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Original article

Reirradiation of relapsed brain tumors in children

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ARTICLE INFO

Article history:
Received 30 June 2011
Received in revised form
6 September 2011
Accepted 7 October 2011

Keywords:
Reirradiation
Late side effects
Conformal radiotherapy
Recurrent brain tumors

ABSTRACT

Aim: The aim of this study was to evaluate toxicity and response to fractionated reirradiation (FR) of relapsed primary brain tumors in children.

Background: The treatment options for recurrent brain tumors in children previously irradiated are limited. Reirradiation is performed with fear due to the cumulative late CNS toxicity and the lack of a significant chance of cure.

Materials and methods: Between 2008 and 2009, eight children with a median age of 14.5 years with a diagnosis of a recurrent brain tumor underwent reirradiation. Initially, all patients were treated with surgery, chemotherapy and radiotherapy. The median time to the first recurrence after the initial treatment was 19.5 months. Intervals between radiotherapy courses were in the range of 5–51 mos. All retreatments were carried out with 3D image-based conformal methods. The total prescription dose was 40 Gy in a fraction of 5×2 Gy/week. The total cumulative dose ranged from 65 to 95 Gy (median: 75 Gy). The median cumulative biologically effective dose was 144 Gy (range: 126–181 Gy).

Results: The median overall survival and progression free survival measured from the beginning of reirradiation was 17.5 and 6.5 months, respectively. During the first evaluation, four patients showed a complete or partial response, two did not respond radiologically. Two children were progressive at the time of reirradiation. Among children with progression that occurred during the first year after reirradiation, only two progressed in the treatment area. The repeated irradiation was well tolerated by all patients. No late complications have been observed.

Conclusion: In the absence of other treatment possibilities, the fractionated reirradiation with highly conformal three-dimensional planning could be a therapeutic choice in case of recurrent brain tumors in children. The control of craniospinal dissemination remains to be the main problem.

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doi:10.1016/j.rpor.2011.10.004

1. Background

Central nervous system (CNS) tumors account for about 20% of all childhood malignancies. Notwithstanding the advances in the treatment of pediatric brain tumors, in particular medulloblastoma, in most series 30–40% of patients develop recurrences which result in death due to tumor progression.[1]

The treatment options for recurrent brain tumors in children previously irradiated are limited. Reoperation and standard dose salvage chemotherapy are used in majority of these patients providing a palliative effect. Reirradiation within the central nervous system may result in temporary local control but is performed with fear due to cumulative late CNS toxicity and the lack of a significant chance of cure. It may be offered only to selected patients with lesions of limited size localized in a "safe" area. This is particularly important in the treatment of children. In the literature there are only few publications concerning this topic. New conformal radiotherapy techniques allow reduction of the treatment volume thereby sparing normal tissue, which consequently decreases the risk of the late toxicity.[2–6] Additionally, radiobiological data suggest at least partial repair of CNS radiation damage after the initial course of radiotherapy. The magnitude of this recovery depends on the total dose and fractionation regimen in the first course and the time elapsed between treatments. Despite this fact, many different reirradiation treatment schemes are used with regard to total dose, size and number of fractions.[7,8]

Due to the low repair capacity of the brain tissue, reflected in the α/β ratio, which is estimated to be approximately 2 Gy, the biologically effective dose (BED) rather than the "physical" irradiation dose, should be considered in the analysis of radiotherapy protocols.[9] Our data were analyzed using this cumulative BED, which is the sum of the BED of the initial irradiation course and the BED of the reirradiation course.

2. Aim

The aim of this study was to evaluate toxicity and response to fractionated reirradiation (FR) of relapsed primary brain tumors in children.

3. Materials and methods

3.1. *Patients*

In the period from January 2008 to September 2009, eight children (5 male, 3 female) with a median age of 14.5 years (range 9–18.5 years) with a diagnosis of a recurrent brain tumor underwent reirradiation at the Radiotherapy Department of MSCM Cancer Centre in Warsaw. Both the clinical data and radiotherapy technical records were reviewed.

The primary histological diagnoses included: six medulloblastoma (MB), one germ cell tumor (GCT) and one non-germ cell tumor (NGCT). Five patients with medulloblastoma were classified as a high risk group, only one (pt. 2 in Table 1) as standard risk.

Table 1 – Children retreatment data.

No.	Histology	RT1 volume	RT1 dose total/fraction [Gy]	RT2 volume	$V_{PTV(RT2)}$ [ccm]	RT2 dose total/fraction [Gy]	TD cum. [Gy]	BED cum. [Gy]	Interval RT1–RT2 [mos]	PFS [mos]	OS [mos]/ outcome	Time to PTV failure [mos]
1	MB	CNS	35.07/1.67	PFT-rec.	4.8	40/2	95	181	51	14	27	21
		TB	55.11/1.67								CNS-meta	
2	MB	CNS	25.05/1.67	Occipital-meta	7.9	40/2	65	126	44	12	26	19
		TB	55.11/1.67	PFT-rec.	15.1	40/2	95	181	50		CNS-meta	
3	NGCT	VS	30.6/1.8	Spine-elective		30.6/1.8			5	5	12	Without LP
		TB	54/1.8	PFT-meta	22.3	40/2	71	138			Death	
4	MB	CNS	35.07 (spine: 40.08)/1.67	Frontal-meta	33.9	40/2	75	144	39	6	17	6
		TB	55.11/1.67								CR	
5	MB	CNS	35.07/1.67	Frontal-meta	8.3	40/2	75	144	39	7	18	Without LP
		TB	55.11/1.67								Spine-meta	
6	MB	CNS	35.07/1.67	PFT-rec.	60.5	28/2	83	157	33	1	6	1
		TB	55.11/1.67								Death	
7	MB	CNS	35.07/1.67	VS-meta	20.4	40/2	75	144	27	1	19	Without LP
		TB	55.11/1.67								VS-meta	
8	GCT	VS	24/1.6	Brain-elective		18/1.8			35	9	9	Without LP
		TB	40/1.6	VS-meta	46.5	40/2	80	152			PR	

RT1, first radiation course; RT2, second radiation course; PFT, posterior fossa tumor; TB, tumor boost; VS, ventricular system; LP, local progression.