

## The results of postoperative radiotherapy in patients with central nervous system hemangioblastoma

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*Introduction.* Hemangioblastoma accounts for 1-2.5% of all central nervous system tumors and about 7-9% of primary posterior fossa tumors. Complete resection results in high local control rate and long overall survival.

*Materials and methods.* Between 1974 and 1996 30 patients with hemangioblastoma were postoperatively irradiated. Six (20%) patients underwent complete resection and six (20%) incomplete resection. In 18 (60%) patients the completeness of resection was doubtful. Mean age was 39 years (range 17-68, median 37). The group consisted of 17 male (57%) and 13 female (43%) patients. Patients in good neurological status accounted for 77% (23 cases). All patients were irradiated with Cobalt 60 unit. The total dose ranged from 40 to 60 Gy given in 20 to 30 fractions during 4 to 6 weeks. One patient received palliative irradiation with a dose of 20 Gy.

*Results.* All 6 patients irradiated after complete resection were alive and without recurrence at the end of the observation. In the analysed group of 24 patients 5- and 10-year overall survival rates were 84% and 65% respectively. In the group of patients with incomplete resection 5- and 10-year overall survival was 42% and was lower than in the group after doubtful-completeness resection, 93% and 69% respectively. Six patients died during the period of observation: 4 patients from recurrent hemangioblastoma, 2 from unknown causes.

*Conclusion.* Postoperative radiotherapy with doses higher than 50 Gy may improve long term survival of patients with hemangioblastoma after uncomplete surgical resection.

### Wyniki pooperacyjnej radioterapii chorych na naczyniaka płodowego centralnego systemu nerwowego

*Wstęp.* Naczyniaki płodowe stanowią ok. 1-2,5% nowotworów centralnego systemu nerwowego oraz ok. 7-9% pierwotnych nowotworów tylnego dołu czaszki. Doszczętny zabieg operacyjny zapewnia wysoki odsetek wyleczeń miejscowych i długoletnie przeżycia bezobjawowe.

*Materiał i metody.* W latach 1974-1996 napromieniano pooperacyjnie 30 chorych na naczyniaka płodowego. U 6 (20%) chorych guz usunięto w całości, u 6 (20%) był to zabieg niedoszczętny, w 18 przypadkach doszczętność zabiegu budziła wątpliwości operującego. Średni wiek chorych wynosił 39 lat (zakres 17-68, mediana 37 lat). Grupa obejmowała 17 mężczyzn (57%) i 13 kobiet (43%). Chorzy w bardzo dobrym i dobrym stanie neurologicznym stanowili 77% (23 chorych). Wszystkich chorych napromieniano w warunkach telegammaterapii 60 Co. Dawki całkowite wynosiły od 40 do 60 Gy podanych w 20 do 30 frakcjach w czasie od 4 do 6 tygodni. Jedną chorą napromieniano paliatywnie dawką 20 Gy.

*Wyniki.* Spośród 6 chorych napromienianych po zabiegach doszczętnych wszyscy żyli bez nawrotu choroby w dniu zakończenia obserwacji. W pozostałej grupie 24 chorych przeżycia 5- i 10-letnie wynosiły odpowiednio 84% i 65%. W grupie po zabiegach niedoszczętnych przeżycia 5- i 10-letnie wynosiły 42% i były niższe niż w grupie po zabiegach o wątpliwej doszczętności (odpowiednio 93% i 69%). W trakcie obserwacji zmarło 6 chorych, u 4 przyczyną zgonu był nawrót naczyniaka, u 2 przyczyna była nieznana.

*Wniosek.* Radioterapia pooperacyjna w dawce  $\geq 50$  Gy może poprawić przeżycia odległe chorych na naczyniaka płodowego po niedoszczętnych zabiegach operacyjnych.

**Key words:** hemangioblastoma, radiotherapy

**Słowa kluczowe:** naczyniak płodowy, radioterapia

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Hemangioblastoma accounts for 1-2.5% of all central nervous system tumors and about 7-9% of primary posterior fossa tumors. Most frequently it develops in the fourth decade of life [1-3]. Generally it is found as a solitary lesion. Multifocality is usually connected with von Hippel – Lindau syndrome (hemangioblastoma of the cerebellum, spinal cord, retina, renal cysts and renal cell carcinoma, cysts of pancreas and epididymis, pheochromocytoma). Hemangioblastoma is thought to be a benign, slowly growing tumor of vascular origin. Nevertheless, being located close to the critical structures of the brain it may bring on severe life-threatening neurological disturbances. Surgical resection is the treatment of choice, especially for solitary hemangioblastoma. Complete resection results in a 75% local control rate and long overall survival [4]. In the case of incomplete resection 5-year overall survival does not exceed 60% and the addition of radiotherapy results in higher local control rates and prolongation of the overall survival [5, 6]. This paper shows the results of postoperative radiotherapy in 30 patients with hemangioblastoma treated in the Centre of Oncology in Cracow between the years 1974 and 1996.

## Materials and methods

Between 1974 and 1996 30 patients with central nervous system hemangioblastoma were treated with radiotherapy in the Centre of Oncology in Cracow. In 27 cases the tumor was located in the cerebellum, in one case in the right hemisphere of the brain, in two cases in the spinal cord. In the two latter cases hemangioblastoma was a part of von Hippel – Lindau syndrome and they had already undergone resection of hemangioblastoma from the cerebellum and the spinal cord several times in the past. One of these patients had a family history of von Hippel – Lindau disease. The other patient was the first case of hemangioblastoma in his family. All patients had undergone surgery: 6 (20%) complete resection, 6 (20%) macroscopically uncomplete resection (in 2 cases proven with postsurgical computed tomography), in 18 (60%) cases the completeness of resection was doubtful (because of the localization of the tumor and severe hemorrhage during surgery). Mean age at the time of diagnosis was 39 years (range 17-68, median 37). The group consisted of 17 male (57%) and 13 female (43%) patients. Neurological status was assessed according to the five step EORTC/MRC scale (Tab. I) [7]. Patients in good neurological status (stage I and II) accounted for 77% (23 cases) of the analysed group. The diagnosis of hemangioblastoma was proven with histopathologic examination in all cases. All patients were irradiated with Cobalt 60 unit. In a majority of patients (27 cases) the technique of two posterior, oblique, wedged fields including posterior fossa was used. In one patient in whom the tumor was localized in the right hemisphere of the brain the three field technique was used. One patient with the tumor located in

the cervical part of the spinal cord was irradiated with two opposed, lateral fields. In one patient, because of poor performance status, only palliative radiotherapy was used – a dose of 20 Gy given in 4 fractions for 5 Gy to one field. It was the patient with von Hippel-Lindau syndrome in whom the recurrence of hemangioblastoma in the thoracic part of the spinal cord was diagnosed. In all other cases the total dose ranged from 40 Gy given in 20 fractions during 4 weeks to 60 Gy given in 30 fractions during 6 weeks. 20 patients (67%) received doses equal or higher than 50 Gy. The dose per fraction ranged from 1.8 Gy to 2.5 Gy. The overall survival was chosen as the criterion of treatment results estimation. The survival rates were estimated with the Kaplan – Meier method.

## Results

Six patients were postoperatively irradiated after undoubted complete resection of hemangioblastoma. All patients from this group were alive and without recurrence at the end of the observation. This group was excluded from further analysis. Detailed analysis of survival and the attempt to establish the prognostic factors was performed in the rest of 24 patients after uncomplete resection or resection, the completeness of which had been doubtful. Clinical data, information about radiotherapy and survival in each individual patient are summarized in Tab. II. Mean observation time was 90 months (range 2-284, median 80). Five and 10-year overall survival rates from the beginning of radiotherapy in the group of 24 irradiated patients were 84% and 65%, respectively. In the group of patients after uncomplete resection 5- and 10-year overall survival was 42% and was lower than in the group after doubtful-completeness resection, 93% and 69% respectively (Fig. 1). Six patients died during the period of observation: 4 patients from recurrent hemangioblastoma, 2 from unknown causes. Among the 18 patients after doubtful-completeness resection one case developed recurrence, which resulted in death after 98 months. In addition two patients in this group died from unknown cause after 33 and 90 months. In the group of 6 patients who had undergone uncomplete resection one patient, irradiated palliatively, died after 2 months because of tumor progression. Among the remaining five patients, irradiated radically, two patients died of recurrence after 58 and 184 months. Improvement of neurological status after radiotherapy was observed in four patients (17%). During radiotherapy five patients (21%) developed acute reactions such as increased intracranial pressure requiring the administration of antioedematic drugs. These reactions had no correlation neither to the fraction dose, nor to the total

Tab. I. Neurological status according to EORTC/MRC scale

I	- no deficit
II	- some deficit, but adequate functioning for useful work
III	- moderate functional impairment with movement difficulties, dysphasia, apraxia, moderate paresis, discrete personality disturbances
IV	- major functional impairment (severe paresis, aphasia, visual impairment, severe personality disturbances)
V	- lack of consciousness or terminal phase

**Tab. II. Clinical data and information about radiotherapy in the group of 24 patients irradiated after uncomplete or doubtful-completeness resections**

No	Age	Sex	NS	Operation	TD [Gy]	FrD [Gy]	Acute reaction	Time of obs. [months]
1.	35	M	1	DC	50.0	2.0		9
2.	43	F	3	U	50.0	2.0		16
3.	68	M	3	DC	50.0	2.0	yes[P]	26
4.	32	F	3	U	60.0	2.0	yes[P]	30
5.	59	M	1	DC	50.0	2.0		37
6.	27	F	2	DC	50.4	2.1		82
7.	42	M	2	U	50.0	2.0		58†r
8.	49	M	1	DC	50.0	2.0		33‡u
9.	17	F	1	DC	50.0	2.0		77
10.	59	M	1	DC	49.3	2.1		76
11.	21	F	1	DC	50.0	2.0		92
12.	42	M	2	DC	50.0	2.0		82
13.	29	F	2	DC	48.0	2.0	yes[P]	21
14.	37	F	2	DC	50.0	2.0		95
15.	32	M	1	DC	60.0	2.0		103
16.	25	F	4	U	20.0	5.0		2†r
17.	25	M	2	DC	50.0	2.0		133
18.	51	M	3	DC	50.0	2.0		98†r
19.	66	M	3	DC	50.0	2.0	yes[P]	90‡u
20.	57	F	2	U	50.0	2.0		184†r
21.	35	F	2	DC	50.0	2.5		243
22.	27	F	2	DC	50.4	2.0		273
23.	42	M	2	DC	50.0	2.5	yes[P]	284
24.	37	M	3	U	48.6	1.8		8

NS - neurological status according to EORTC/MRC; TD - total dose; FrD - dose per fraction; Time of obs. - time of observation; M - male; F - female; U - uncomplete resection; DC - doubtful-completeness resection; P - increased intracranial pressure; †r - death from recurrence; ‡u - death from unknown cause

dose. Two patients (8%) developed symptoms of neuroinfection during radiotherapy, which resolved after antibiotics and had no influence on the course of treatment. Treatment results of the analysed group of patients are summarized in Tab. III according to therapeutic and clinical factors. Although a small number of patients in each subgroup does not allow for a reliable statistical analysis, there seems to be undoubtful correlation between completeness of surgical resection (uncomplete vs doubtful-completeness) and the chance of cure. Data from Tab. III also shows that age, sex, the neurological status and the total dose of irradiation may have influence on the final outcome.

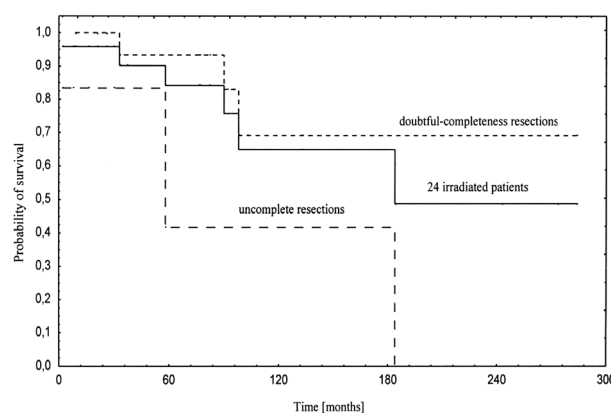


Fig. 1. Overall survival in the group of 24 irradiated patients and survival in subgroups after uncomplete and doubtful-completeness resections

**Tab. III. Treatment results in the group of 24 irradiated patients according to therapeutic and clinical factors**

Factor		5-year survival	10-year survival
Sex	male 13 (54%)	79%	47%
	female 11 (46%)	91%	91%
Age	<50 yr 18 (75%)	79%	79%
	>50 yr 6 (25%)	100%	33%
NS*	I + II 17 (71%)	86%	86%
	III + IV 7 (29%)	86%	0%
Operation	uncomplete 6 (25%)	42%	42%
	doubtful completeness 18 (75%)	93%	69%
Dose	>50 Gy 20 (83%)	87%	67%
	<50 Gy 4 (17%)	75%	0%

NS\* - neurological status according to EORTC/MRC

## Discussion

Hemangioblastoma occurs rarely, therefore papers dealing with this type of tumor usually discuss small groups of patients who had been treated during a long period of time. This renders the assessment of the applied method of treatment difficult. It also concerns the efficacy of radiotherapy. In Polish literature there have been published until now only two papers concerning radiotherapy for hemangioblastoma, describing groups of 14 and 15 patients respectively. One of these two series con-

cerns patients treated with ortovoltage therapy between 1954-1961 [5, 8]. In these reports the presentation of results has a descriptive character and includes, also because of a short follow-up period, no information about the survival rates and no attempt to assess neither the therapeutic nor clinical factors. Results of postoperative radiotherapy of the central nervous system hemangioblastoma obtained in the Centre of Oncology in Cracow do not differ from those quoted in literature [3, 5]. The analysed material involves patients irradiated between the years 1974 and 1996, after macroscopically incomplete resections and doubtful-completeness resections. There is a consent that surgery is the treatment of choice for central nervous system hemangioblastoma. Complete resection assures high local control and overall survival rates, and there are no indications for postoperative radiotherapy. Postoperative radiotherapy improves overall survival only in patients after incomplete resections [3, 5, 6]. In our material we have shown that overall survival depends on the completeness of surgical resection and adjuvant radiotherapy after incomplete resection. A review of literature dealing with radiotherapy of hemangioblastoma suggests that a total dose greater than 40 Gy increases the probability of local control and prolongs overall survival. Sung et al. suggest that a total dose less than 40 Gy (20-36 Gy) results in 55% and 27% of 5- and 10-year survival, respectively, whereas for doses ranging 40-55 Gy it is 91% and 57%, respectively [3]. Smalley et al. observed better local control rates for doses higher than 50 Gy. Strategy assuming delivery of a total dose of 55-60 Gy seems to be especially indicated in patients after macroscopically incomplete resection [6]. The neurological status of the patients before radiotherapy and their age also have significant influence on the results of treatment. Long term results are poorer in patients above the age of 50 and with severe neurological deficits. Postoperative radiotherapy may improve neurological status even in 40% of patients [8]. The chance of improving treatment results is thought to lie in stereotactic radiotherapy which offers the possibility of delivering higher total doses to the tumor with simultaneous sparing of normal tissues. It may be an alternative for conventional radiotherapy, especially in the case of multifocal involvement or in case of unresectable tumors [4, 9, 10].

## Conclusion

Our own experience and data from literature indicate that postoperative radiotherapy with doses higher than 50 Gy may improve long term survival of patients with hemangioblastoma after incomplete surgical resection.

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