NOWOTWORY Journal of Oncology • 2004 • volume 54
Number 1 • 28–30

Radiotherapy of malignant melanoma cerebral metastases – results of treatment

Katarzyna Pudełek, Jan Skołyszewski

Aim. The aim of the study was to evaluate the efficacy of radiotherapy in the treatment of malignant melanoma brain metastases.
Material and methods. 20 patients with malignant melanoma brain metastases treated with palliative radiotherapy at the Centre of Oncology in Kraków between 1990 and 2000. In 8 cases the patients were irradiated twice daily (39 Gy in 13 fractions of 300 cGy) and in 12 cases once daily (20-40 Gy in 5-10 fractions of 400 cGy).
Results. The overall 2-year survival rate in the entire group of 20 palliatively irradiated patients was 5%. The median survival was 5.5 months.
Conclusion. Radiation therapy is effective in the palliative management of malignant melanoma brain metastases.

Wyniki leczenia napromienianiem chorych z przerzutami czerniaka złośliwego do mózgu

Cel. Ocena roli radioterapii w leczeniu chorych na czerniaka złośliwego z przerzutami do mózgu na podstawie doświadczeń Centrum Onkologii w Krakowie.
Materiał i metody. W latach 1990-2000 w Centrum Onkologii w Krakowie leczono napromienianiem 20 chorych na czerniaka złośliwego skóry z przerzutami do mózgu. U wszystkich chorych zastosowano paliatywne napromienianie całego mózgu. 8 chorych napromieniano dwa razy dziennie dawką 39 Gy w 13 frakcjach po 300 cGy. 12 chorych napromieniano raz dziennie i otrzymali oni dawkę 20-40 Gy w 5-10 frakcjach po 400 cGy.
Wyniki. W całej omawianej grupie odsetek przeżyć dwuletnich wyniósł 5%. Mediana przeżycia wyniosła 5.5 miesięcy.
Wniosek. Radioterapia jest skuteczną metodą paliatywnego leczenia chorych z przerzutami czerniaka złośliwego do mózgu.

Key words: malignant melanoma, brain metastases, radiation therapy
Słowa kluczowe: czerniak złośliwy, przerzuty do mózgu, radioterapia

Introduction

Malignant melanoma represents 1% of all neoplasms in men, and 1.5% in women in Poland. In 98% of cases it primarily affects the skin. The standardised incidence rates are 2.5/100.000 for men, and 2.6/100.000 for women, and the standardised mortality rates are 1.5/100.000 and 1.2/100.000, respectively [1, 2]. The incidence of malignant melanoma is increasing steadily, some epidemiological studies even show its twofold increase in every decade [1, 3, 4].

The treatment of choice is surgery. Radiotherapy is used for incompletely removed primary tumours, inoperable local recurrences and skin, nodal, bone and cerebral metastases [1, 3, 5, 6]. Due to the rather disappointing results of radiotherapy, malignant melanoma was believed to be a neoplasm of low radiosensitivity. However, the use of high dose per fraction (hypofractionation) renewed interest in this treatment [7, 8].

The aim of this study is to evaluate the role of palliative radiotherapy in the treatment brain metastases of malignant melanoma of the skin.

Material and methods

Between 1990 and 2000, twenty melanoma patients (14 men, 6 women; mean age 48 years; range 27 – 76 years) with brain metastases were palliatively irradiated at the Maria Skłodowska-Curie Memorial Cancer Center and Institute of Oncology in Kraków. Mean history of melanoma was 7 months (range:1 – 24 months), and the mean Karnofsky performance status was 80% (range: 60% – 90%).

In 7 patients, the primary tumour was located on the trunk, in another 7 – on the extremities, in 4 – in the head and neck

Department of Radiation Oncology
The Maria Skłodowska-Curie Memorial Cancer Center and Institute of Oncology, branch Kraków, Poland

region, while in 2 cases the location of the primary tumour remained unknown. All our patients had brain metastases and stage IV disease, according to the UICC classification [9]. Brain metastases were the only localization of disease at the time of treatment.

In our group of 20 patients radiotherapy was the only treatment method of brain metastases, all were treated with whole brain megavoltage Co60 radiotherapy; 12 patients were irradiated with a 400cGy dose per fraction – 10 patients received a total dose of 20 Gy in 5 fractions and 2 received 40 Gy in 10 fractions. The remaining 8 patients were irradiated twice daily with a 300 cGy dose per fraction, receiving a total tumour dose of 39 Gy in 13 fractions over 8.5 days of treatment (they were not irradiated during weekends). The interval between the fractions was at least 6 hours.

During irradiation 16 patients received corticosteroids either for increased intracranial pressure or to reduce the risk of radiation-induced oedema of the brain; 14 patients received dexamethasone orally (12 mg *per die*), and 2 patients received intravenous dexamethasone (24 mg *per die*). Thirteen patients received 100 mg of Phenobarbital orally, to prevent seizures; (6 patients once daily and 7 – twice daily).

Patient survival was determined from day 1 of radiotherapy to the day of death. At the time of this analysis, all 20 patients were dead; in all cases the date of death was known. Overall survival was calculated using the Kaplan-Meier method and the chi square test was used to compare the survival rates.

Results

One patient (5%) survived two years. The curve depicting the overall survival of our patients is shown in Figure 1.

The median survival of 20 patients with brain metastases estimated from the onset of radiotherapy, was 5.5 months. Survival was longer (median of 7.5 months) in those 8 patients who were irradiated twice daily with a 300 cGy dose per fraction, as compared with the 12 patients irradiated once daily with a 400 cGy dose per fraction (median – 3 months). However, the difference is not statistically different, probably due to the small number of patients. The curves comparing the overall survival of patients irradiated twice daily and once daily are shown in Figure 2.

Radiotherapy was well tolerated, no patient developed severe acute side effects following irradiation.

All our patients eventually died of distant metastases.

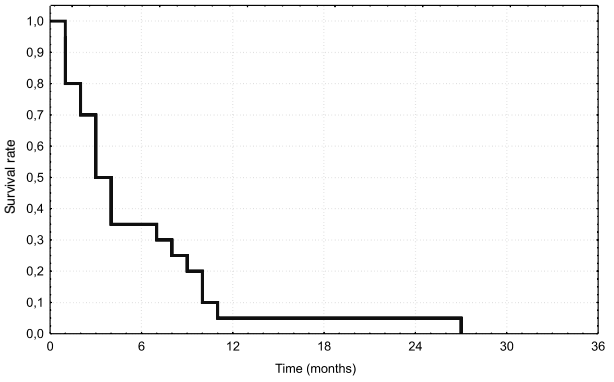

Figure 1. Overall survival in 20 patients treated with palliative radiotherapy for brain metastases of malignant melanoma

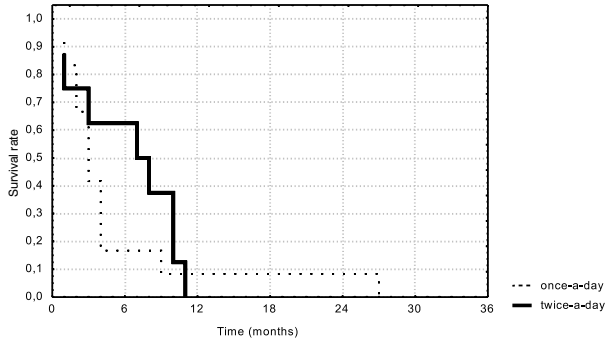

Figure 2. The survival of patients irradiated once daily vs. twice daily

Discussion

The results of therapy of melanoma cerebral metastases are poor and the choice of optimal treatment modalities remains a problem. Some authors believe that surgery combined with radiotherapy could improve treatment results [10,1 1].

Rate et al. presented results of radiotherapy for metastatic malignant melanoma to the brain and to the bones. The median survival of 77 patients with brain metastases was 14 weeks. Statistically improved survival was observed in patients who underwent subtotal or total resection of a solitary brain metastasis prior to radiotherapy (median – 36 weeks); while no improved survival was observed in patients with a solitary brain metastasis treated by radiotherapy alone (median – 16 weeks) [11].

Seegenschmiedt et al. presented their 20-year clinical experience with palliative radiotherapy in 121 patients with locally advanced, recurrent or metastatic malignant melanoma in stages UICC IIB/III/IV. The patients received a total dose of 20-66 Gy, fraction dose 2-6 Gy. Complete response was achieved in 17% of the UICC IV patients. On the last follow-up, 6% of the UICC IV patients were still alive. External beam radiotherapy provided effective palliation in malignant melanoma. The UICC staging system was an excellent prognostic factor for tumour response [12].

Ellerhost et al. presented results of whole brain irradiation in 87 patients with metastatic melanoma. The median survival of the entire populace was 19 weeks. Improved survival was noted in patients who underwent resection of all brain metastases (45 weeks) and in those with no extracranial disease (45 weeks). The authors suggest that whole brain irradiation may provide palliation for melanoma patients with brain metastases [10].

Kirova et al assessed the response rate and efficacy of palliative radiation therapy in patients with metastatic melanoma. Nine patients had brain metastases and were treated with 30 Gy of irradiation in 10 fractions or 20 Gy in 5 fractions. 57% of the patients with brain metastases had remission and good palliation of symptoms, 29% did not respond, and 1 patient showed aggravation of disease. Thus, the authors believe that short-course radiotherapy has a role to play in the palliation of metastatic melanoma [13].

It is difficult to compare the results of radiotherapy presented in literature, as the groups of patients treated in different centres are highly diversified. In our study, the overall 2-year survival of the entire group was 5%, and was similar to the results published by other authors. Patients receiving palliative radiotherapy for metastatic malignant melanoma to the brain survived 6 months. Our results suggest that radiotherapy may be effective in the palliative management of brain metastases. Better results obtained in the group of patients irradiated twice daily should be confirmed in further studies. Similarly to Rate and Ellerhost [10, 11] we have proven the efficacy of palliative radiotherapy in metastatic disease.

In all our patients, distant metastases were the ultimate cause of treatment failure. This observation is in keeping with the data of the other authors [11, 12]. Thus, it seems that the possible improvement of results is to be looked for in the new and better methods of systemic therapy.

Katarzyna Pudełek MD
Department of Radiation Oncology, Center of Oncology
Maria Skłodowska-Curie Memorial Institute,
Garncarska 11
31-115 Kraków, Poland

References

1. Skowronek J, Mackiewicz A, Żygulska-Mach H. *Czerniak złośliwy*. Poznań: Termedia Wydawnictwa Medyczne; 1998, 17-20, 63-99.
2. Zatoński W, Tyczyński J. *Nowotwory złośliwe w Polsce w 1992 roku*. Warszawa: Centrum Onkologii – Instytut w Warszawie; 1995, 58.
3. Ruka W, Towpik E (red). *Rozpoznanie kliniczne i leczenie czerniaka skóry. WHO Melanoma Programme*. Warszawa: Wydawnictwo PFESO; 1998, 11, 56-57.
4. Solan MJ, Brady LW, Binnick SA et al. Skin. Melanoma. In: Perez CA, Brady LW, *Principles and Practice of Radiation Oncology*. 3rd Edition. Philadelphia: Lippincott-Raven Publ;1998, 737-740.
5. Bishop JF. *Cancer Facts*. Amsterdam: Harwood Academic Publishers; 1999, 255-265.
6. Meder J, Fijuth J, Dańczak-Ginalska Z. Ocena wyników napromieniania chorych na czerniaka złośliwego wysokimi dawkami frakcyjnymi. *Nowotwory* 1985; 35: 42-6.
7. Overgaard J. Radiation treatment of malignant melanoma. *Int J Radiat Oncol Biol Phys* 1980; 6: 41-4.
8. Wideł M. Eksperymentalne i kliniczne aspekty radiobiologii czerniaka złośliwego. *Nowotwory* 1996; 46; 742-60.
9. Sobin LH, Wittekind Ch. *UICC TNM Classification of Malignant Tumours*. Fifth Edition. New York: Wiley and Sons, Inc. Publ.; 1997; 118-121.
10. Ellerhost J, Strom E, Nardone E et al. Whole brain irradiation for patients with metastatic melanoma: a review of 87 cases. *Int J Radiat Oncol Biol Phys* 2001; 49: 93-97.
11. Rate WR, Solin LJ, Turissi AT. Palliative radiotherapy for metastatic malignant melanoma: brain metastases, bone metastases, and spinal cord compression. *Int J Radiot Oncol Biol Phys* 1988; 15: 859-64.
12. Seegenschmiedt MH, Keilholz L, Altendorf-Hofmann A et al. Palliative radiotherapy for recurrent and metastatic malignant melanoma: prognostic factors for tumor response and long-term outcome: a 20-year experience. *Int J Radiat Oncol Biol Phys* 1999; 44: 607-18.
13. Kirova YM, Chen J, Rabarijaona LI et al. Radiotherapy as palliative treatment for metastatic melanoma. *Melanoma Res* 1999; 9: 611-3.

Paper received: 23 May 2003
Accepted: 19 August 2003