

Radiotherapy of brain metastases: A 20-case report

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Abstract

Introduction: Brain metastases represent the most common malignant brain tumors, affecting 20-40% of cancer patients. This article examines the efficacy of in toto encephalic radiotherapy in the treatment of these metastases. Historically, before the advent of radiotherapy, the prognosis for brain metastases was poor, with a median survival of one month. In toto brain radiotherapy has played a crucial role in improving survival and local control of lesions. The aim of this study was to analyze the epidemiological, clinical and therapeutic characteristics of patients treated by this method.

Material and Method: This prospective descriptive study included patients with brain metastases treated with total encephalic radiotherapy (TER) between January and April 2021. Inclusion criteria were related to diagnosis of brain metastases and exclusive use of total encephalic radiotherapy. Data were collected from medical records and analyzed using Microsoft Excel. Quantitative and qualitative data were processed to provide information on the characteristics of the study population.

Results: Results show that the mean age of patients was 58.55 years, with a predominance of the 50-59 age group. Brain metastases were mainly from bronchopulmonary cancer (45%) and breast cancer (25%). In terms of symptoms, 90% of patients were symptomatic, while 10% were asymptomatic. The majority of patients (85%) had more than 3 brain metastases on MRI. As for treatment, 70% received radiotherapy at a dose of 30 Gy in 10 fractions, while other regimens were used for the remaining cases.

Conclusion: Brain metastases remain a major problem in oncology, with significant consequences for patient survival and quality of life. Although stereotactic radiotherapy is gaining in popularity, this study highlights the persistent role of in toto encephalic radiotherapy in the treatment of certain brain metastases. Despite advances in other therapeutic modalities, EIT continues to play an important role in the management of these tumors.

Keywords: Radiotherapy; Brain; Metastasis; Stereotactic; Quality of life

1. Introduction

Cerebral metastases are the most frequent malignant tumors of the brain. Between 20% and 40% of cancer patients develop brain metastases during the course of their disease [1].

Bronchopulmonary cancer is the leading cause of brain metastases (34%), followed by breast cancer (30%) and melanoma [1].

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Without the advent of radiotherapy, the prognosis was appalling due to rapid neurological deterioration, with a median survival of 1 month [2].

For many years, in toto encephalic radiotherapy was the cornerstone of treatment for brain metastases, achieving two objectives: potentially curative for metastases in place, and prophylactic in the remaining brain tissue [3].

Median survival has thus increased from 3 to 6 months, with 50% local control [4] [5].

We report the epidemiological, clinical and therapeutic results of patients with brain metastases treated at our institution with in toto encephalic radiotherapy.

2. Material and method

2.1. Type of study and period

This is a prospective descriptive study of patients with brain metastases, irrespective of the primary cancer, treated with in toto encephalic radiotherapy over the period January to April 2021.

2.2. Objectives

The aim of our study is to determine and analyze the epidemiological, clinical and therapeutic characteristics of patients treated with TBRT for brain metastases, and to deduce the remaining indications for this technique.

2.3. Study population

2.3.1. - Inclusion criteria

Patients with brain metastases, whatever the primary cancer, treated with radiotherapy to the entire brain.

2.3.2. - Non-inclusion criteria

- Patients treated with another radiotherapy technique, in particular stereotactic.
- Patients with primary brain cancer.

2.4. Data collection

Data were collected from medical records, using Ambre and MOSAIQ software.

2.5. Analysis methods

- Data were entered and analyzed in Microsoft Excel.
- Histograms and other figures were produced using Microsoft Excel.
- For quantitative variables, we assessed the minimum, maximum, mean and standard deviation. For all qualitative variables, frequency and percentage were calculated.

2.6. Ethical considerations

We collected data using anonymous forms, in strict compliance with confidentiality requirements.

3. Results

Patient characteristics are summarized in Table 1.

The mean age of our patients was 58.55 years (42-78 years). The most represented age group was 50-59, with 8 patients, or 40% (figure 1). The sex ratio was 0.82. Bronchial cancer was the most frequently found primary (45%), followed by breast cancer in 25% of cases. The other primary cancers were all represented at 5% (chondrosarcoma, endometrium, melanoma, pancreas, prostate and maxillary sinus) (figure 2). 45% of patients had a WHO score of 1 and 35% a WHO score of 2. 15% of patients were classified WHO 3 and one patient was classified WHO 0, i.e. 5% of the study population. 18 patients were symptomatic, i.e. 90%, and 2 had no neurological signs, i.e. 10%. The primary tumor was in complete or partial response in 40% of patients, and 10% had stable primary disease. In 50% of patients, the primary tumour

was progressive. 85% of our patients had more than 3 brain metastases on MRI, and 10% had 3 brain lesions. Carcinomatous meningitis was found in one patient, i.e. 5% of the study population.

Table 1 Patients and treatment characteristics

		n (%)
Mean age (years)	Mean (range)	58.55 (42-78)
staff by age	<50	4 (20)
	50-59	8 (40)
	60-69	4 (20)
	≥70	4 (20)
Gender	Men	9 (45)
	Women	11 (55)
Primary location	Lung	9 (45)
	Breast	5 (25)
	Chondrosarcoma	1
	melanoma	1
	Prostate	1
	Endometrial	1
	pancreas	1
	maxillary sinus	1
PS	0-1	10 (50)
	2-3	10 (50)
Symptoms	HTIC	7 (35)
	motor deficit	4 (20)
	confusion	3 (15)
	facial paralysis	1 (5)
	speech disorder	2 (10)
	convulsions	1 (5)
	frontal syndrome	1 (5)
	cognitive disorders	1 (5)
Control of the primary tumor	Evolutionary	10 (50)
	Response	8 (40)
	Stable	2 (10)
number of lesions on MRI	>3	17 (85)
	3	2 (10)
	carcinomatous meningitis	1 (5)
Extracerebral metastases	Node	10
	Bone	9
	Lung	9
	Liver	7
	Pleural	3

	Mediastinal	1
	Pericardial	1
	sigmoïde	1

18 patients, or 90%, had extra-brain metastases. The most common metastatic sites were lymph nodes, bone, lung and liver.

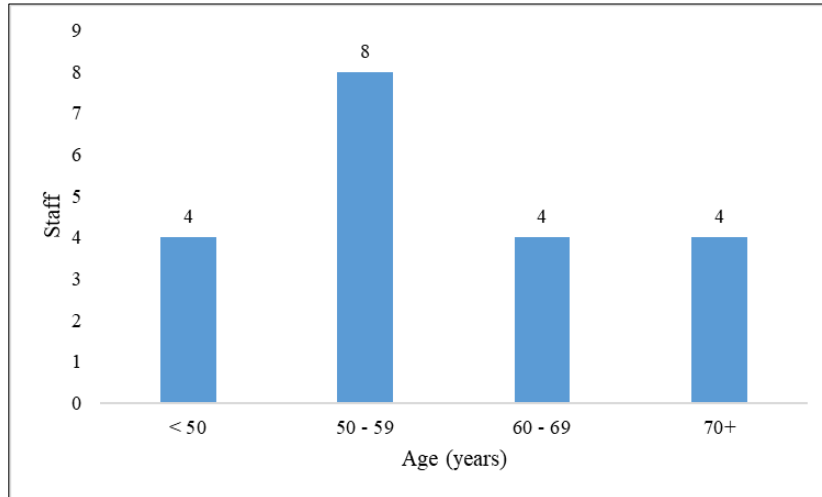


Figure 1 Age distribution

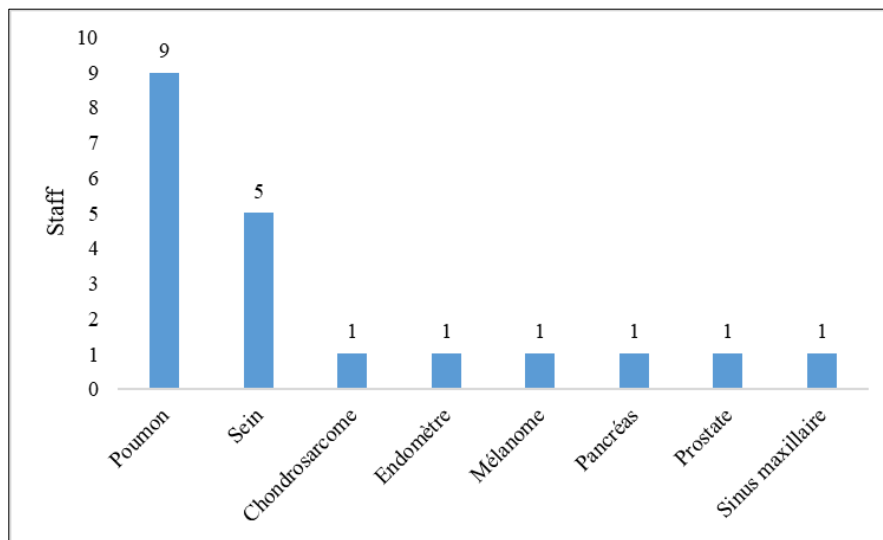


Figure 2 Distribution by primary cancer

70% of patients received radiotherapy at a dose of 30 Gy in 10 fractions of 3 Gy. The 20 Gy regimen in 5 fractions of 4 Gy was delivered in 10% of patients. 5% received 37.5 Gy in 15 2.5 Gy fractions and 27 Gy in 9 3 Gy fractions (figure3).

In terms of tolerability, 90% of patients were free of acute toxicity.

10% did not complete radiotherapy and had 6 sessions out of the 10 planned because of a deterioration in their general condition. Late toxicity was not assessed.

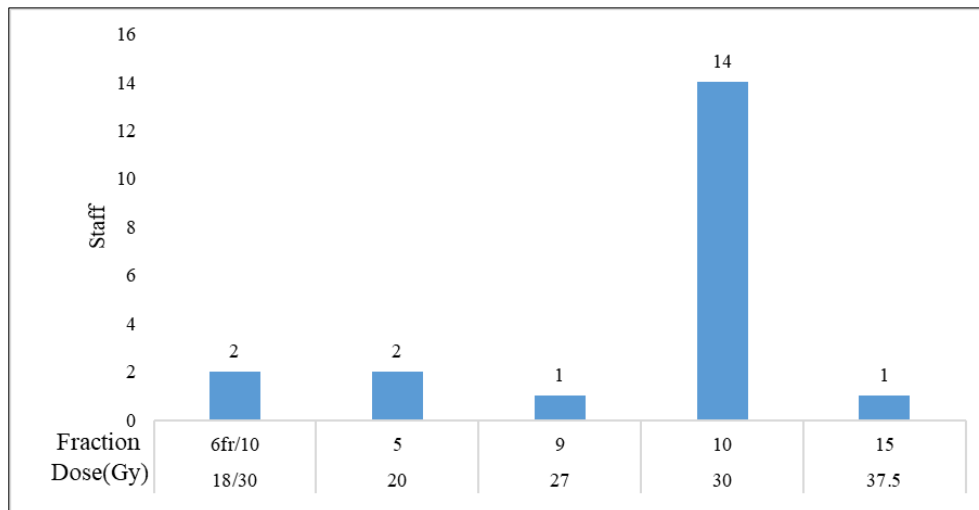


Figure 3 Distribution by dose and fractionation

4. Discussion

Patients with brain metastases constitute a growing population due to the increased efficacy of systemic treatments, but also to improved imaging techniques which increase the detection rate [3].

In France, there are 30,000 new cases of brain metastases per year [6].

The average age of our patients was 58.55 years, and women were more frequently represented than men. A study carried out at the Dakar Cancer Institute found an average age of 45.88 years, with 42 women versus 8 men [7]. The primary cancers most likely to cause brain metastases are bronchial, breast and melanoma cancers [8]. In our study, this was found with lung cancer coming in first place, followed by breast cancer. Mané's 2018 study found 70% breast cancer and 14% bronchial cancer [7].

90% of our patients were neurologically symptomatic, requiring rapid and effective management. 50% of our patients were in good general condition (WHO 0-1). In the various prognostic scores proposed for the management of patients with brain metastases, general condition was the most frequently found factor. Poor PS has been identified as a poor prognostic factor.

Historically, the management of brain metastases was based on corticosteroids, followed by whole-brain irradiation [9]. Patients untreated or treated solely with corticosteroids had a median survival time of around one month, but an early randomized trial showed its value in combination with whole-brain irradiation [10] [2]. Whole-brain irradiation with different fractionations has resulted in median overall survival times of around three to six months, and one-year survival rates of around 10% [2] [4] [11].

50% of our patients had a progressive primary tumor, which has been identified as a poor prognostic factor in prognostic scores.

However, for the other half of patients with controlled primary disease (stability and remission), TIS was justified as increasing survival.

Whole-brain irradiation was considered the gold standard treatment for multiple brain metastases [12]. In our study, 85% of patients had more than 3 brain metastases, and one patient (5%) had carcinomatous meningitis.

TIS increases local control by reducing the risk of recurrence at the initial site and in the rest of the brain.

In the EORTC trial, Kocher et al. demonstrated that the addition of TIS to stereotactic radiotherapy or surgery significantly reduced relapse rates in the initial metastatic site and in the rest of the brain [13].

Furthermore, the trial reported by Chougule et al, which compared radiotherapy under stereotactic conditions with or without irradiation of the entire brain, demonstrated a superior local control rate with the combination, respectively 91% versus 62% [14].

Several studies have demonstrated the cognitive toxicity of EIT [15] [16] [17] [18] [19].

In 2016, Brown et al. demonstrated the deterioration in cognitive function and quality of life at 3 and 12 months in patients who had received EIT radiotherapy [20]. The benefit-risk balance must therefore be carefully assessed in relation to patient prognosis.

In a study presented at ASTRO 2020, stereotactic radiotherapy was shown to preserve cognitive function better than EIT radiotherapy [21].

In the RTOG 0614 study, the administration of memantine to patients treated with EIT prolonged the time to onset of cognitive decline [22].

Hippocampal sparing has also been evaluated in the preservation of cognitive function in patients treated with EIT.

In the NRG Oncology CC001 study, hippocampal sparing in patients treated with EIT combined with memantine resulted in less cognitive decline, compared with the group that did not benefit from hippocampal sparing [23].

The presence of extracerebral metastases has been identified in various prognostic scores as a poor prognostic factor.

In our study, 80% of patients had synchronous extracerebral metastases, and the sites most frequently affected were lymph nodes, bone and lung.

The regimen of 30 Gy in 10 fractions of 3 Gy was prescribed in 80% of our patients. However, two of them received only 6 of the 10 prescribed sessions, due to a deterioration in their general condition.

As for the radiotherapy regimen, three prospective RTOG trials included more than 1,800 patients and evaluated nine different fractionations without noting any significant difference in terms of survival [5] [24].

In some trials, 37.5 Gy in 15 fractions of 2.5 Gy and 3 weeks was the reference [25]. However, the protocol with 30 Gy in ten 3 Gy fractions is the most reported fractionation in retrospective series and was the reference in the EORTC trial, whereas that with 20 Gy in five 4 Gy fractions was not considered inferior to the previous fractionation in the elderly [26] [13] [27].

The most conventional is 30 Gy in 10 fractions of 3 Gy over 2 weeks. This limits neurological symptomatology, but is also palliative, as this dose is too low for lasting control of encephalic metastatic disease.

The 37.5 Gy regimen in 15 fractions over 3 weeks is optimized to limit long-term neurocognitive complications for patients with an assumed long life expectancy.

Finally, 20 Gy in 5 fractions over one week is a more rapid regimen for fatigued patients with short life expectancy.

Our study has shown that, despite the increasing use of stereotactic radiotherapy, TIA remains an indication for certain patients with brain metastases.

However, the cognitive toxicity of TIA is a limiting factor for patients with better survival.

As a result, TIA would be of particular benefit to patients whose survival is not long, enabling them to improve their neurological symptoms and thus their quality of life during the few months they have left to live.

Hippocampal sparing could be an interesting prospect in this treatment technique for the preservation of cognitive functions.

In any case, we must always optimize the benefit/risk balance in order to offer our patients appropriate management, and this necessarily involves the RCP.

Abbreviations

- TIS: encephala in toto
- EORTC: European Organization for Research and Treatment of Cancer
- RTOG: Radiation Therapy Organization Group

5. Conclusion

Cerebral metastases are the most frequent malignant tumors of the brain. For many years, in toto encephalic radiotherapy has been the cornerstone of treatment for brain metastases. Despite the increasing use

Compliance with ethical standards

Disclosure of conflict of interest

No conflict of interest to be disclosed.

Statement of informed consent

Informed consent was obtained from all individual participants included in the study.

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