toxicity. To decrease the potential detrimental effect of whole brain irradiation (WBRT) [4], focalized external beam irradiation could be used as an alternative to WBRT, provided the pattern of disease recurrence is mainly extracerebral. There are currently no valid data available on the feasibility and efficacy of focalized external beam irradiation of the tumor bed after resection of a single brain metastasis. Therefore, we initiated a phase I/II trial to define the site of first recurrence after focalized radiotherapy treatment and to question the widely accepted dogma of WBRT.

2. Patients and methods

Between April 1991 and December 1993, 12 patients were included in a prospective phase I/II study aimed at assessing the feasibility of focalized external irradiation after surgical resection for a single brain metastasis. Metas-

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tases from small cell lung cancer and malignant lymphoma were not eligible. In order to exclude other secondary lesions within the brain, all patients were submitted to both brain tomodensitometry (CT) and nuclear magnetic resonance (NMR). For the present phase I/II study, eligibility criteria included that the primary tumor had to be controlled and that no other extracranial metastases were discovered.

The postoperative irradiation was delivered after three-dimensional computer-assisted treatment planning (TPS). The CT slices required for spatial reconstruction of the target were obtained in a head immobilization mask (ORFIT Raycast, Uehlinger Pfiffner AG, Switzerland). The transfer of CT images to the TPS was done by an Ethernet link. The region of interest was irradiated conformally with multiple static beams (two to three beams) and individualized cerrobend blocks. A total dose of 50.4 Gy was applied on the ICRU-50 point (intersection of the beams). Patients received daily fractions of 1.8 Gy, five times per week. These treatments were performed with a linear accelerator producing at least 6 MV photons. The median time between surgery and initiation of radiotherapy was 26 days (range 8–72 days). Only five patients were kept on steroids during irradiation. No anticancer chemotherapy was applied except for one patient with testicular embryonal carcinoma.

Table 1

Characteristics of the 12 patients

	n
Sex	
Male	6
Female	6
Age (years)	
Median	58
Range	21–77
WHO performance status	
1	1
2	2
3	8
4	1
Primary tumor	
Lung	4
Breast	3
Melanoma	1
Testicular	1
Renal and lung	1 (renal origin)
Ovary and breast	1 (ovarian origin)
Colon and prostate	1 (colon origin)
Histology of the primary tumor	
Adenocarcinoma	10
Melanoma	1
Embryonal carcinoma	1
Location	
Supratentorial	11
Infratentorial	1
Interval from primary diagnosis to brain metastasis (months)	
Median	9
Range	0–12

Table 2

Improvement in terms of performance status following treatment

WHO performance status	Before surgery	After surgery	After radiotherapy
1	1	2	5
2	2	6	5
3	8	3	1
4	1	1	1

WHO, World Health Organization.

After completion of the external radiation therapy, the patients were followed on a regular basis until death. Radiological follow-up with CT and/or NMR was done on a regular basis or if disease progression was suspected based on clinical symptoms.

3. Results

The patient characteristics are listed in Table 1. Strikingly, a large majority had an adenocarcinoma from various origins, which is a common feature in the case of a single brain metastasis. As illustrated in Table 2, we observed an improvement in terms of performance status after treatment by surgery and radiotherapy for these patients bearing single brain metastases. This clearly illustrates the potential advantage of treating those patients as far as quality of life is concerned. The median survival was 7.2 months (range 2.4–50.4 months). Eleven of the 12 patients died from their disease. Seven of those died because the tumor recurred in the brain. Four patients died from extracranial metastatic disease. One of the latter also presented with intracranial failure. Only one patient is currently alive without evidence of disease 4 years after treatment. Overall, eight of the 12 patients developed intracranial failure. The distribution of brain failures has been listed according to their locations in Table 3. Interestingly, there were no failures reported inside the treated area, i.e. in-field, as the sole site of recurrence. However, failures outside the treated volume are the main reason for intracranial failure. Most of those brain failures were multiple; four patients developed multiple foci and two patients presented carcinomatous meningitis. Only two out of eight patients had only one site of brain failure. There is only one patient alive in this series; he presented with a brain metastasis from a clear cell adenocarcinoma of the kidney. The patient with a primary

Table 3

Distribution of intracranial recurrences

No failure	IF	OF	M	IF + OF	M + IF + OF	Total
4	0	3	2	2	1	8

IF, in-field; OF, out-field; M, meningeal.

embryonal carcinoma of the testicle, which progressed during external irradiation, received chemotherapy but died 1 year after radiation treatment.

This phase I/II study was stopped after only 12 patients due to the unacceptably high rate of central nervous system failures.

4. Discussion

Despite the reported series [2,3,5–7] of an increased survival after treatment of solitary brain metastases, especially in patients submitted to surgery, our results were disappointing. We observed a high intracranial failure rate (eight out of 12) and a short median survival (7.5 months) after resection and focalized external radiation therapy. Noordijk et al. [3] reported a median survival of 10 months in 32 patients after resection followed by accelerated whole brain radiation therapy at a dose of 40 Gy (b.i.d. in 2 weeks). Patchell et al. [2] described a median survival of 40 weeks in their series of 25 patients treated with surgery and hypofractionated WBRT (36 Gy in 12 fractions).

One could argue against the use of high-dose multifractionated treatment in this population of patients characterized by a short median survival [8]. However, this treatment schedule was chosen because of concern regarding late toxicity in patients for whom potential long survival after resection of a solitary brain metastasis has been described. In the present series, a high dose (50.4 Gy) focalized irradiation yielded a high in-field local control. However, the out-field intracranial progression rate and subsequent death rate is unacceptable. Therefore, the dogma which states that the concept of a 'solitary' brain metastasis is merely an illustration of the lack of resolution of current radiological imaging techniques in detecting the presence of micrometastatic disease seems to be illustrated by our results on a small number of patients.

We conclude that focalized external radiotherapy after resection of a solitary brain metastasis is not a safe procedure as far as intracranial control is concerned. Should we question the role of WBRT after stereotactic radiation therapy of a 'solitary' brain metastasis, or rather the impact of a high-dose stereotactic boost added to moderate doses of WBRT in a randomized trial?

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