Case Series

Stereotactic Radiosurgery in the Treatment of Sarcoma Brain Metastasis

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Abstract

CNS metastases from systemic sarcoma are exceedingly rare and difficult to treat, as the lesions appear late in the course of the disease. The situation is even more complicated by the fact that sarcoma is considered a radioresistant tumor of mesenchymal origin. Adjuvant CyberKnife radiosurgery (CKSRS) as a treatment option has not been described in the management of secondary central nervous system involvement from systemic sarcoma, but can offer good local control and increased progression free survival without interfering with the need of ongoing systemic therapy. We therefore report our experience of 4 lesions in 2 patients treated with CKSRS in this setting.

Clinical Presentation:

Case A: While undergoing adjuvant radiation for a pulmonary artery sarcoma, patient A presented with a generalized seizure. A right 2cm frontoparietal lesion was identified and resection was performed. The patient was subsequently treated electively with CKSRS. Serial MRI demonstrated a significant decrease in size in the treated lesion with no evidence of residual or recurrent disease at 30 months. The patient remains clinically stable since the time of radiosurgery.

Case B: A 60-year-old woman with a history of metastatic chondroblastic osteosarcoma complained of new onset of headaches combined with a right visual field cut and anomia. Two separate lesions were identified on MRI and a open resection was performed on the larger of the lesions. Postoperative CKSRS was performed subsequently to the resection cavity and a second native lesion. Effective local tumor control was seen after treatment. A delayed recurrence of the resected lesion was retreated at 5 months. Repeat CKSRS was required for this lesion and third out-of-field lesion at 5-months after the initial CKSRS. The CNS sites remained well controlled until the patient succumbed due to systemic disease progression 19 months after initial treatment.

Conclusion: Based on this report and available information in the literature, CyberKnife radiosurgery appears to be a suitable approach for patients with secondary central nervous system involvement from systemic sarcoma.

INTRODUCTION

Sarcomas account for about 0.7% of all systemic cancers. Once clinically diagnosed, secondary central nervous system involvement from systemic sarcoma is an extremely rare event, occurring in only 1 to 8% of various subtypes of sarcoma in unselected autopsy reports [1]. An increased use of radiation therapy and systemic chemotherapy have led to some improved outcome, though these treatment regimen seem to be more suitable and effective for systemic disease control but remain rather ineffective in cases of brain metastasis [2,3].

The prognosis of patients with brain metastases is dismal, showing a mean survival of 1-2 months in untreated patients. Overall median survival has increased to only 4-5 months with therapy [4]. Due to its rarity and its usually late presentation in the course of systemic disease, the best CNS treatment still remains unclear. Resection remains a mainstay of surgical management but the decision what modality to choose and when to treat remains under debate. Though SRS is intuitively suitable in this setting, to our knowledge CyberKnife radiosurgery (CKSRS) as an increasingly available and effective treatment option has not been reported in the management of intracranial sarcoma metastasis in the primary or adjuvant setting. Here, we report the successful CKSRS treatment of 5 lesions in 2 patients harboring intracranial sarcoma metastasis.

CASE SERIES

Case A

A 65-year-old man underwent a right parietal craniotomy in 2011 for resection of a symptomatic brain metastasis from a recently diagnosed lung lesion which was identified and treated as a high grade intimal sarcoma of the pulmonary artery. At the time of his initial hospitalization, he presented with acute left facial numbness and left hand clumsiness in the setting of a generalized seizure.
His past medical history included prostatectomy due to early stage prostate cancer in 2009 and a recent pneumonectomy due to the pulmonary artery sarcoma. He was simultaneously being treated via adjuvant involved field radiation to the mediastinum. Chemotherapy was not performed.

Standard MRI of the brain showed a ca. 22mm right sided contrast medium enhancing, hemorrhagic intra-axial mass centered within the right parietal lobe (Figure 1).

Preoperative steroids were given because significant vasogenic edema was noted on MRI. This greatly and rapidly improved his symptoms and mental status. Due to the profound and symptomatic edema, image guided open microscopic resection of the lesion was performed and the histopathology was consistent with a pulmonary artery sarcoma with brain invasion (Figure 2,3).

The patient underwent adjuvant post resection cavity radiation to the resection cavity via CKSRS two weeks after surgical intervention. SRS target volume was delineated at 14.18cc and he was planned with a prescription dose of 2400 cGy to be given in 3 fractions of 800 cGy to the 75% isodose line (Figure 4).

At the time of CKSRS the patient had a nonfocal postoperative neurological examination, including a negative Romberg test. His Karnofsky score was 80.

Serial MRI scans post-CKSRS demonstrated no further contrast enhancement and a significant decrease in the volume of the radiosurgically treated tumor area. The most recent follow-up MRI at 30 months post SRS remained unchanged from his 6-months postop imaging. No out-of-field recurrences have been observed in this patient during his follow-up and he remains clinically stable since the time of his radiosurgery.

**Case B**

A 60- year old woman with a history of metastatic chondroblastic osteosarcoma originating in the left femur complained of new onset of headaches combined with a right visual field cut and anemia.

MRI was performed and revealed two intracranial lesions: a ca. 17 mm left occipital lesion inside a ca. 4cm hemorrhagic focus and a second ca. 5 mm left subinsular region ring-enhancing mass, both suspicious for metastasis (Figure 5).

Of note, parenchymal focal extension of subarachnoid and subdural hemorrhage in the left occipital region could be seen and remained stable on sequential scans.

A gross total open microscopic resection of the left-sided hemorrhagic occipital intraaxial lesion was performed and was histopathologically diagnosed as malignant spindle cell tumor consistent with her primary sarcoma (Figure 6).

The patient then opted for postoperative adjuvant stereotactic CyberKnife radiation therapy to treat both areas. A prescription dose of 2400cGy was given to the left occipital resection cavity (Volume 9.74cc) in 3 fractions of 800cGy each to the 76% isodose line. A single fraction treatment of 2000cGy to the left subinsular lesion (Volume: 2.52cc) was delivered to the 75% isodose line during the same setting (Figure 7).

Initially, the patient did exquisitely well postinterventionally. However, follow up films revealed a 2.5 cm intracranial marginal recurrence just superior to the resection cavity of the previously treated occipital lesion at about 5 months after the index surgery (Figure 8).
Figure 3 There was patchy positivity for CD31 (A) and keratin cocktail (B). C: Representative section of the brain metastasis showing a hypercellular tumor sharply circumscribed from surrounding brain parenchyma. D: High power view of the brain metastasis showing a similar morphological appearance to the pulmonary artery intimal sarcoma (compare with "Figure 2B") (A, B: immunohistochemical stains for CD31 and pancytokeratin cocktail, respectively – 10X objective. C-D: Hematoxylin and eosin, C: 5X, D: 20X objective).

Figure 4 A CyberKnife’s treatment planning software can be seen which was used to determine the size of the area that should be targeted by radiation and the radiation dose. The optimal radiation delivery plan for treatment was calculated showing a prescription dose of 2400 cGy to the 75% isodose line.

Given her stable systemic disease at that time, we recommended a re-resection and a second round of focal CKSRS. The patient was consented and taken to the OR for elective surgery. She tolerated the second procedure very well and was discharged to home on the fourth postoperative day. Postoperative radiation was performed 16 days after surgery to the new resection cavity (Volume 19.06cc) with a dose of 2400cGy in 3 fractions to the 75% isodose line as well as a small new lesion in the left frontal lobe (Volume: 1.51cc), which received 1600 cGy to the 61% isodose line (Figure 9).

The patient remained stable since the CKSRS at these sites on follow up scans over the course of her remaining life and she passed away 19 months after the initial treatment of her CNS disease.

**DISCUSSION**

Brain metastases from systemic sarcoma are an uncommon problem. These metastatic deposits usually occur late during the course of the disease - most likely when these patients harbor concurrent pulmonary metastasis [5]. CNS disease is rarely the site of primary presentation or of a relapse [6]. The site and number of tumor metastasis are important factors affecting prognosis [7].

A mean survival of only 1-2 months is expected if the patient
Figure 5 MRI revealed two intracranial lesions: (A) a 5 mm left subinsular region ring-enhancing mass and a (B-D) 17 mm left occipital lesion inside a 4 cm hemorrhagic focus.

Figure 6 Showing the histopathologically diagnosed as malignant spindle cell tumor consistent with her primary sarcoma.
remains untreated. The overall median survival may increase to 4-5 months with therapy [4]. Prophylactic treatment of sarcoma metastases to the brain has been considered by several authors and Metha and colleagues as well as Marsa and colleagues have suggested whole-brain radiation therapy at the time of initial chemotherapy [8]. However, Gercovich and colleagues [2] as well as Espana and colleagues [9] noted the frequent co-occurrence of brain and lung metastases but suggested to defer prophylaxis until lung metastases appear.

Though surgery and radiotherapy are the favored modes
of therapy, treatment of metastatic sarcoma to the brain is complicated by its relative radioresistance and the frequently encountered chemoresistance of sarcoma cells [3].

Therefore, surgical excision remains a mainstay of treatment as long as the patient has a good performance status. If surgery is performed, the establishment of tumor-free margins remains critical in the prevention of local recurrence. However, due to the highly aggressive and infiltrative nature of this tumor type, negative surgical margins are often difficult to achieve (see our patient B).

GammaKnife radiosurgery has been reported in the past as a primary adjuvant treatment after neurosurgical excision and CKRS treatment has been generally reported as well-tolerated and initially effective in the management of a few patients with sarcomatous intracranial metastases [10]. However, even after successful initial treatment, many patients, including those who received additional fractionated whole-brain radiotherapy, developed progressive new brain disease [10].

In the study of Joshua and colleagues, mean survival post GKRS was about 8 months leading the authors to the conclusion that the patients overall disease and health status play a more critical role in the life expectancy of cancer patients with secondary central nervous system involvement from systemic sarcoma [11] which is an observation also reflected in the RPA (Recursive Partitioning Analysis) of other intracranial metastasis as revealed in the classic RTOG (Radiation Therapy Oncology Group) trials [12].

Recently, Otani et al. [2013] published the case of a 41-year-old woman diagnosed with intracranial metastatic synovial sarcoma receiving CyberKnife radiosurgery after surgical resection, which lead to resolution of her neurological deficits [13].

We also opted for CyberKnife SRS in our 2 patients. The radiosurgical target volumes were contoured in detail on fused MR/CT images and were measured at 2.52cc and 1.51cc for the two lesions treated with primary SRS treatment and 14.18cc, 9.74cc and 19.06cc respectively in our post resection cavity lesions treated with SRS. The prescription doses were 2000cGy and 1600cGy for lesions undergoing primary SRS and 2400cGy for the respective post resection cavities. These prescription doses were selected based upon tumor location and volume.

Bindal et al. showed that a Karnofsky score greater than 70 is associated with a more favorable prognosis [14] and a significant
improvement of 20 points could be achieved in our patients following CyberKnife SRS therapy. We do realize that the achieved results in these two patients appear very good and exceed the previously reported expected course. Further studies are therefore necessary to validate this treatment modality and its applicability in more detail.

CONCLUSION

Well-selected patients with brain metastases from radioresistant primary tumors who undergo SRS (stereotactic radiosurgery) may survive longer than historical controls undergoing whole brain radiotherapy only. CKSRS therefore appears to be a potentially more effective treatment option in this setting. Repeat radiosurgical treatments may also be feasible for patients presenting with focal tumor recurrences in the setting of controlled systemic disease, but this indication requires great caution with respect to the biological effects of the accumulated dose on adjacent critical structures and the induction of possible radiation necrosis in areas receiving overlapping high dose treatment. However, given the overall dismal prognosis of this patient population and the lack of any other suitable alternatives, further studies are required to elucidate the risk and benefits of SRS in this patient population.

REFERENCES


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