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Title: Sarcomatous brain metastases; Recent University of Florida Experience

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Abstract:

**Background:**

Brain metastases occurring in patients with sarcoma are rare and are not routinely screened for. Their development portends a poor prognosis with published survival ranging from 1.67 to 9.8 months after diagnosis<sup>1-5</sup>. Some studies advocate for aggressive management of patients, while others have demonstrated uniformly poor outcomes. The paucity of literature regarding management of such patients makes deciding on morbid interventions difficult. The purpose of this study is to describe the recent University of Florida experience of managing the unique subset of sarcoma patients and their outcomes.

**Questions/Purposes:**

We sought to characterize this unique subset of patients with metastatic sarcoma specifically with regard to patient factors, disease factors, treatment, and the time course of their disease from initial diagnosis.

**Patients and Methods:**

This descriptive study is a retrospective case series. The prospectively collected musculoskeletal oncology database of the University of Florida was queried to identify patients who had been treated for bone or soft tissue sarcoma and who developed brain metastasis. We identified 11 patients (8 males and 3 females) managed from 2000 to 2015 who had been followed up for a mean of a 51.9 months ( $\pm 23.2$ ) from the time of initial diagnosis to death or time of last follow up. We the evaluated this patient population with regard to a variety of disease and treatment related characteristics.

**Results:**

The 11 patients had the primary diagnoses of high grade sarcoma; osteosarcoma (4), undifferentiated pleomorphic sarcoma (3), leiomyosarcoma of bone, myxofibrosarcoma, spindle cell sarcoma, and neurofibrosarcoma. 6 of the 11 patients with soft tissue sarcoma were managed with radiotherapy and wide local excision for their primary. All 4 patients with the diagnosis of osteosarcoma were treated with chemotherapy and wide resection of the tumor. One patient who had widespread metastatic disease when referred to the surgical oncologist received only palliative radiotherapy to the primary sarcoma. Patients were diagnosed at a mean age of 52 years ( $\pm 19.9$ ) for their primary sarcoma, and with brain metastasis at a mean interval of 45.8 months ( $\pm 56.9$ ). The presentation of the brain metastasis included hemiparesis, headaches, visual disturbances, and nausea.

Features of the metastasis was as follows; cerebellar (2), dural-based (4), and parenchymal (5). 3 of 11 patients had been managed for local recurrence. All 11 patients developed metastases at other sites (bone and/or lung), with 2 of the patients having other metastases when first diagnosed. Treatment included whole brain radiotherapy, chemotherapy, radioisotopes, radiosurgery and resection (Table 1). The median duration from diagnosis of brain metastasis to death was 80 days. The two patients surviving at last follow-up were at 13.8 and 29.6 months from diagnosis of their brain metastasis. Both of them had cerebellar metastases. The longest surviving study subject was managed with resection of gross tumor and adjuvant radiosurgery (AWD at 29.6 months), while the other patient had been managed with radium and several radiosurgery treatments (AWD at 13.8 months).

### **Conclusions:**

Patients treated for sarcoma who develop brain metastasis do very poorly; with most patients succumbing soon after diagnosis. Mean survival after diagnosis of brain metastasis was 2.7 months in the 9 of 11 patients who succumbed to disease. All patients in the study had also suffered from metastatic disease at other sites. Interesting findings included a patient who developed brain and lung metastases 17 years after management of his primary, and a long term survivor alive at 29.6 months after diagnosis and treatment of brain metastasis. Our study is limited by the size of the series, a limitation inherent to the study of this uncommon event, as well as by the inclusion only of sarcomas arising from extremities and pelvis. Our study supports formal radiological evaluation for brain metastasis in patients with sarcoma with neurologic symptoms and with disease metastatic to other sites.

Table 1: Summary of patient characteristics

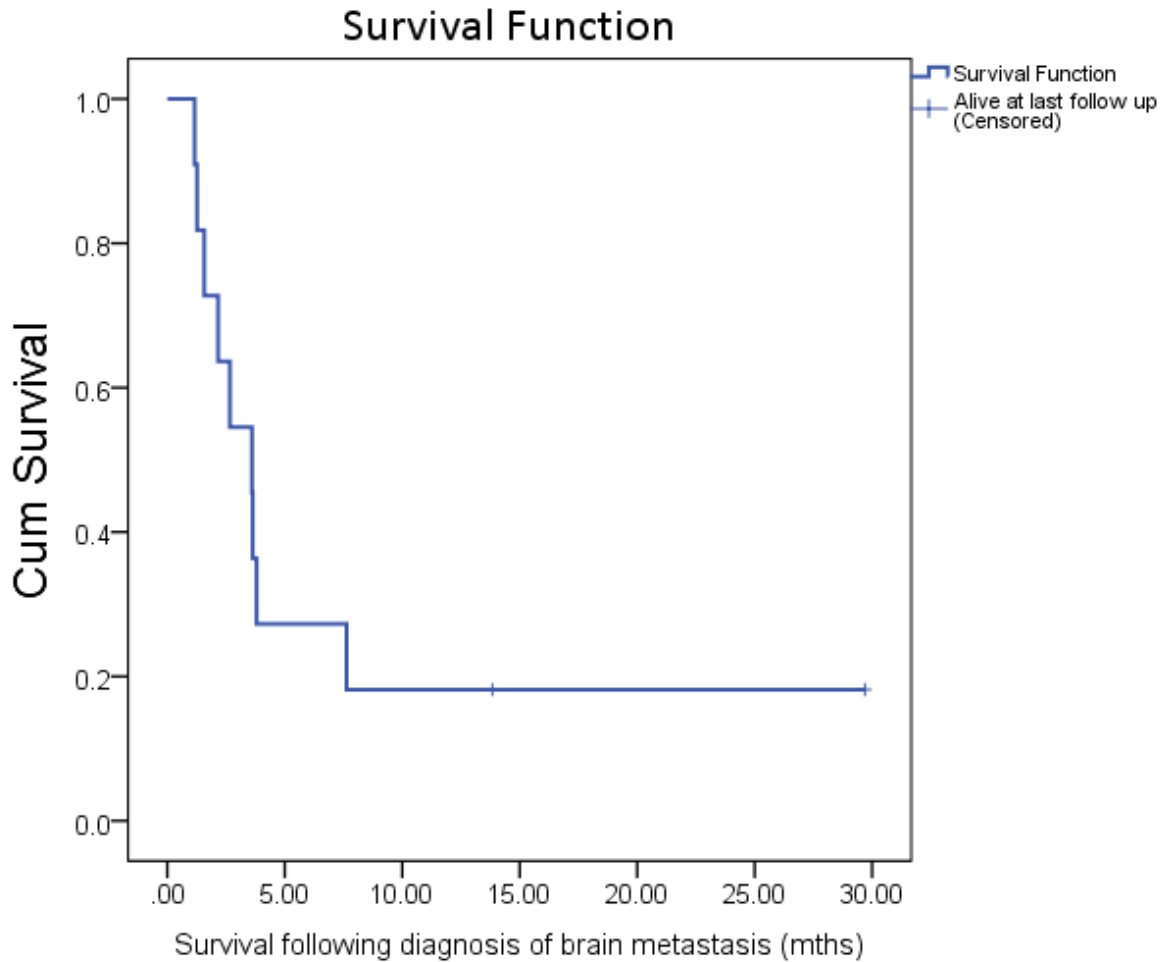
Case #	Primary Sarcoma diagnosis	Site of disease	Age at diagnosis (y)	Gender (M/F)	Treatment of primary	Presentation of brain met	Interval to brain met (m)	Location of brain met	Management of brain met	Local recurrence?	Location of other metastasis	Interval to other met (m)	Interval from other met to brain met (m)	Duration of f/u (m)	Survival following diagnosis of brain met (m)	Survival following initial diagnosis (m)
1	UPS	Right shoulder (around coracoid)	51	M	RT, WLE	Headache and imbalance	53	Right cerebellum	Gross total resection & SRS	No	Lung / Right posterior diaphragm	14	39	80	Alive at 29.6 m	AWD at 77 m
2	UPS	Left anterior thigh	56	M	RT, WLE	Nausea and vomiting	19	Right frontal lobe, involving pre-central gyrus	3D-CRT	Yes	Lung	9	10	20	1.2	13
3	Leiomyosarcoma of bone	Right distal femur	56	M	CTX, WLE	Headache, Orbital pain	31	Intracranial	Whole brain RT	No	Bone (T8 10, 11, L1,2, Ilium) / Bilateral lungs	9	22	38	7.6	38
4	Osteosarcoma; Fibroblastic	Left distal femur	18	M	CTX, WLE	Nausea and vomiting	44	Right temporal lobe (Dural-based)	SRS	No	Lung / Right distal femur	17	27	47	2.2	47
5	Osteosarcoma; Chondroblastic	Left distal femur	68	F	CTX, WLE	Blurred vision	9	Bilateral frontal lobes (Dural-based)	Pazopanib, Sirolimus	No	Bilateral lung / Bone (Left prox hum, glenoid, proximal femora)	0	9	10	1.6	10
6	UPS	Right posterior thigh	56	F	RT, WLE	Orbital pain and proptosis	52	Right frontal lobe (Dural-based)	RT	No	Lung / Bone	12	40	53	1.3	53
7	Osteosarcoma; telangiectatic	Right distal femur	78	M	CTX, WLE	Left hemiparesis and headaches	21	Right frontal lobe (Dural-based)	Gross total resection	Yes	Lung	15	6	25	3.8	25
8	Myxofibrosarcoma	Left posterior thigh	67	M	RT, WLE	Left hemiparesis	10	Right parietal lobe	SRS	No	Lung	4	6	12	3.6	13
9	Spindle cell sarcoma	Left navicular	55	F	Palliative RT	Headache and nausea	7	Right occipital lobe. Bilateral frontal lobes	Whole brain RT	No	Lung / Left inguinal node	0	7	11	3.6	11
10	MPNST in setting of NF1	Left buttock (arising from sciatic nerve)	55	M	RT, WLE	Right sided weakness, and sensory aphasia	49	Left parieto-occipital lobe	Gross total resection & Whole brain RT	Yes	Lung	44	5	52	2.7	52
11	Osteosarcoma	Left distal femur	12	M	CTX, WLE	No symptoms. Noted on Tc-99 bone scan	209	Bilateral cerebellar hemispheres (left then right), Bilateral frontal lobes	Radium radioisotope. SRS	No	Bone (Ischium) / Lung	209	0	223	Alive at 13.8 m	AWD at 223 m

All sarcomas were High-grade

Abbreviations:

CTX: Chemotherapy. WLE: Wide Local Excision. RT: Radiotherapy. SRS: Stereotactic radiosurgery. 3D-CRT: 3D Conformal RT. IMRT: Intensity Modulated RT. AWD: Alive with disease.

Figure 1: Kaplan-Meier Survival plot: Time of diagnosis of brain metastasis to death/last follow-up



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