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Sarcoma Metastatic to the Brain: Results of Surgical Treatment [Clinical Study]

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ABSTRACT TOP

WE REPORT ON 21 patients surgically treated for intraparenchymal brain metastasis from sarcoma, including six osteosarcomas, four leiomyosarcomas, three malignant fibrous histiocytomas, two alveolar soft-part sarcomas, two Ewing's bone sarcomas, one extraskeletal osteosarcoma, one extraskeletal Ewing's sarcoma, and two unclassified sarcomas. Median survival after craniotomy was 11.8 months. Patients with a preoperative Karnofsky performance score of > 70 survived for 15.7 versus 6.6 months for those with a Karnofsky performance score ≤ 70. Patients undergoing complete resection survived 14.0 versus 6.2 months for patients undergoing incomplete resection. Patients with evidence of lung metastases at the time of surgery survived 11.8 months, which was similar to the 10.5-month survival for patients with disease limited to the brain. The two patients with alveolar soft-part sarcoma are alive at 16 and 25 months after surgery. We conclude that surgery is effective in treating selected patients with sarcoma metastatic to the brain and that patients with metastasis from alveolar soft-part sarcoma may have a relatively good prognosis if they are surgically treated. The complete removal of all brain metastases and a Karnofsky performance score > 70 are associated with a favorable prognosis, whereas the presence of concurrent lung metastases is not a contraindication to surgery.

Article Outline

Figures/Tables

Brain metastasis is a common complication of systemic cancer, with 15 to 20% of all patients dying of cancer developing brain metastases 2,4. Brain metastasis from sarcoma is a rare event. Overall, 1 to 8% of patients with sarcoma of various histologies develop intraparenchymal brain metastases 3,7,13,22,24,37,44. The only exception is in patients with alveolar soft-part sarcoma (ASPS) in whom the incidence is 33% 27. Use of chemotherapy is thought to increase the incidence of brain metastasis secondary to improving systemic control of the disease and to failure of many chemotherapeutic agents to cross the blood-brain barrier 13,15,16. Nevertheless, brain metastasis from sarcoma is rare and, as a result, there is no report in the literature of the results of treatment in a series of patients.

PATIENTS AND METHODS TOP

Twenty-one patients underwent surgical treatment for brain metastasis from sarcoma between January 1, 1980 and December 31, 1992. We present six patients with osteosarcoma, four with leiomyosarcoma, three with malignant fibrous histiocytoma, two with ASPS, two with Ewing's bone sarcomas, one with extraskeletal osteosarcoma, one with extraskeletal Ewing's sarcoma, and two with unclassified sarcomas. Histology for all patients was verified at M. D. Anderson Cancer Center. Only patients with parenchymal metastases were included in this report. Patients with bone or dural metastases were excluded.

The goal of all surgical procedures was gross total excision. Complete removal was defined as removal of all known lesions in the brain, whether single or multiple. Patients were considered to have undergone incomplete resection if they had multiple lesions with one or more lesions remaining unresected after surgery. Cause of death was classified as follows: patients who died with stable systemic disease and advancing neurological disease because of brain metastasis were labeled neurological deaths, patients with stable neurological function and advancing systemic disease were labeled systemic deaths, and patients with progressing neurological and systemic disease were labeled combined deaths.

Whole-brain radiation therapy (WBRT) for patients consisted of 30 Gy in 10 fractions given over 2 weeks, except for patient 13 who received preoperative WBRT of three fractions at 375 cGy each and postoperative WBRT of 30 Gy in 12 fractions. Patients 10, 13, and 18 underwent resection of two lesions each. In each instance, two craniotomies were performed in the same operation.

Karnofsky performance score (KPS) was determined by immediate preoperative neurological examination. Three responses to surgery were defined. Patients were considered: 1) to have improved if the KPS improved within 30 days of surgery; 2) to have stabilized if within 30 days of surgery the KPS neither improved nor worsened; or 3) to have worsened if the KPS declined from preoperative levels 30 days after surgery. Operative mortality was defined as death from any cause within 30 days of craniotomy.

Survival curves were drawn using the Kaplan-Meier product-limit method 21. The Cox-Mantel log-rank test was used to evaluate the differences between two or more survival curves 9. Because of the small number of patients available for this study, there may have been insufficient statistical power to detect important differences in survival to a *P* value less than 0.05.

RESULTS TOP

Patient characteristics before craniotomy are shown in Table 1. Median age at the time of the initial diagnosis of cancer was 28 years. Median time from the initial diagnosis of cancer to diagnosis of brain metastasis was 17 months (range, 0-124 months). Median preoperative KPS was 80 (range, 50-100). Six patients (29%) had multiple brain metastases at the time of surgery. All patients received systemic chemotherapy before brain metastases developed, except patient 20 who presented with brain metastasis.

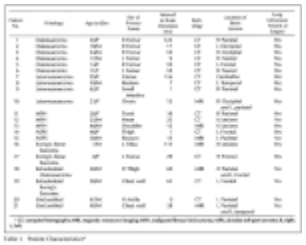
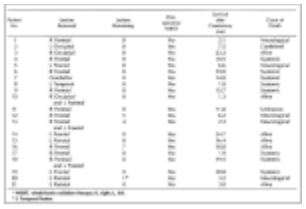


Table 1. Patient Characteristics[a]

Median survival after the initial diagnosis of cancer was 29 months. The results of surgery for brain metastases are shown in Table 2. After craniotomy, median survival for all patients was 11.8 months (Fig. 1). Six-, 12-, and 24-month survival rates were 75, 47, and 28%, respectively. There were no 5-year survivors although six patients were alive at the end of the study, the longest with a 24.7-month survival. Patients with a preoperative KPS > 70 survived 15.7 months versus 6.6 months for those with a KPS ≤ 70 (*P* = 0.13) (Fig. 2). Patients in whom all lesions were removed survived 14.0 months, whereas patients who had one or more known lesions remaining after surgery survived 6.2 months (Fig. 3). Patients with concurrent lung metastases at the time of surgery survived 11.8 months, which was similar to the 10.5-month survival of patients with disease limited to the brain (*P* = 0.43) (Fig. 4). No patient had evidence of systemic metastasis in any location other than the lungs. Survival of patients with soft-tissue sarcomas was also similar to that of patients with osseous sarcomas (11.8 versus 10.5 months; *P* = 0.60).

Table 2. Results of Surgery[a]



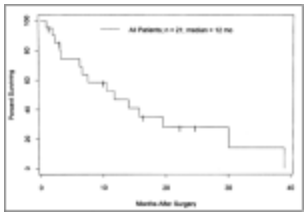


Figure 1. Survival of all patients with surgically treated sarcoma metastatic to the brain.

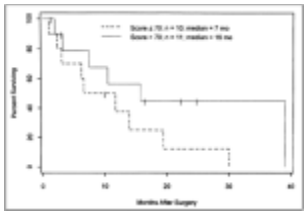


Figure 2. Survival of patients with preoperative Karnofsky performance score (KPS) > 70 versus those with KPS ≤ 70. Patients with a higher score tended to survive longer (*P* = 0.13).

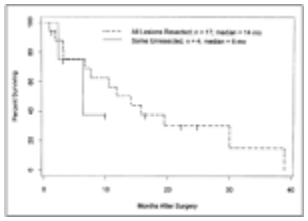


Figure 3. Survival of patients undergoing removal of all known lesions versus those with one or more known lesions unresected.

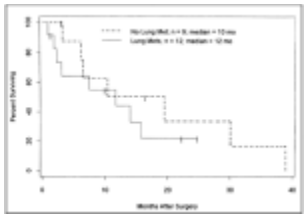
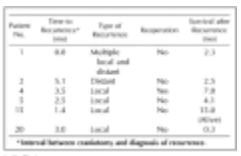


Figure 4. Survival of patients with concurrent lung metastases versus those without lung metastases at the time of craniotomy. No patient had systemic metastases in any location other than the lungs. This difference was not significant (*P* = 0.43).

Of the 15 patients who died, five (33%) died of neurological causes alone, eight (53%) of systemic disease alone, and one (7%) of both neurological and systemic disease. One (7%) patient died of unknown causes, and six patients were alive at last follow-up.

Recurrence of disease in the brain is detailed in Table 3. Overall, tumors recurred in six patients, four of whom had osteosarcoma. One patient (patient 4) underwent reoperation for a recurrent tumor. He survived 7.0 months more, and disease did not recur again in the brain; however, the patient died of widespread systemic metastases. Median survival after recurrence for the five patients not undergoing reoperation was 2.5 months. There was no significant reduction in the recurrence rate among patients who received postoperative WBRT versus those who did not (*P* = 0.77).

Table 3. Recurrence in the Brain



Response to surgery was as follows: 13 (65%) symptomatic patients improved postoperatively and 7 (35%) remained neurologically stable. No patient had progressive worsening of symptoms. One patient was asymptomatic pre- and postoperatively. One patient died 29 days after surgery.

DISCUSSION TOP

This study is the first to analyze the results of treatment for a series of patients with brain metastases from sarcoma. Our data suggest that preoperative KPS is an important prognostic indicator for such patients. Patients undergoing removal of all known lesions also tended to survive longer. Surprisingly, patients with concurrent lung metastases did no worse than patients with no evidence of systemic disease. Therefore, the presence of lung metastases is not a contraindication to surgery in patients with sarcoma.

Multiple brain metastases TOP

Our study includes six patients with multiple brain metastases who were treated with surgery. Until recently, the presence of multiple lesions was considered a contraindication to surgery. We recently reported on the results of surgery in patients with multiple brain metastases of various histologies 5. That study indicates that patients with multiple metastases who undergo removal of all lesions have a similar prognosis to patients undergoing surgery for a single brain metastasis, whereas patients who do not have all lesions removed have a significantly poorer prognosis. In this study, there was a large difference in the median survival between patients who underwent removal of all known lesions and those who did not.

Literature review TOP

Many rare histological types of sarcoma metastatic to the brain are included in this report. Patient 19 is the first reported case of brain metastasis from extraskeletal Ewing's sarcoma. Patient 18 is the second reported case of brain metastasis from extraskeletal osteosarcoma 39. Patient 12 is the third reported case with brain metastasis from malignant fibrous histiocytoma of the heart 20,40. A review of the literature for the histological types of sarcoma metastatic to the brain parenchyma reported in our series is summarized in Table 4.

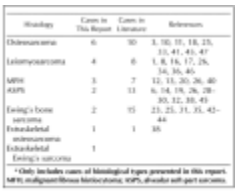


Table 4. Literature Review of Pathologically Verified Cases of Brain Metastasis from Sarcoma[a]

Prognosis of surgically treated alveolar soft-part sarcoma TOP

Seven cases of surgically treated brain metastasis from ASPS are reported in the literature 6,26,29,30,32,38,45. One of these does not provide follow-up data 38. The remaining six cases from the literature, plus our two cases of brain metastases from ASPS, are shown in Table 5. Only two of these eight patients have died, both of whom were treated in the 1950s. All the others have follow-ups ranging from 12 months to 5 years. These survival data are strikingly different from the expected survival of patients undergoing craniotomy for brain metastasis of other histologies 4. These data suggest that aggressive surgical resection of brain metastases should be performed in patients with ASPS and can result in a particularly favorable prognosis. This can be explained biologically by the slow-growing, indolent nature of this disease 28. We recommend aggressive removal of all accessible brain metastases in patients with ASPS who are not terminally ill.

Table 5. Cases of Surgically Treated Alveolar Soft-Part Sarcoma

CONCLUSION TOP

We conclude that surgery is effective in treating selected patients with sarcoma metastatic to the brain and that patients with metastasis from ASPS may have a relatively good prognosis if they are surgically treated. The removal of all known brain metastases and a KPS > 70 are associated with a favorable prognosis, and the presence of concurrent lung metastases is not a contraindication to surgery.

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