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Postoperative irradiation for adult patients with intracranial meningiomas

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Purpose. To present our own experience in postoperative irradiation of adult patients with intracranial meningioma.

Material and methods. From January 1975 to December 1995, 76 patients with intracranial meningiomas received postoperative irradiation. Conventional treatment techniques and standard doses 50-60 Gy (median dose 51 Gy) were administered.

Results. Treatment tolerance was very good. The-10 year actuarial overall survival (AOS) in the whole group was 69%. Patients with benign meningiomas (40 cases) had better prognosis in comparison to the patients with malignant variants of this tumor. 10-year AOS were 77% and 50% respectively. This difference was statistically significant ($p=0.0125$). Age and gender of patients, tumor location, and extent of surgery did not influence AOS

Conclusion. Fractionated radiation therapy appears to be an effective and well tolerated treatment in postoperative management of adult patients with intracranial meningioma.

Wyniki pooperacyjnej radioterapii dorosłych chorych na oponiaki śródczaszkowe

Cel pracy. Przedstawienie doświadczeń własnych w pooperacyjnym napromienianiu dorosłych chorych na oponiaki śródczaszkowe.

Materiał i metoda. W okresie od stycznia 1975 roku do grudnia 1995 roku, w Klinice Radioterapii Centrum Onkologii w Krakowie napromieniano pooperacyjnie 76 dorosłych chorych na oponiaki śródczaszkowe. Stosowano klasyczne techniki i frakcjonację, dawka całkowita na guz wahała się od 50 do 60 Gy (mediana 51 Gy).

Wyniki. Przy bardzo dobrej tolerancji leczenia 10-letnie aktualizowane przeżycie całkowite wyniosło 69%. W grupie 40 chorych na oponiaki łagodne odsetek 10-letnich aktualizowanych przeżyć całkowitych wyniósł 77% w porównaniu do 50% dla chorych z oponiakami złośliwymi. Różnica w przeżyciach była statystycznie znamienne ($p=0,0125$). W analizie jednowariantowej nie wykazano wartości rokowniczej wieku i płci chorych, umiejscowienia guza oraz stopnia doszczętności zabiegu operacyjnego.

Wniosek. Klasycznie frakcjonowane pooperacyjne napromienianie chorych na oponiaki śródczaszkowe jest bezpieczną i skuteczną metodą leczenia.

Key words: meningioma, radiotherapy

Słowa kluczowe: oponiaki, radioterapia

Introduction

Meningiomas constitute about 15% of all intracranial tumors in adults. They are usually benign masses that rarely invade the substance of the brain, thus potentially allowing for curative surgery. Twenty percent are anaplastic [1, 2]. Surgery is the basic treatment method, however, it should be stressed that despite the progress in microsurgery the total removal of meningioma is impossible in some cases. External beam irradiation

would seem to be beneficial for aggressive meningiomas and allows to inhibit or delay local recurrence [3-5].

The aim of this paper is to assess the value of postoperative radiotherapy in adult meningioma patients.

Material and methods

The study population was referred to the Maria Skłodowska-Curie Memorial Cancer Center in Kraków for radiation therapy from neurosurgical centres. Between January 1975 and December 1995, 76 patients with histologically confirmed diagnosis of intracranial meningioma underwent postoperative irradiation. The studied group consisted of 41 women and 35 men. The oldest patient was 66, the youngest 20 years of age.

There were 40 cases of benign and 36 of malignant meningiomas (according to the WHO classification). Patient characteristics according to histology are shown in Table I.

Table I. Patients characteristics

| Characteristics | Benign meningioma | Malignant meningioma |
|--------------------|-------------------|----------------------|
| Age (years) | | |
| 50 and less | 10 | 11 |
| More than 50 | 30 | 25 |
| Gender | | |
| Female | 21 | 20 |
| Male | 19 | 16 |
| Tumor location | | |
| Convexity | 11 | 15 |
| Falx, parasagittal | 11 | 8 |
| Other | 18 | 13 |
| Surgery | | |
| Partial resection | 38 | 27 |
| Total resection | 2 | 9 |

Radiotherapy started 4 to 10 weeks after surgery and was given with a Cobalt-60 unit.

Whole brain irradiation (19 cases of malignant meningioma treated between 1975 and 1984) was delivered by the means of two opposed lateral fields. The tumor dose of 50 Gy in 25 fractions in 5 weeks was calculated on the central axis of the treatment fields at the midplane of the skull. The treatment fields were then reduced to cover the known tumor-bearing area plus 2-3 cm of surrounding healthy brain tissue, and a 10 Gy "boost" was given in 5 fractions over 5 days. From 1985, the treatment volume covered the tumor residual with a margin of 2-3 cm, and a dose of 60 Gy in 30 fractions was given over 6 weeks.

Supportive treatment

Systemic anticonvulsants (Phenytoine or Phenobarbital) were administered to all patients during irradiation. Dexamethasone (12-20 mg/day) was given only as symptomatic medication required to control cerebral edema.

Statistical considerations

The cause-specific failure was unknown in a large proportion of patients (60%), and for this reason the overall survival was determined as the endpoint in the present series. Survival plots were generated using the Kaplan-Meier method, and then data was analyzed using the Gehan modification of the Wilcoxon rank-sum analysis for comparing arbitrarily censored samples [6, 7].

Results

The treatment was generally well tolerated. During radiotherapy, 14 patients (18%) showed improvement in neurological function, in 62 cases neurological deficits were assessed as steady. The 10-year actuarial overall survival in the entire group of 76 patients was 69% (Figure 1). The Kaplan-Meier survival curves according to histology are presented in Figure 2.

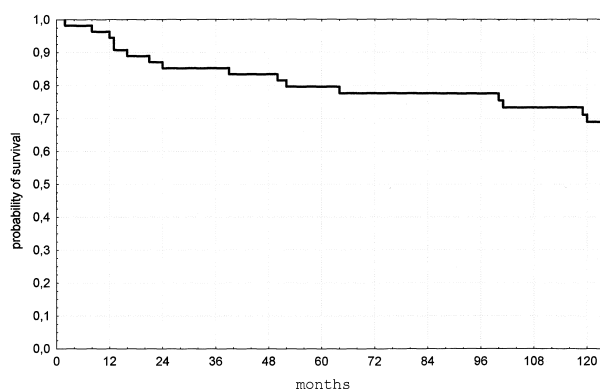


Figure 1. Actuarial overall survival of 76 patients

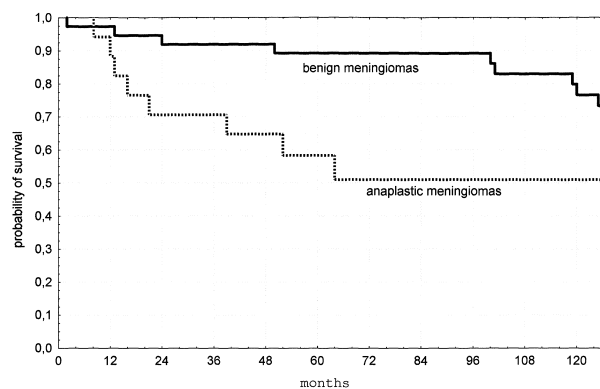


Figure 2. Actuarial overall survival according to the histology

The 10-year actuarial overall survival for patients with benign and malignant variants of meningioma was 77% and 50%, respectively (two-tailed Gehan P-value = 0.0125).

The age and gender of patients, tumor location and the extent of surgery was not a prognostic factor for survival.

Discussion and conclusions

Our observations of clinical population features of adult patients with intracranial meningiomas are similar to those reported by other authors. The majority of patients were in the fifth and sixth decade of age, and the most common site of tumor is brain convexity [1, 2, 8]. The high ratio (47%) of malignant forms is interesting. In this respect, our group resembles the series from the Maria Skłodowska-Curie Memorial Cancer Center in Warsaw, where the reported ratio of malignant tumors was 43% [9]. It suggests a similar selection of patients resulting from similar indications for adjuvant irradiation in meningioma patients. In other reports, malignant meningiomas do not exceed 25% [10-12].

In the present series 5- and 10-year actuarial overall survival rates were 80% and 69%, respectively. Our results are comparable with observations of Bataini from Institute Curie (Paris) [13]. An interesting study from another French center (CHU Bordeaux) of 91 meningioma patients treated with radiotherapy was reported

by Maire et al. Contemporary techniques were used, a median dose of 52 Gy was given and the 5- and 10-year survival rates were 71% and 40%, respectively [14].

Univariate analysis of our results demonstrates that malignant histology is an important adverse prognostic factor for survival. All published reports have shown poor treatment outcomes in patients with malignant (anaplastic) meningioma. These tumors widely infiltrate adjacent tissues, and recur early following even "complete" surgical excision and after adequate contemporary radiotherapy [10, 13, 15]. These observations are confirmed by the National Cancer Data Base (NCDB) report, covering the population of over 9000 patients with meningioma treated in USA in the years 1985 – 1992. The overall 10-year survival rates for patients with benign and malignant meningioma were 70% and 51%, respectively [16]. An important study was published by Milosevic from the Princess Margaret Hospital (Toronto) covering the treatment outcomes in 59 patients, including 42 (71%) with malignant and 17 with atypical meningioma. The 5-year actuarial overall and disease-specific survival (DSS) was 28% and 34%, respectively. In multivariate analysis, age below 58 years and a radiation dose higher than 50 Gy were independent prognostic factors associated with higher DSS [17].

In this analysis, patient age was found not to be a prognostic factor for survival, contrary to other authors. The Kepka et al. series, with pathoclinical characteristics resembling our material, age over 50 years had a negative effect on prognosis [9]. Authors from the NCDB have also confirmed the role of age in the outcome of patients with meningioma. The actuarial 10-year survival rates were 50% and 81%, respectively for patients at ages above and below 60 years of age [16]. Similar observations were reported by Goldsmith and Leibel [10, 18].

We found no relationship between tumor location and patient outcome, nevertheless one should mention the opinion of Ayerbe et al. on the adverse influence on prognosis in case of tumors located on the cerebral convexity [2, 13, 15, 16].

In the present study, the extent of surgery (total vs partial resection) did not result in significant differences in survival. The prognostic value of this therapeutic factor is a point of controversial reports in the literature, probably resulting from subjective assessments of resection. Kepka et al. compare the results obtained in two groups: patients with total tumor removal vs. patients with subtotal, partial resections or biopsies. 5-year survival rates were 75% and 54%, respectively ($p=0.06$). Separate assessment of results according to tumor histology (benign vs, anaplastic) results in pronouncing the extent of surgery to be not of prognostic value [9].

Primary treatment in the management of meningioma is surgery, with radiotherapy as an important postoperative measure in selected patients with malignant histology, or after incomplete resection. Salazar has combined several studies and found a 58% recurrence rate following gross total resection and a 90% recurrence rate following subtotal resection of malignant menin-

giomas, which fell to 36% and 41%, respectively when surgery was followed by external beam irradiation [19]. Barbaro et al. has shown, that 60% of no irradiated patients suffered recurrence, as compared to 32% of those who had received radiation therapy [8]. Taylor found an incidence of recurrence of 49% in patients receiving postoperative irradiation vs 81% when no radiotherapy was performed after subtotal resection [12]. Mirabell et al. have presented similar findings [20]. An interesting study on malignant meningioma was published by the Baylor College of Medicine in Houston. The 5-year actuarial disease-free survival was 39% in patients with complete resection, whereas none of the patients after incomplete resection survived five years. Postoperative radiotherapy as a planned part of the initial treatment increased the 5-year survival from 15% to 80% ($p=0.002$) [21].

Our results compare favorably with previously published reports. External fractionated radiotherapy is well tolerated, the recommended radiation dose and target volume average at least 60 Gy with the 2-3 cm margin. The effectiveness of higher radiation doses must be weighted against possible complications, especially in patients with benign meningioma, because of the long survival of patients and a potential risk of radio-necrosis.

Based on the published data and the experience at our Institution we suggest that patients with malignant meningiomas should undergo postoperative irradiation.

The role of radiotherapy in the treatment of benign meningiomas after subtotal resection is still debated, should irradiation be given postoperatively or at the time of progression? Prospective randomized multicenter trials would be required to clear these issues.

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