# **Cystic metastases**

Metastases in form of a cyst.

# Etiology

Metastatic brain tumors are normally composed of cystic components, however, the reasons for the cyst formation have not been clearly investigated <sup>1)</sup>. Stem <sup>2)</sup> reported that the brain cyst fluid protein always presents in the inflammatory exudates. Cumings <sup>3)</sup> also reported that the cyst fluid formation may be correlated with the tumor degeneration. Gardner et al <sup>4)</sup> found that fluid accumulating in brain tumors runs in the normal drainage route, since there are no lymphatic vessels in the tumors.

Gamma knife radiosurgery (GKRS) is occasionally a useful tool for maintaining good brain status in patients with brain metastases (METs). Conversely, Ishikawa et al. experienced patients with delayed cyst formation (DCF) several years after GKRS, a complication not previously reported <sup>5)</sup>.

# **Differential diagnosis**

The main challenge in discrimination between intracranial cystic lesions is to differentiate benign inflammatory cystic lesions (as cerebral abscess) from malignant cystic lesions (as Bladder cancer intracranial metastases and cystic glioma) which have totally different management.

Cerebral abscess.

Hydatid cyst.

Other intra-axial cysts, e.g. intracranial arachnoid cyst, neuroglial cyst, porencephalic cyst.

The most common tumors are, hemangioblastoma, pilocytic astrocytoma, ganglioglioma, pleomorphic xanthoastrocytoma, tanycytic ependymoma, intraparenchymal schwannoma, desmoplastic infantile ganglioglioma.

Cystic meningioma is a rare form of intracranial meningioma. Meningiomas are typically solid tumors but may rarely have cystic components. The diagnosis of cystic meningioma is clinically challenging as the finding of multiple intra-axial tumors, including metastatic tumors, is relatively common. We report a case of cystic meningioma initially diagnosed as a metastatic tumor from a recurrence of acute lymphoid leukemia. However, postoperative histopathological examination demonstrated an atypical meningioma<sup>6)</sup>.

# **Case series**

## 2017

Between December 2007 and February 2015, 38 consecutive patients with 40 cystic metastases underwent Ommaya reservoir implantation at our institution. The patient characteristics, treatment

parameters, and all available clinical and neuroimaging follow-ups were analyzed retrospectively.

The rate of volume reduction was significantly related to the location of the tube tip inside the cyst. By placing the tip at or near the center, 58.7% reduction was achieved, whereas reduction of 42.6% and 7.7% occurred with deep and shallow tip placement, respectively (p=0.011). Although there was no additional surgery in the center placement group, additional surgeries were performed in 5 out of the 23 deep and shallow cases due to inadequate volume reduction. No other factors were correlated with successful volume reduction.

For adequate volume reduction using the Ommaya reservoir in the treatment of cystic brain metastases prior to stereotactic radiosurgery, the tip of the reservoir tube should be placed at the center of the cyst <sup>7)</sup>.

#### 2016

Lee et al. retrospectively reviewed the clinical, radiological, and dosimetry data of 37 cystic brain metastases of 28 patients who were treated with GKRS. Cyst drainage was performed in 8 large lesions before GKRS to decrease the target volume. The mean target volume was 4.8 (range, 0.3-15.8) cc at the time of GKRS, and the mean prescription dose was 16.6 (range, 13-22) Gy.

The actuarial median survival time was 17.7  $\pm$  10.2 months, and the primary tumor status was a significant prognostic factor for survival. The actuarial local tumor control rate at 6 and 12 months was 93.1 and 82.3%, respectively. Among the various factors, only prescription dose (>15 Gy) was a significant factor related to local tumor control after multivariate analysis (p = 0.049). Cyst volume or cyst/total tumor volume ratio did not influence local control after GKRS, when the target volume was reduced to about 15 cc after cyst drainage.

According to this results, they suggest that stereotactic radiosurgery should be considered as one of the treatment options for cystic brain metastases, when large tumor volume can be reduced by surgical drainage before radiosurgery, especially for patients with a controlled primary tumor <sup>8)</sup>.

A study involved 48 patients who were diagnosed with cystic metastatic brain tumors between January 2008 and December 2012 in the Department of Neurosurgery of Nanfang Hospital Southern Medical University (Guangzhou, China). Every patient underwent Leksell stereotactic frame, 1.5T magnetic resonance imaging (MRI)-guided stereotactic cyst aspiration and Leksell GKRS. Subsequent to the therapy, MRI was performed every 3 months. The results indicated that 48 cases were followed up for 24-72 months, with a mean follow-up duration of 36.2 months. Following treatment, 44 patients (91.7%) exhibited tumor control and 4 patients (8.3%) experienced progression of the local tumor. During this period, 35 patients (72.9%) succumbed, but only 2 (4.2%) of these succumbed to the brain metastases. The total local control rate was 91.7% and the median overall survival time of all patients was 19.5 months. The 1-year overall survival rate was 70.8% and the 2-year overall survival rate was 26.2%. In conclusion, these results indicated that the method of stereotactic cyst aspiration combined with GKRS was safe and effective for patients with large cystic brain metastases. This method is effective for patients whose condition is too weak for general anesthesia and in whom the tumors are positioned at eloquent areas. This method enables patients to avoid a craniotomy, and provides a good tumor control rate, survival time and quality of life <sup>9</sup>.

# 2015

In a review, Kim et al. describe the characteristics of cystic brain metastasis and evaluate the combined use of stereotactic aspiration and radiosurgery in treating large cystic brain metastasis. The results of several studies show that stereotactic radiosurgery produces comparable local tumor control and survival rates as other surgery protocols. When the size of the tumor interferes with radiosurgery, stereotactic aspiration of the metastasis should be considered to reduce the target volume as well as decreasing the chance of radiation induced necrosis and providing symptomatic relief from mass effect. The combined use of stereotactic aspiration and radiosurgery has strong implications in improving patient outcomes <sup>10</sup>.

## 2014

Between February 2005 and March 2012, a total of 24 patients underwent GKR after cyst aspiration for 29 cystic metastatic brain tumors. The median age was 60 years (range, 18-81). The number of male patients was 18 and that of female patients 6. Most of the patients were in class II (87.5%) based on the data of the Radiation Therapy Oncology Group using recursive partitioning analysis. We analyzed the changes in tumor volume, the local control rate, intracranial progression-free survival (PFS) and overall survival (OS).

Before aspiration, the mean total tumor volume was 32.7 cm(3) (range, 12.1-103.3) and cystic volume was 18.6 cm(3) (range, 8-72.3). The mean duration of cyst drainage was 1 day (range, 1-2). The mean amount of aspiration was 16.8 cm(3) (range, 6-67.4). After aspiration, the total mean volume was 12.4 cm(3) (range, 3.7-38.1) and cystic volume was 2.0 cm(3) (range, 0.1-9.5). The nature of the cyst was serous in 18, serous and hemorrhagic in 3, and serous and necrotic in 8. The median prescription dose was 16 Gy (range, 14-20). There was no treatment-related complication. The local control rate was 58.6% (17/29). The median survival to local recurrence was  $6.0 (\pm 1.42)$  months. During the follow-up period, an Ommaya reservoir was placed in 3 patients. Insertion of an Ommaya reservoir and whole-brain radiotherapy (WBRT) or GKR were done in 2 patients, WBRT in 2, GKR in 1 and operation in 1. The median intracranial PFS and OS after intracranial metastasis was  $5.2 (\pm 0.42)$  and  $6.8 (\pm 0.38)$  months.

Cyst aspiration and GKR were feasible and safe but not very efficient, which could be an alternative option for large cystic metastases in patients who could not expect longer survival time <sup>11</sup>.

#### 2013

Ebinu et al. reviewed a prospectively maintained database of brain metastases patients treated between 2006 and 2010. All lesions with a cystic component were identified, and volumetric analysis was done to measure percentage of cystic volume on day of treatment and consecutive follow-up MRI scans. Clinical, radiologic, and dosimetry parameters were reviewed to establish the overall response of cystic metastases to GKRS as well as identify potential predictive factors of response.

A total of 111 lesions in 73 patients were analyzed; 57% of lesions received prior whole-brain radiation therapy (WBRT). Lung carcinoma was the primary cancer in 51% of patients, 10% breast, 10% colorectal, 4% melanoma, and 26% other. Fifty-seven percent of the patients were recursive partitioning analysis class 1, the remainder class 2. Mean target volume was 3.3 mL (range, 0.1-23 mL). Median prescription dose was 21 Gy (range, 15-24 Gy). Local control rates were 91%, 63%, and

37% at 6, 12, and 18 months, respectively. Local control was improved in lung primary and worse in patients with prior WBRT (univariate). Only lung primary predicted local control in multivariate analysis, whereas age and tumor volume did not. Lesions with a large cystic component did not show a poorer response compared with those with a small cystic component.

This study supports the use of GKRS in the management of nonsurgical cystic metastases, despite a traditionally perceived poorer response. Our local control rates are comparable to a matched cohort of noncystic brain metastases, and therefore the presence of a large cystic component should not deter the use of GKRS. Predictors of response included tumor subtype. Prior WBRT decreased effectiveness of SRS for local control rates <sup>12</sup>.

#### 2012

Between 2005 and 2010, 25 cystic metastases in 25 patients were treated at Dokkyo Medical University. The patients first underwent MRI and stereotactic aspiration of the cyst while stationary in a Leksell stereotactic frame; immediately afterward, the patients underwent a second MR imaging session and Gamma Knife treatment. Tumor volume reduction, tumor control rate, and overall survival were examined.

Tumor volume, including the cystic component, decreased from 8.0-64.2 cm(3) (mean 20.3 cm(3)) to 3.0-36.2 cm(3) (mean 10.3 cm(3)) following aspiration, and the volume of 24 of 25 lesions decreased to less than 16.6 cm(3), which is equivalent to the volume of a 3.16-cm sphere. At least 20 Gy was delivered to the entire lesion in 24 of 25 cases. Good tumor control was obtained in 16 of 21 cases that could be evaluated during a median follow-up period of 11 months (range 1-27 months); however, reaccumulation of cyst contents was observed in 2 patients who required Ommaya reservoir placement.

The 1-day aspiration plus GKS procedure is an effective and time-efficient treatment for large cystic brain metastases <sup>13)</sup>.

#### 2009

Hydrofiber dressing is a sodium carboxymethylcellulose hydrocolloid polymer with high fluidabsorptive capacity. This material was originally used as a dressing for exudative wounds. Hydrofiber dressing was used for 8 patients with cystic-type metastatic brain tumor. Tumor removal was performed after hydrofiber dressing was inserted into the cyst cavity to transform the tumor into a solid-type tumor.

Transformation of cystic-type metastatic brain tumors into smaller solid-type tumors using hydrofiber dressing facilitated en bloc resection of tumor. The dressing also absorbed residual cyst fluid and was thus also effective in preventing intraoperative dissemination of tumor cells. This approach enabled ideal en bloc resection in all patients. There were no adverse events.

These findings suggest hydrofiber dressing may be useful in surgery for cystic-type metastatic brain tumors  $^{14)}$ .

#### 2008

Between January 2001 and November 2005, 680 consecutive patients with brain metastases underwent GKS at our hospital, 30 of whom were included in this study (18 males and 12 females, mean age 60.6 +/- 11 years, range 38-75 years). Inclusion criteria were: 1) no prior whole-brain radiation therapy or resection procedure; 2) a maximum of 4 lesions on preoperative MR imaging; 3) at least 1 cystic lesion; 4) a Karnofsky Performance Scale score >or= 70; and 5) histological diagnosis of a malignant tumor.

Non-small cell lung carcinoma was the primary cancer in most patients (19 patients [63.3%]). A single metastasis was present in 13 patients (43.3%). There was a total of 81 tumors, 33 of which were cystic. Ten patients (33.3%) were in recursive partitioning analysis Class I, and 20 (66.6%) were in Class II. Before drainage the mean tumor volume was 21.8 ml (range 3.8-68 ml); before GKS the mean tumor volume was 10.1 ml (range 1.2-32 ml). The mean prescription dose to the tumor margin was 19.5 Gy (range 12-25 Gy). Overall median patient survival was 15 months. The 1- and 2-year survival rates were 54.7% (95% confidence interval 45.3-64.1%) and 34.2% (95% confidence interval 23.1-45.3%). Local tumor control was achieved in 91.3% of the patients.

The results of this study support the use of a multiple stereotactic approach in cases of multiple and cystic brain metastasis <sup>15)</sup>.

#### **Case reports**

#### 2015

A study describes the first case of histopathologically-confirmed brainstem metastasis originating from lung adenosquamous carcinoma, and discusses the outcomes of treatment by stereotactic aspiration combined with gamma knife radiosurgery (GKRS). A 59-year-old female presented with a cystic mass (15×12×13 mm; volume, 1.3 cm3) located in the pons, two years following surgical treatment for adenosquamous carcinoma of the lung. The patient received initial GKRS for the lesion in the pons with a total dose of 54.0 Gy, however, the volume of the mass subsequently increased to 3.9 cm3 over a period of three months. Computed tomography-guided stereotactic biopsy and aspiration of the intratumoral cyst were performed, yielding 2.0 cm3 of yellow-white fluid. Histology confirmed the diagnosis of adenosquamous carcinoma. Aspiration provided immediate symptomatic relief, and was followed one week later by repeat GKRS with a dose of 12.0 Gy. The patient survived for 12 months following the repeat GKRS; however, later succumbed to the disease after lapsing into a two-week coma. The findings of this case suggest that stereotactic aspiration of cysts may improve the effects of GKRS for the treatment of cystic brainstem metastasis; the decrease in tumor volume allowed a higher radiation dose to be administered with a lower risk of radiation-induced side effects. Therefore, stereotactic aspiration combined with GKRS may be an effective treatment for brainstem metastasis originating from adenosquamous carcinoma<sup>16</sup>.

#### 2009

A 71-year-old man who was admitted to the emergency department after an episode of loss of consciousness. On neurological examination a left hemiparesis was observed. The patient's previous history entailed a total cystectomy and radical prostatectomy 7 months ago because of a transitional

cell carcinoma (TCC) of the urinary bladder. Brain imaging work-up revealed a cystic lesion with perifocal edema in the right frontal lobe. The patient was operated and the histological diagnosis was consistent with a metastatic carcinoma, with morphological, histochemical and immunohistochemical features comparable to those of the primary tumor. Postoperative the patient was in excellent neurological state and received complementary chemotherapy and total brain irradiation. Additional imaging and laboratory examinations excluded other metastatic lesion. The patient died 18 months later due to systemic disease. Although intracranial metastases from TCC of urinary bladder have a low incidence, in follow-up examinations any alterations in neurological status in these patients should be thoroughly evaluated <sup>17)</sup>.

Cystic brain metastases from small-cell lung carcinomas are exceedingly rare and neurosurgical operations are not suitable for those cases considering invisible micrometastases. A 34-year-old female patient presented with small-cell lung carcinoma that metastasized to the brain as a solitary cyst with a thin wall 24 months after a good partial response to initial chemoradiotherapy. The brain mass volume and the main symptom of left hemiplegia, which made the Karnofsky performance status (KPS) fall to 30%, did not respond to whole brain irradiation. Therefore, an Ommaya reservoir was inserted, which dramatically improved the KPS to 70%. This minimally invasive surgical strategy is suitable even for patients with a poorer KPS bearing cystic brain metastases <sup>18)</sup>.

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