Journal of Clinical Neuroscience 22 (2015) 955–958

Contents lists available at ScienceDirect

Journal of Clinical Neuroscience

journal homepage: www.elsevier.com/locate/jocn

Clinical Study

Hypofractionated stereotactic radiotherapy in medium-sized to large arteriovenous malformations

Peter Lindvall [a,*], David Grayson [a], Per Bergström [b], A. Tommy Bergenheim [a]

[a] Department of Clinical Neuroscience, Neurosurgery, Umeå University, 901 85 Umeå, Sweden
[b] Department of Radiation Sciences, Oncology, Umeå University, Umeå, Sweden

ARTICLE INFO

Article history:
Received 23 September 2014
Accepted 16 December 2014

Keywords:
Arteriovenous malformations
Linear accelerator
Radiosurgery
Treatment results

ABSTRACT

We have reviewed treatment results in terms of obliteration and complications in 24 patients with medium to large sized cerebral arteriovenous malformations (AVMs) (mean volume 18.5 ± 8.9 cm^3; range: 10–42) treated with hypofractionated stereotactic radiotherapy (HSRT). AVMs are congenital lesions associated with a high morbidity and mortality. Radiosurgery is one option for treatment. However, in larger AVMs with volumes exceeding 10 cm^3 obliteration rates are less favourable and radiation induced complications more frequent. For larger AVMs, volume-staged radiosurgery is one option while another option may be the use of HSRT. Patients were treated with 6–7 Gy in five fractions to a total dose of 30–35 Gy (mean total dose 32.9 ± 1.6 Gy [standard error of the mean]). Sixteen patients (69.6%) showed obliteration after a mean time of 35.2 ± 14.8 months (range: 24–60). Only one patient (4.2%) experienced symptomatic radionecrosis. Our treatment with HSRT seems safe and efficient for treatment of medium to large sized AVMs. Treatment results seem to be in line with volume-staged radiosurgery and may be an alternative for AVMs not suitable for single fraction radiosurgery.

1. Introduction

Cerebral arteriovenous malformations (AVMs) are congenital lesions associated with a high morbidity and mortality [1]. Stereotactic radiosurgery is one option in the treatment of AVMs and obliteration rates for both Gamma Knife (Elekta, Stockholm, Sweden) and linear accelerator (LINAC) have been reported to be between 80–90% for small AVMs [2–4]. With increasing AVM size treatment results are, however, less favourable, with decreasing obliteration rates and increasing radiation related complications [5,6]. The rate of complications is a function of total dose and volume of radiation delivered and as a consequence, one strategy in large AVMs has been to reduce the dose to minimise complications. This may negatively affect the obliteration rates even if complications are maintained at an acceptable level. Different strategies have evolved to solve this problem. Volume-staged Gamma Knife radiosurgery has been reported to be successful in AVMs >15 cm^3 [7,8]. Another strategy may be the use of hypofractionated stereotactic radiotherapy (HSRT) [3,9,10]. By using hypofractionation a treatment benefit may be achieved exploiting the proposed difference in the α/β ratio between the AVM target cells and the normal late responding tissue [11,12]. A higher total radiation dose may be delivered than with single fraction radiosurgery and without an increased rate of complications. We present our results in AVMs $\geqslant$10 cm^3 treated with HSRT.

2. Materials and methods

As all patients in this retrospective study were treated according to our clinical routine there was no need for a formal approval by the Regional Ethical Committee. All patients have given their informed consent for publication of data given the fact that no individual patient could be identified.

HSRT has been used for the treatment of cerebral AVMs at Umeå University Hospital since 1986. Seventy-eight patients had been treated with this modality by the end of 2013. Twenty-four of these patients had an AVM with a volume $\geqslant$10 cm^3 (range: 10–42; mean 18.5 ± 8.9 cm^3) and treatment results from these patients were evaluated. The technique of HSRT at Umeå University Hospital has been described previously [3,13]. Digital subtraction angiography and a contrast enhanced CT scan with 1.25–2.5 mm slices were performed with a relocatable non-invasive stereotactic frame, either the Laitinen stereoadapter or more recently the Fixster frame [14–16]. These investigations were used for delineation and positioning of the target. AVM volumes were

* Corresponding author. Tel.: +46 90 785 00 00.
E-mail address: peter_lindvall_nkk@hotmail.com (P. Lindvall).

http://dx.doi.org/10.1016/j.jocn.2014.12.015
0967-5868/

calculated in the 3D dose-planning system (TMS-Helax or recently Oncentra Masterplan; Nucleotron, Columbia, MD, USA) and a 2 mm margin was added to the AVM nidus to create the planning target volume. Treatment was delivered in five fractions using a 6 MV linear accelerator (Dynaray CH-6, BBC until 1992 and thereafter a Clinac 2300CD; Varian Medical Systems, Palo Alto, CA, USA). Patients were examined with a contrast enhanced CT scan or an MRI 1 year following treatment in order to diagnose a possible reaction to the radiation therapy. Follow-up with a digital subtraction angiography was performed 2 years after treatment and in patients with incomplete obliteration subsequent angiographies were performed at 1–2 year intervals until complete obliteration of the AVM without evidence of remaining draining veins.

Values are reported as means ± standard error of the mean and range. Statistical evaluation included a t-test for comparison of means. Pearson correlation analysis and logistic regression was used for analyses of association between variables. A Kaplan–Meier plot was used for evaluation of AVM obliteration following treatment.

3. Results

Twenty-four patients (13 women, 11 men) with an AVM volume $\geqslant 10\ cm^3$ (range: 10–42; mean 18.5 ± 8.9, median 15.5) were treated with HSRT. Sixteen AVM (66.7%) had been embolised prior to HSRT and in these patients the AVM volumes were calculated post embolisation. Nine patients (37.5%) presented with intracranial haemorrhage whereas the rest of the patients presented with seizures, headache or focal neurological symptoms. The mean age at the time of treatment was 45.6 ± 16.4 years (range: 18–74). The patient and AVM characteristics as well as treatment outcome are shown in Table 1. The modified radiosurgery-based AVM grading scale (Table 1) [17] was also used for classification (AVM score = 0.1 × volume + 0.02 × age + 0.5 × location). The mean score was 2.76 ± 0.96 (range: 1.26–5.28). HSRT was delivered in five fractions with 6–7 Gy in each fraction. The mean total dose was 32.9 ± 1.6 Gy (range: 30–35). Six patients (25%) were treated with 7 Gy in five fractions and the rest of the patients with 6–6.5 Gy in five fractions. The mean AVM volume was not significantly larger in patients treated with <35 Gy ($p = 0.39$).

Four patients died during the follow-up period. Three patients (12.5%) died of intracerebral haemorrhages from a ruptured AVM before proven obliteration after a mean time of 28.2 ± 35.6 months (range: 4–69) following treatment. Another patient, whom at latest follow-up 9 years after treatment still did not show obliteration, died from unrelated causes. One additional patient declined angiographic follow-up after treatment. Overall, 16 patients (69.6%) showed obliteration after a mean time of 35.2 ± 14.8 months (range: 24–60; Fig. 1). Excluding one patient with symptomatic radiation necrosis, the obliteration rate without new neurological deficits was 65.2% (15/23). Three patients have so far not shown

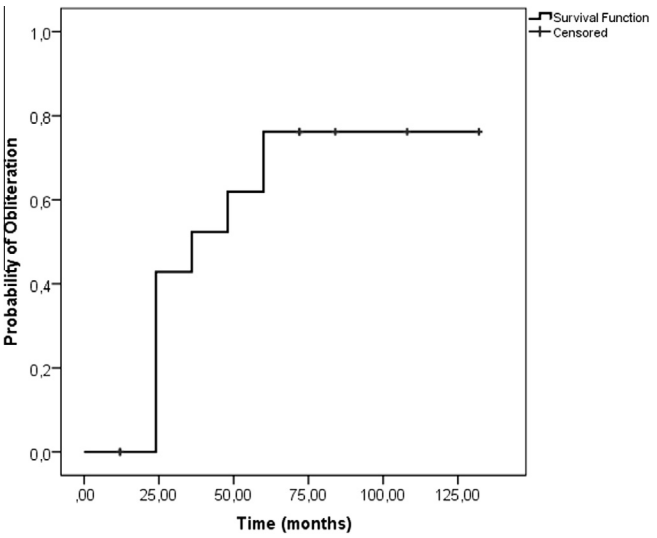

Fig. 1. Kaplan–Meier plot showing the angiographic obliteration rates in patients with arteriovenous malformations following hypofractionated stereotactic radiotherapy

Table 1
Patient and AVM characteristics with previous treatments and outcomes

Sex	Age (years)	Clinical presentation	Previous treatment	AVM volume (cm^3)	AVM score*	Location	Total dose (Gy)	Outcome
F	65	Seizure	None	10.0	2.30	Frontal	30.0	O
M	33	SAH	None	15.0	2.16	Cerebellar	32.5	O
F	47	Vertigo	Embol	13.0	2.24	CC	32.5	O
F	44	SAH	Embol	16.0	2.48	Parietal	32.5	O
F	74	Dysphasia	Embol	28.0	4.28	Parietal	30.0	FH
M	55	Headache	Embol	30.0	4.10	Occipital	32.5	O
M	46	Seizure	None	12.0	2.12	Frontal	32.5	O
F	18	Headache	Embol	35.0	3.86	Occipital	32.5	NO
F	48	ICH	Embol	11.0	2.06	Parietal	32.5	O
M	48	Seizure	Embol	29.0	3.86	Frontal	35.0	O
F	30	ICH	Embol	18.0	2.40	Frontal	35.0	O
M	54	Seizure	None	42.0	5.28	Temporal	30.0	NO
M	65	Incidental	None	12.0	2.50	Occipital	32.5	O
M	44	SAH	Embol	15.0	2.38	Temporal	35.0	O
F	60	Headache	Embol	23.0	3.50	Parietal	32.5	O
M	36	Seizure	None	18.0	2.52	Temporal	35.0	O
F	72	SAH	Embol	11.0	2.54	Frontal	35.0	FH
F	22	ICH	Embol	11.0	1.54	Occipital	35.0	NO
M	54	Seizure	None	10.3	2.11	Temporal	35.0	LF
M	18	ICH	Embol	10.0	1.36	Cerebellar	32.5	NO
M	57	Hemiparesis	None	17.6	2.82	BG	32.5	FH
F	44	SAH	Embol	18.4	2.72	Frontal	32.5	O
M	18	Seizure	Embol	12.5	1.61	Occipital	32.5	O
F	42	Headache	Embol	26.6	3.50	Parietal	32.5	O

* modified radiosurgery-based AVM grading scale [17] AVM score = 0.1 × volume + 0.02 × age + 0.5 × location.
AVM = arteriovenous malformation, BG = basal ganglia, CC = corpus callosum, Embol = embolisation, F = female, FH = fatal haemorrhage, ICH = intracerebral haemorrhage, LF = lost to follow-up, M = male, NO = non-obliterated, O = obliterated, SAH = subarachnoid haemorrhage.