24

Gamma Knife Radiosurgery After Stereotactic Aspiration for Large Cystic Brain Metastases

Do Hoon Kwon and Won Hyoung Park
Department of Neurological Surgery
Asan Medical Center, College of Medicine, Univ. of Ulsan, Seoul, Korea

1. Introduction

Large cystic metastatic brain tumors can be treated with surgical resection, radiation therapy and stereotactic radiosurgery. However, single treatment modality is not effective to improve the quality of life for patients harboring these tumors. In most cases, cystic tumor can not be resected totally due to its eloquent location or patient's physical condition after chemotherapy. Radiotherapy alone is not possible due to large volume with mass effect and its effectiveness is not evaluated. Stereotactic radiosurgery alone is also dangerous due to its large volume. Therefore, in the management of large cystic metastatic brain tumors, multimodality treatment, cyst aspiration and radiosurgery with the same stereotactic frame is one option.

2. Treatment and outcome

2.1 Mechanism of cyst formation

Cystic metastatic brain tumors are common from lung cancer, and non small cell lung cancer is the most common pathology. Sometimes, even in the same pathology, multiple metastatic tumors have cystic and/or solid component.

The cause of cyst formation was not clearly established. Stem et al. suggested that the relatively large amounts of protein in cystic fluid resembled that present in inflammatory exudates, which could be the result of increased permeability of pathologic vessels and mesodermal reactive processes. Cumings et al. also suggested that formation of cystic fluid could be explained by tumor degeneration followed by transudation of fluid from blood vessels. Alternatively, Gardner et al. suggested that fluid accumulating in brain tumors is merely interstitial fluid without its normal drainage route because of the absence of lymphatics in the surrounding brain.

2.2 Surgical treatment

Conventionally, the presence of a large cystic brain tumor has been regarded as an indication for surgery. Yoshida and Morii advocated surgical treatment for patients with large cystic lesions, providing rapid relief of neurological symptoms caused by mass effect. However, if the lesions are located deep in the brain or adjacent to eloquent area, surgical

procedures may result in severe neurologic deficits. In addition, surgical procedures are not possible nor effective for patients in poor general condition or those with multiple lesions.

2.3 Stereotactic radiosurgery

From the past decade, stereotactic radiosurgery, particularly with Gamma Knife, have gained increasing relevance in the treatment of cerebral metastatic tumors. The increasing use of this technique is attributable to minimal invasiveness, a substantial reduction in hospitalization time and cost with an excellent local tumor control rates even in radioresistant tumor types and a very low associated morbidity. Moreover, although there had been no direct randomized clinical comparisons of Gamma Knife Radiosurgery with other surgical-radiation protocols, the results of Gamma Knife Radiosurgery in patients with solitary lesions were similar or superior to those obtained using other methods. If the tumors are located in the eloquent areas or in the deep locations, or have large cystic component, it is difficult to remove the tumor completely. Also, large cystic brain metastases do not appear suitable for radiosurgery, because the volume of the lesion is the limiting factor for radiosurgery given that it correlates with radiation induced complication.
Pan et al. reported that tumors with large cystic components (> 10 cc) were not effectively controlled by Gamma Knife Radiosurgery alone.

2.4 Cyst aspiration and stereotactic radiosurgery

In large cystic tumors, Gamma Knife Radiosurgery after stereotactic cyst aspiration could be the better treatment modality than surgical resection or Gamma Knife Radiosurgery alone.
Stereotactic cyst aspiration is a safe and effective procedure. Stereotactic cyst aspiration reduced tumor volume in most of our cases and relieved the neurologic symptom rapidly. The mean volume reduction after aspiration was about 76% compared to the preradiosurgical tumor volume in our results and we could increase the prescription dose to the tumor margin.
The high viscosity of cystic contents can make aspiration difficult. But even in the case of intratumoral hemorrhage which was noted in MR images before radiosurgery, aspiration was not difficult because hemorrhage was mixed with cystic fluid.
Collapsed cystic tumor after aspiration became smaller than initial tumor volume, but remained as a irregular shape. These irregular shaped mass made dose planning difficult in the radiosurgical procedure and needed multiple small isocenters.
This treatment method is composed of two stereotactic procedures with a single frame application. Stereotactic cyst aspiration and Gamma Knife Radiosurgery are performed with a single frame application on the same day with pre and post operative MR guidance. When large cystic tumors were multiple or even septated, aspiration is relatively easy and not difficult to perform under MR guidance. As we experienced several cases of cystic fluid reaccumation in the follow-up period after radiosurgery, Ommaya reservoir was applied after cyst aspiration.
Combined methods, aspiration and radiosurgery were performed in the same day if patient's condition was permitted. But in some cases, the two procedure time was too long, when the patient had have multiple brain metastases or patient's condition was unable to have frame fixation for several hours. In that case, we performed stereotactic cyst aspiration and Ommaya insertion first and delayed Gamma Knife Radiosurgery several days later. The time period of

Ommaya insertion and Gamma Knife Radiosurgery was usually within 7 days, because some cases had have rapid tumor progression or reaccumulation of the cystic fluid.
Applying Ommaya reservoir can make repeated aspiration without difficulty during and after radiosurgery.

2.5 Treatment result

The result of cyst aspiration combined with radiosurgey was rarely reported in the literature. Franzin et al. reported that preoperative tumor volume (mean volume 21.8 cc) was decreased about 46% postoperatively(mean volume 10.1 cc) and he could irradiate above 18 Gy to the tumor margin. He also reported that 92.3% of tumor control rates, overall median survival time was 15 months, the acturarial survival rates at 1 and 2 years was 54.7% and 34.2%, respectively and 26.3% of patients died from neurological progression.
In our study, preoperative tumor volume(mean 24.2cc) decreased about 76% postoperatively(mean 5.6cc), irradiated 20 Gy to the tumor margin. Our results showed that the tumor control rates were 50%, the overall median survival was 17.6 months and 11.1% of the patient died from progression of the brain metastases after treatment (Table 1, 2), (Fig 1, 2).

Characteristics	Number of patients (%)
Age	
<65 years	26 (76.0)
>65 years	8(24.0)
Sex	
Male	17 (50.0)
Female	17 (50.0)
Tumor volume, mean	pre 24.2cc post 5.6cc
Marginal dose, mean	20 (13-25) Gy
Primary tumor	
Non small cell lung cancer	17 (50.0)
Small cell lung cancer	2 (5.9)
Breast cancer	7 (20.1)
Ovarian cancer	2 (5.9)
Colorectal cancer	2 (5.9)
Endometrial carcinoma	2 (5.9)
Hepatocellular carcinoma	1 (2.9)
Malignant melanoma	1 (2.9)
Number of metastases	
1	20 (55.6)
2	8 (22.2)
3	1 (2.9)
>4	5 (14.7)
RPA Classification	
Class I	18 (52.9)
Class II	11 (32.4)
Class III	5 (14.7)

RPA: Recursive partitioning analysis

Table 1. Clinical characteristics of the 34 study patients.

Outcome	Number of patients (%)
Tumor control	17 (50.0)
Local tumor progression	8 (23.5)
Remote tumor progression	9 (26.5)
Death	27(50.0)
Brain metastasis progression	3 (11.1)
Unrelated illness	14 (51.9)
Primary cancer progression	10 (37)

Table 2. Outcomes of the 34 study patients.

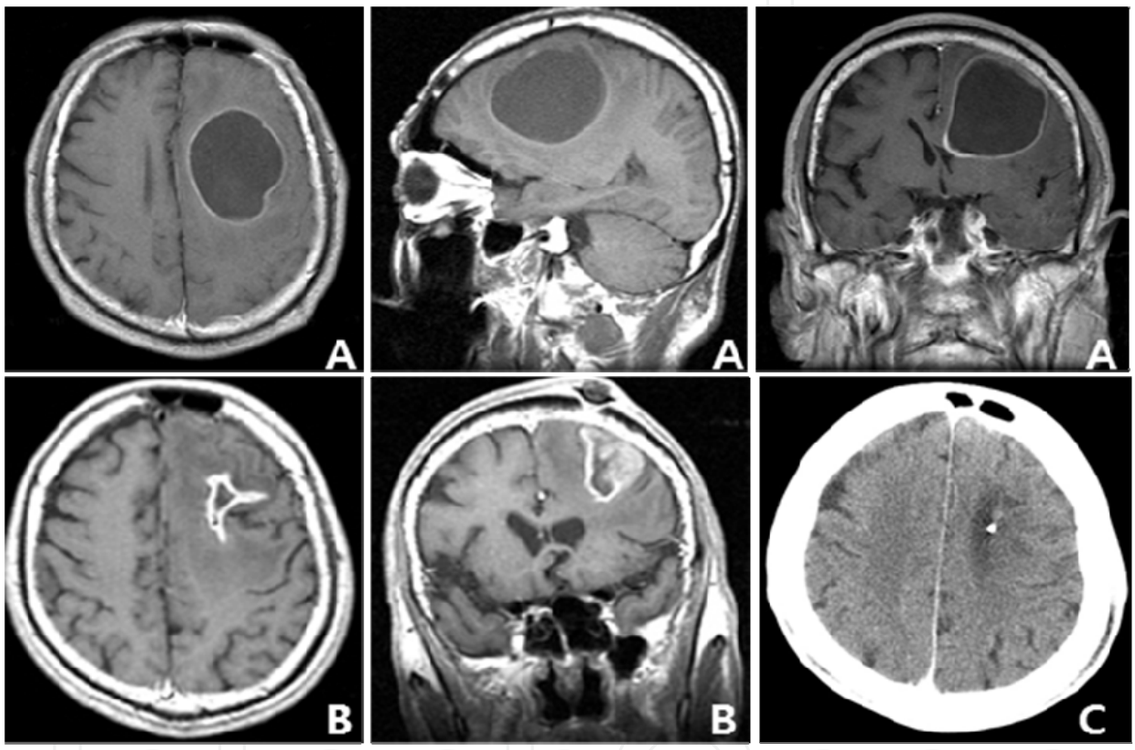


Fig. 1. Gadolinium-enhanced T1-weighted MR image of a 63-year-old man with a large cystic brain metastasis developing from non small cell lung cancer. A : Before aspiration : initial cyst volume, 36.0 cc. B : After cyst aspiration, volume, 8.0 cc. The prescription dose was 20 Gy. C : Enhanced CT scan obtained 6 months postradiosurgery showing no definite enhancing tumor.

Tendulkar et al. reported that median survival was reported to be 8.7 months after subtotal resection for single brain metastasis and 10.6 months after gross total resection of a single brain metastasis. Although it is difficult to directly compare these findings, the results of Gamma Knife Radiosurgery after stereotactic cyst aspiration of large cystic metastases were as good as that of gross total surgical resection of single brain metastasis.
The results of combined treatment modality, median survival and tumor control rates are nearly the same as the results of radiosurgery for solid metastatic brain tumors as reported in Coffey, Flickinger et al., Lutterbach et al. and Sansur et al.

Patient's prognosis is related to numerous parameters, such as KPS score, RPA class, age, location, number of cerebral lesions, character of primary tumor. Among them, RPA class is known as the most important prognostic factor.

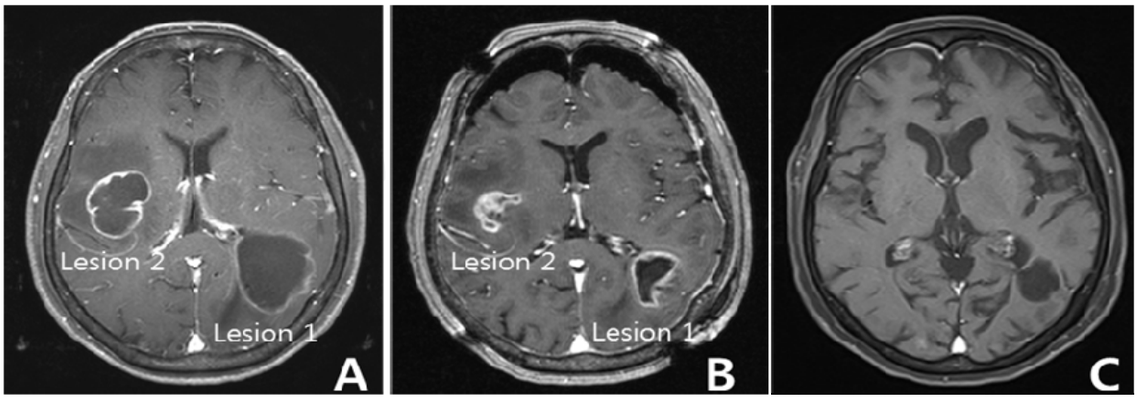


Fig. 2. Axial gadolinium-enhanced T1-weighted MR image of a 70-year-old woman with two large cystic brain metastases developing from breast cancer. A : Before aspiration : initial cyst volume of lesion 1, 34.7 cc; of lesion 2, 11.0 cc. B : After cyst aspiration : cyst volume of lesion 1, 8.0 cc ; of lesion 2, 0.9 cc. The prescription dose was 23 Gy for lesion 1 and 25 Gy for lesion 2. C : Image obtained 12 months postradiosurgery showing no definite enhancing tumors.

Tendulkar et al. reported that patients with unresectable brain metastases classified into RPA class I, II, and III, the median survival time was 7.1 months, 4.2 months and 2.3 months respectively. Lutterbach et al. reported median survival time as 13.4, 9.3 and 1.5 months in RPA class I, II and III, respectively. We observed median survival of 17.8 months, 10.9 months, and 6.1 months in RPA classes I, II and III, respectively. These data and our results confirmed that RPA class is an important tool to predict the patient prognosis in metastatic brain tumors. Moreover, some patients in RPA class III were too weak to permit general anesthesia. But, this combined treatment modality does not require general anesthesia. These findings further reinforce the efficacy of Gamma Knife Radiosurgery after stereotactic cyst aspiration for unresectable cystic brain metastases.

Perfoming Ommaya insertion and cyst aspiration just before Gamma Knife Radiosurgery is the most recommended procedure when the metastatic tumors have a large cyst even patient 's condition is not good after chemotherapy or poor general condition.

2.6 Complications

Ommaya reservoir insertion carries risks such as infection, leptomeningeal dissemination or tumor recurrence along the tube site. We have one case of this complication, tumor recurrence along the tube site, but there was no procedure related mortality nor morbidity.

Another possible complications include hemorrhage, neurosurgical deficits and seizures. The mortality rate in several large series has been less than 1%, and complication rates vary from 0% to 7%.

The complications of stereotactic radiosurgery are related to the effects of radiation on the brain and structures in proximity to the lesions. Significant early complications include

seizures and worsening neurological deficits, but they are very rare. Approximately one-third of patients experiences mild transient symptoms, including headache, nausea and dizziness. Late complications occur 6 to 9 months after the procedure and can include neurologic symptoms according to the tumor location. Patients may become symptomatic from radiation necrosis or local brain edema in the follow-up periods.

Franzin et al. reported that there was no acute complication and 7.6% of the patients experienced radionecrosis after stereotactic aspiration and Gamma Knife Radiosurgery of cystic brain metastases.

3. Conclusion

Cyst aspiration and stereotactic radiosurgery with a same stereotactic frame reduced tumor volume, relieving acute symptoms, permitting decrease in radiation dose to the brain, increasing tumor control rates, increasing median survival, decreasing the associated risks of radiation necrosis and post-radiation complications. Our results support the usefulness and safety of stereotactic radiosurgery after cyst aspiration for large cystic metastatic brain tumors.

4. Acknowledgement

The authors report no conflict of interest concerning the materials or methods used in this study or the findings specified in this chapter.

5. References

Andrews DW, Scott CB, Sperduto PW, et al (2004). Whole brain radiation therapy with or without stereotactic radiosurgery boost for patients with one to three brain metastases : phase III results of the RTGO 9585 randomized trial. Lancet 363 : 1665-1672

Arnold SM, Patchell RA (2001). Diagnosis and management of brain metastases. Hemato Oncol Clin North Am 15 : 1085-1107

Bernstein M, Parrent A (1994). Complication of CT guided stereotactic biopsy of intra-axial brain lesions. J Neurosurg 81 : 165-168

Borgelt B, Gelber R, Kramer S, et al (1980). The palliation of brain metastases : final results of the first two studies by the Radiation Therapy Oncology Group. Int J Radiat Oncol Bio Phys 6 : 1-9

Coffey RJ (1995). Stereotactic radiosurgical treatment of brain metastases in Cohen AR, Haines SJ (Ed) : Minimally invasive Techniques in Neurosurgery. Baltimore : Williams & Wilkins, 1995, pp139-143

Cumings JN (1950). The chemistry of cerebral cysts. Brain 73 : 244-250, 1950

Diener-West M, Dobbins TW, Phillips TL, Nelson DF (1989). Identification of an optimal subgroup for treatment evaluation of patients with brain metastases using RTGO study 7916. Int J Radiat Oncol Bio Phys 16 : 669-673

Flickiner JC (2001). Radiotherapy and radiosurgical management of brain metastases. Curr Oncol Rep 3 : 484-489

Franzin A, Vimercati A, Picozzi P, et al (2008). Stereotactic drainage and Gamma Knife radiosurgery of cystic brain metastasis. J Neurosurg 109 : 259-267

Gardner WJ, Collis JS, Lewis LA (1963). Cystic brain tumors and the blood-brain barrier. Comparision of protein fractions in cyst fluids and sera. Arch Neurol 8 : 291-298

Kim MS, Lee SL, Sim SH (1999). Brain tumors with cyst treated with Gamma Knife Radiosurgery : Is Microsurgery Indicated? Stereotact Funct Neurosurg 72 (Suppl 1) : 38-44

Kondziolka D, Firlik AD, Lunsford LD (1998). Complications of stereotactic brain surgery. Neurol Clin 16 : 35-54

Lohr F, Pirzkall A, Hof H, Fleckenstein K, Debus J (2001). Adjuvant treatment of brain metastases. Semin Surg Oncol 20 : 50-56

Lunsford LD, Martines AJ (1984). Streotactic exploration of the brain in the era of computed tomography. Surg Neurol 22 : 222-230

Lutterbach J, Cyron D, Henne K, Ostertag CB (2003). Radiosurgery followed by planned observation in patients with one to three brain metastases. Neurosurgery 52 : 1066-1074

Mandell L, Hilaris B, Sullvian M, Sundaresan N, Nori D, Kim JH, (1986). The treatment of single brain metastasis from non-oat cell lung carcinoma : surgery and radiation versus radiation therapy alone. Cancer 58 : 641-649

Mingione V, Oliveira M, Prasar D, Steiner M, Steiner L (2002). Gamma surgery for melanoma metastases in the brain. J Neurosurg 96 : 544-551

Muacevic A, Kreth FW, Horstmann GA, et al (1999). Surgery and radiotherapy compared with gamma knife radiosurgery in the treatment of solitary cerebral metastases of small diameter. J Neurosurg 91 : 35-43

Pan HC, Sheehan J, Stroila M, Steiner M, Steiner L (2005). Gamma knife radiosurgery for brain metastases from lung cancer. J Neurosurg 102: 128-133

Park WH, Jang IS, Kwon DH, et al (2009). Gamma Knife radiosurgery after stereotactic aspiration for large cystic brain metastases. J Korean Neurosurg Soc 46: 360-364

Patchell RA, Tibbs PA, Walsh JW, et al (1990). A randomized trial of surgery in the treatment of single metastases to the brain. N England J Med 322 : 494-500

Pullicino P, Thompson EJ, Moseley IF, Zilkha E, Shortman RC(1979). Cystic intracranial tumors. Cyst fluid, biochemical changes and computerized tomographic findings. J Neurol Sci 44 : 77-85

Tendulkar RD, Liu SW, Barnett GH, et al (2006). RPA classification has prognostic significance for surgically resected single brain metastasis. Int J Radiat Oncol Biol Phys 66 :810-817

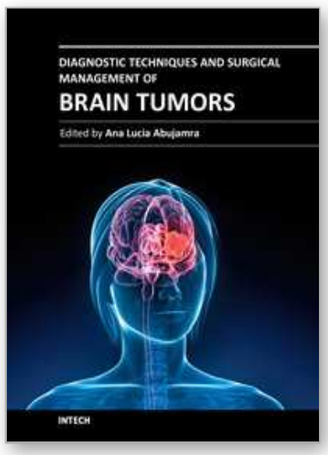
Sansur CA, Chin LS, Ames JW, et al (2000). Gamma knife radiosurgery for the treatment of brain metastases. Stereotact Funct Neurosurg 74 : 37-51

Stem K (1939). Chemical study of fluids obtained from cerebral cysts : report on 56 cases. Brain 62 : 88

Weissman DE (1988): Glucocorticoid treatment for brain metastases and epidural spinal cord compression : a review. J Clin Oncol 6 : 543-551

Werner-Wasik M, Rudoler S, Preston PE, et al (1999). Immediate side effects of stereotactic radiotherapy and radiosurgery. Int J Radiat Oncol Biol Phys 43 : 299-304

Yoshida S, Morii K (2004). The role of surgery in the treatment of brain metastasis : a retrospective review. Acta Neurochir (Wien) 146 : 767-770



Diagnostic Techniques and Surgical Management of Brain Tumors
Edited by Dr. Ana Lucia Abujamra

ISBN 978-953-307-589-1
Hard cover, 544 pages
Publisher InTech
Published online 22, September, 2011
Published in print edition September, 2011

The focus of the book Diagnostic Techniques and Surgical Management of Brain Tumors is on describing the established and newly-arising techniques to diagnose central nervous system tumors, with a special focus on neuroimaging, followed by a discussion on the neurosurgical guidelines and techniques to manage and treat this disease. Each chapter in the Diagnostic Techniques and Surgical Management of Brain Tumors is authored by international experts with extensive experience in the areas covered.

INTECH
open science | open minds

InTech Europe
University Campus STeP Ri
Slavka Krautzeka 83/A
51000 Rijeka, Croatia
Phone: +385 (51) 770 447
Fax: +385 (51) 686 166
www.intechopen.com

InTech China
Unit 405, Office Block, Hotel Equatorial Shanghai
No.65, Yan An Road (West), Shanghai, 200040, China
中国上海市延安西路65号上海国际贵都大饭店办公楼405单元
Phone: +86-21-62489820
Fax: +86-21-62489821

IntechOpen