ORIGINAL ARTICLE

The Role of Stereotactic Cyst Aspiration for Glial and Metastatic Brain Tumors

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ABSTRACT: ***Objective:*** To evaluate the role of stereotactic cyst aspiration in the context of multimodality management of cystic glial and metastatic tumors, we retrospectively reviewed our experience with 38 patients during a 10-year interval. ***Methods:*** All 38 patients had one or more computed tomography or magnetic resonance imaging guided stereotactic cyst aspirations. Twenty-seven patients had glial neoplasms and 11 had metastatic brain tumors. Twenty-two patients underwent cyst aspiration as the initial treatment modality while 15 patients had cyst aspiration following previous treatments. ***Results:*** In the immediate postoperative period, 19 of the 27 (70%) patients with gliomas and nine of the 11 (82%) patients with metastatic tumors experienced symptomatic improvement. No procedure-related morbidity was encountered. Twelve patients (31.5%) eventually required a catheter-reservoir system. Thirty-seven percent of patients with cystic glial neoplasms and 18% of patients with metastatic tumors had delayed cytoreductive surgery by craniotomy subsequent to stereotactic cyst aspiration. Reduction in tumor volume following aspiration facilitated Gamma knife radiosurgery in seven patients. ***Conclusion:*** Single stereotactic aspiration is a low risk procedure that provides immediate relief of symptoms in patients with cystic brain tumors. It appears to be valuable together with the use of other therapeutic strategies.

RÉSUMÉ: Le rôle de l'aspiration stéréotaxique de kystes situés dans les tumeurs gliales et métastatiques du cerveau. ***Objectif:*** Dans le but d'évaluer le rôle de l'aspiration stéréotaxique de kystes dans le contexte du traitement multimodal de tumeurs kystiques gliales et métastatiques, nous avons procédé à une revue rétrospective de notre expérience chez 38 patients sur une période de dix ans. ***Méthodes:*** Les 38 patients ont eu une ou plusieurs aspirations de kystes sous guidage stéréotaxique par tomodensitométrie ou par RMN. Vingt-sept patients avaient une néoplasie gliale et 11 avaient des tumeurs cérébrales métastatiques. Vingt-deux patients ont subi une aspiration de leur kyste comme traitement initial alors que 15 patients ont subi une aspiration suite à une autre modalité thérapeutique. ***Résultats:*** Dans la période postopératoire immédiate, 19 des 27 patients porteurs d'un gliome (70%) et 9 des 11 patients porteurs de tumeurs métastatiques (82%) ont eu une amélioration de leurs symptômes. Il n'y a pas eu de morbidité associée à la procédure. Douze patients (31.5%) ont éventuellement eu besoin d'un système cathéter/réservoir. Trente-sept pourcent des patients porteurs de néoplasies gliales kystiques et 18% des patients porteurs de tumeurs métastatiques ont éventuellement subi une chirurgie cytoréductrice par crâniotomie suite à l'aspiration stéréotaxique de kystes. La diminution du volume de la tumeur suite à l'aspiration a facilité la radiochirurgie Gamma-Knife chez 7 patients. ***Conclusion:*** L'aspiration stéréotaxique unique est une procédure à faible risque qui amène un soulagement immédiat des symptômes chez les patients porteurs de tumeurs cérébrales kystiques. Cette procédure semble être utile en association avec d'autres stratégies thérapeutiques.

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Tumor-associated cysts are well-defined entities distinct from benign cysts such as arachnoid, neuroepithelial, leptomeningeal, and porencephalic cysts. Some authors distinguish true cysts from pseudocysts on the basis of imaging characteristics. A true cyst is lined by a thin wall of contrast enhancement and has smooth inner margins. A pseudocyst is characterized by a thick wall with irregular margins and is usually seen in malignant tumors undergoing necrosis.[1]

The exact mechanism of cyst formation in brain tumors is unknown, although cysts may arise from the degeneration of the tumor tissue (necrobiosis) which might give rise to cyst fluid rich in endogenic cerebral proteins.[2] Cyst fluid may contain high levels of glial fibrillary acidic protein, S-100 protein, endolase, B-endorphin, and thymidine kinase.[3] Another potential cause of tumor-associated cyst formation is blood brain barrier

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disruption.[4] The opening of endothelial cell junctions can give rise to excessive fluid deposition in the tumor ultimately leading to cyst formation. Vasogenic peritumoral edema resolves by drainage into the CSF or by degradation by proliferating glial elements. A mismatch of edema formation and resolution may eventually result in microcyst formation which subsequently becomes confluent forming a larger cyst cavity. Lohle et al[4] noted a predominance of plasma proteins (>92%) in tumor cyst fluid. They suggested that endogenous cerebral proteins constitute only a minor proportion of proteins in the cyst fluid and that the majority of protein enters the cyst from plasma through open endothelial junctions and endothelial fenestrations which are the morphological sites of blood brain barrier disruption. Strugar et al[3] in a study of 34 primary brain tumors reported a high correlation between the presence of vascular endothelial growth/permeability factor (VEG/PF) and the occurrence of perivascular brain edema, tumor-associated cysts, and tumor enhancement irrespective of tumor grade.

Tumor-associated cyst formation can occur in a variety of glial and metastatic brain tumors. However, the management of cystic glial or metastatic tumors is not straight forward. Surgical resection of the tumor is often the preferred management approach. When resection is not always possible, a multimodality approach including stereotactic cyst aspiration, radiation therapy, radiosurgery, radioactive isotope instillation, cyst reservoir placement and chemotherapy may be employed for control of solid tumor growth and symptomatic cyst expansion.

While tumor-associated cysts are common, little has been written regarding the therapeutic strategies, outcomes of cyst management and the effect on patient symptomatology. The role of single cyst aspiration and the potential therapeutic benefits of this approach have not been well-characterized. A single stereotactic aspiration of cyst contents can reduce cerebral mass effect and improve patient symptomatology. Because such cysts frequently re-accumulate, insertion of catheter-reservoir systems may eventually be required to facilitate percutaneous interval cyst drainage.[5-7] We report a series of patients who had primary glial or metastatic cystic brain tumors treated by stereotactic aspiration. We assess the role of stereotactic aspiration to improve symptoms, to facilitate other minimally invasive treatment strategies and to avoid higher risk surgical procedures.

Methods

We retrospectively examined the medical and imaging records of 38 patients who underwent 53 cyst aspiration procedures as part of multimodality treatment for cystic brain tumors. Twenty-seven patients had glial neoplasms and 11 had metastatic brain lesions (Table 1). In all patients, management included at least one computed tomography (CT) or magnetic resonance imaging (MRI) guided stereotactic cyst aspiration performed between 1987 and 1998. Twenty-two patients presented for cyst aspiration as the initial treatment modality while 16 patients presented for aspiration following other treatment (Table 2). Stereotactic cyst aspiration was performed as a single surgical procedure to reduce mass effect or in conjunction with biopsy, catheter-reservoir placement, or Gamma knife radiosurgery.

Table 1: Demographics of cystic tumors (n=38)

		No. of Patients
Gender		
	Male	21 (55%)
	female	17 (45%)
Location		
	Lobar	25 (65%)
	Deep	13 (34%)
Histology		
	Low grade glial tumor	9 (24%)
	Malignant glial tumor	18 (47%)
	Metastatic tumor	11 (29%)

Procedure

The Leksell model G stereotactic system was used for target localization with MR or CT guidance. In 27 of the 53 procedures, cyst volumes were measured with computer assisted intraoperative imaging technique prior to aspiration. In the remaining cases the preoperative cyst volume was calculated from preoperative images. Under conscious sedation, a small twist drill craniostomy (for single aspiration) or burr hole (for catheter placement) was fashioned. After durotomy, a biopsy cannula was passed to the target. Cyst aspiration was achieved first by passive drainage with the patient in a supine position or by gentle suction when necessary. Our goal was to evacuate at least two-thirds of the cyst volume. The recovered volume was compared to the volume of the cyst estimated during preoperative planning. An immediate postoperative CT was performed routinely in the operating room to rule out hematoma and evaluate cyst morphology. After successful aspiration, seven patients underwent Gamma knife radiosurgery within 48 hours after the aspiration. All seven patients underwent intraoperative Gamma knife stereotactic MRI following cyst aspiration in order to define the lesion following collapse of the cyst.

Morbidity and survival data (both from the time of diagnosis and from the time of initial cyst aspiration) were assessed. Additionally, the effect of tumor location and cyst volume were evaluated. The effect of cyst aspiration on subsequent tumor management was assessed.

Table 2: Adjunctive therapies for cystic tumors (n=38)

Tumor Histology	No. of Patients	Pre or Postoperative Adjunctive Therapies		
		XRT	Chemotherapy	Radiosurgery
Low grade glial tumors	9	4	0	7
Malignant glial tumors	18	17	11	4
Metastatic tumors	11	11	11	5

XRT – Fractionated radiation therapy

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Table 3: Improvement after stereotactic cyst aspiration

Tumor Histology	No. of Patients	Improved after aspiration
Low grade glial tumors	9	7 (78%)
Malignant glial tumors	18	12 (67%)
Metastatic tumors	11	9 (82%)
Total	38	28 (74%)

RESULTS

Cystic glial tumors

There were 15 males and 12 females with the following cystic glial tumors: ependymoma (n=1), pilocytic astrocytoma (n=6), astrocytoma (n=2) anaplastic astrocytoma (n=2), anaplastic mixed glioma (n=3) and, glioblastoma multiforme (GBM) (n=13). Eleven patients presented for cyst aspiration following interventions that included craniotomy (n=6), stereotactic biopsy (n=5), fractionated radiation therapy (n=7), Gamma knife radiosurgery (n=3), ventriculo-peritoneal shunt (n=2) or stereotactic radioisotope implantation (n=1). Concomitant biopsy was performed in 18 patients including the 16 patients who presented for cyst aspiration as their initial therapy. One patient with an ependymoma was diagnosed and operated upon approximately 20 years prior to development of a cystic component. One patient was diagnosed with an astrocytoma nine years prior to cyst aspiration and biopsy at the time of this procedure revealed a GBM. This patient died nine months after aspiration.

The volumes of fluid drainage varied from 1.5 to 45 cc. The percentage of calculated cyst volume drainage at the time of initial aspiration varied from 67% to 100% (mean = 79%). Nineteen of these 27 patients showed significant clinical improvement in the immediate postoperative period (Table 3). The remaining eight patients did not show appreciable improvement, but did not deteriorate. During the aspiration procedure one patient complained of headache that resolved within hours. Another patient with a pontine cyst developed ipsilateral V_1 trigeminal pain during the procedure. Blood tinged aspirate was noted in one patient with a pineal cyst, but a post-operative CT showed no hemorrhage. Procedure-related morbidity such as hematoma, infection, or new neurologic deficit was not encountered.

Adjuvant therapies

Eleven patients eventually required repeated drainage procedures either by repeat stereotactic aspiration (N=1), or by reservoir placement (N=10) and aspiration. In these patients, initial drainage volume varied from 6.5 cc to 40 cc, volumes which represented 67% to 100% of the calculated cyst volume. The histology from patients that required a repeat aspiration included: pilocytic astrocytomas (n=3), astrocytoma (n=1), anaplastic astrocytoma (n=1), GBM (n=6). Transient improvement in clinical status was noted after nine of 12 repeat aspiration procedures.

Radiosurgery was performed in three patients within 24 hours of aspiration to capitalize on the reduced tumor volume. Radiosurgery was performed in an additional three patients within three weeks. Adjuvant chemotherapy or fractionated radiation therapy was performed in all patients with anaplastic astrocytoma or glioblastoma either prior or subsequent to cyst aspiration. Ten patients underwent delayed craniotomy and

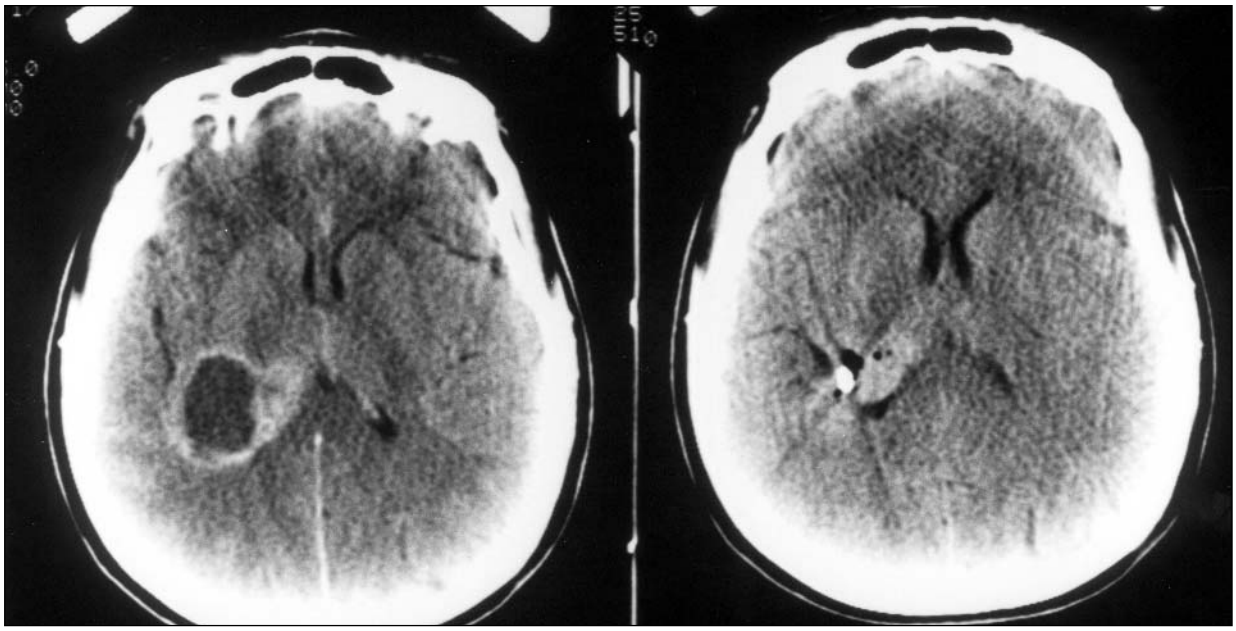

Figure 1: *Axial contrast enhanced CT scan showing a large cystic tumor (left). The Axial CT scan of the same patient immediately after stereotactic aspiration and reservoir placement showing complete cyst evacuation (right).*

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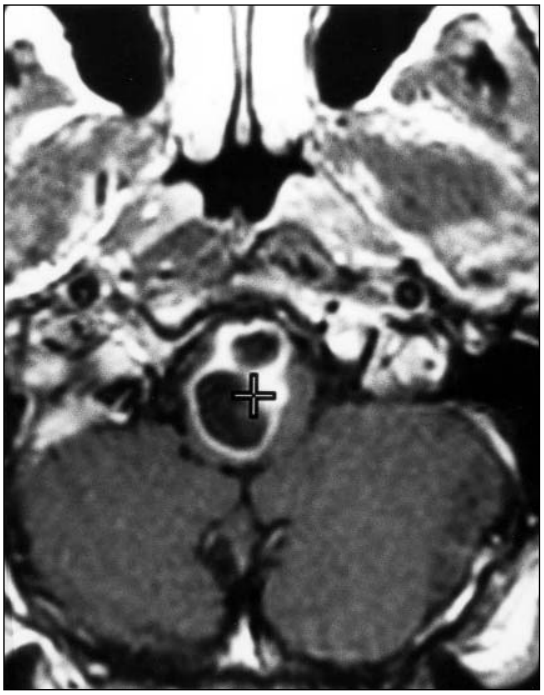

Figure 2 A: *Axial T1-weighted contrast enhanced MR image showing a large cystic medullary glial tumor.*

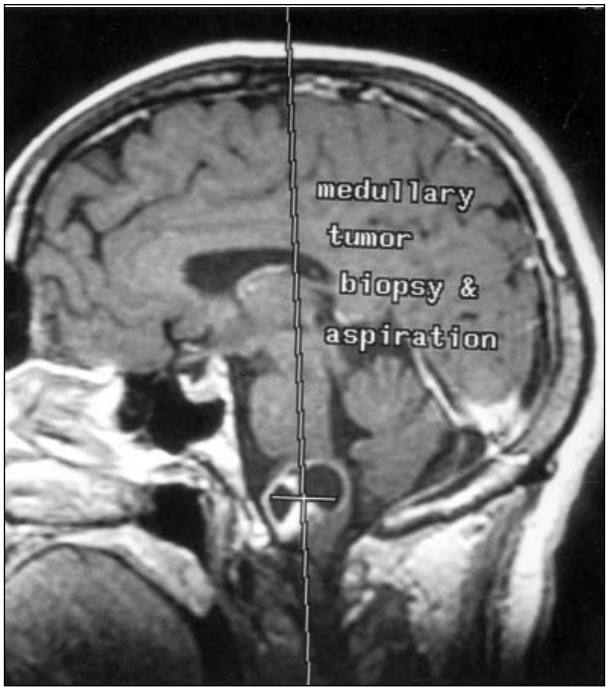

Figure 2 B: *Sagittal T1-weighted contrast enhanced MR image showing the trajectory of planned stereotactic aspiration of cystic medullary tumor.*

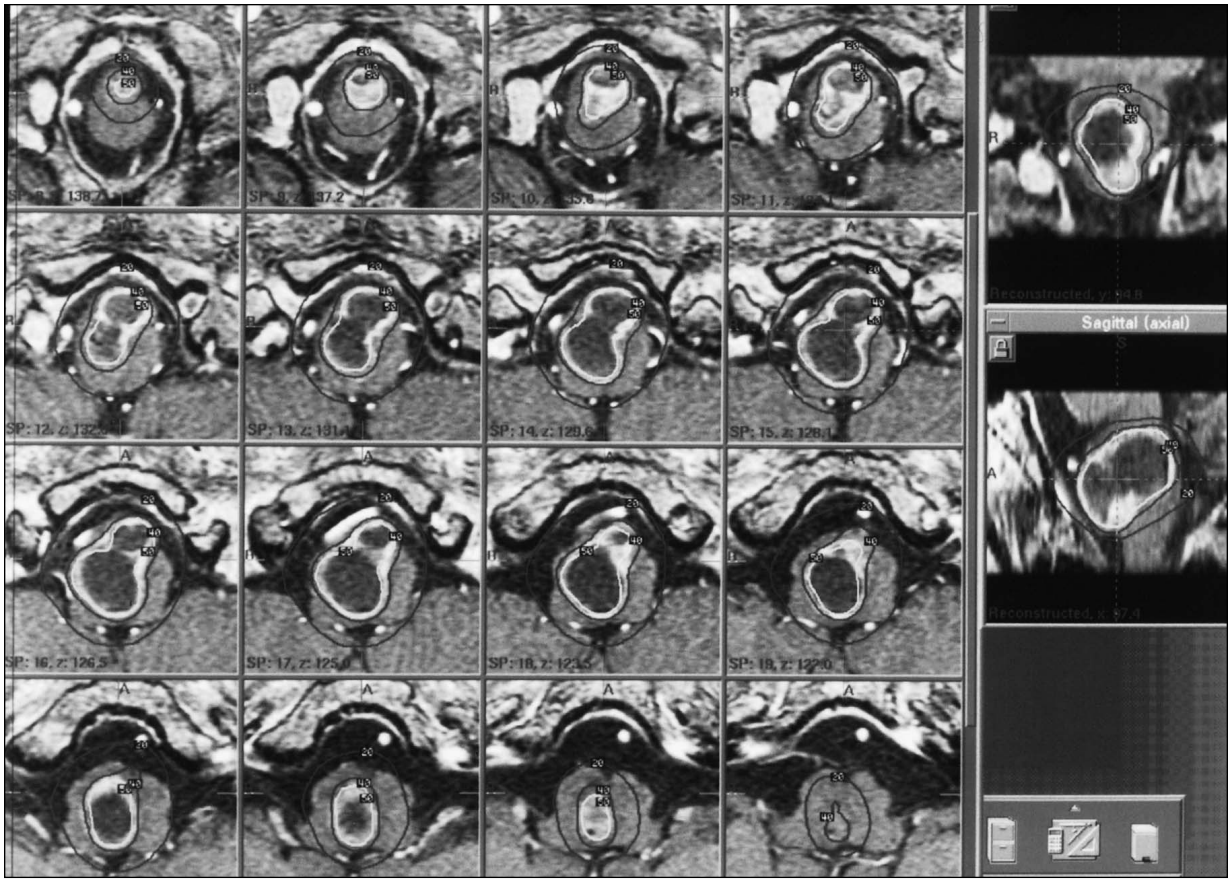

Figure 2 C: *A radiosurgery plan for cystic medullary tumor immediately after partial stereotactic aspiration. The 50%, 40%, and 20% isodose lines are shown in axial MR images with sagittal and coronal reconstructions.*

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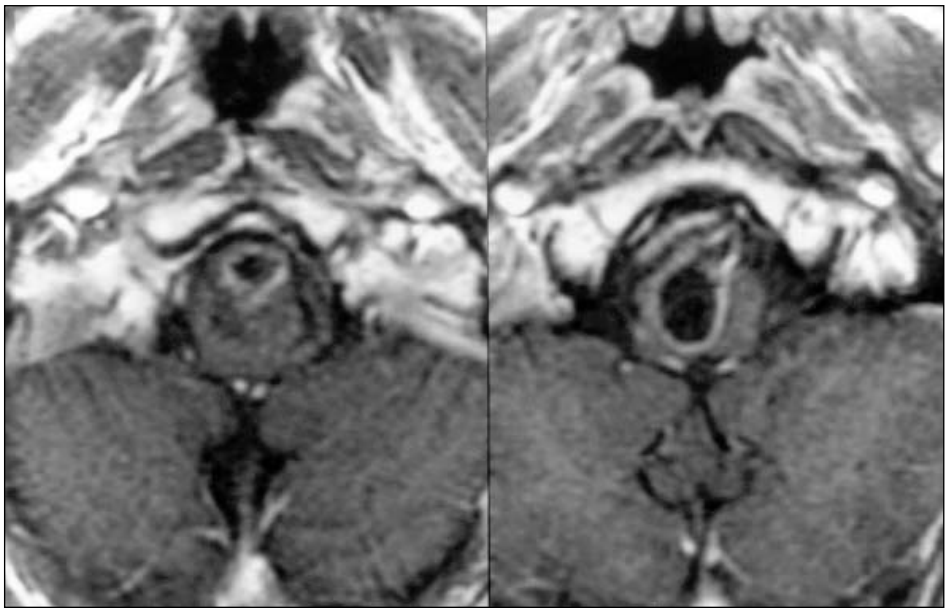

Figure 2 D: *The axial MR scans of the same patient 10 months after stereotactic aspiration and radiosurgery showing stable appearance of the cyst.*

cytoreductive surgery between three weeks to five years of their first aspiration procedure.

Survival

All six patients with deeply located pilocytic astrocytoma (pons=1, midbrain=1, hypothalamus=3, occipital lobe=1) remain alive with a median survival of 81 months (range 15 months to 134 months) from the time of diagnosis and 19 months (range nine months to 104 months) from the time of initial aspiration. The two patients with astrocytoma remain alive at 17.5 and 80 months from diagnosis and 17 months and 44 months from initial aspiration. The patient with ependymoma is alive 21 years from diagnosis and 12 months from initial aspiration. Four of five patients with anaplastic astrocytoma or anaplastic mixed glioma remain alive at a median interval of 54.5 months from diagnosis and 50 months from initial cyst aspiration; one patient died 24 months after diagnosis and five months after initial cyst aspiration. Median survival for patients with GBM was 6.5 months (range 1.5-27) after diagnosis and five months (range 1-21) post initial cyst aspiration.

Cystic metastatic tumors

There were five males and six females with the following cystic metastatic brain tumors: adenoid cystic carcinoma (n=1), adenocarcinoma (parotid) (n=1), small cell carcinoma of the lung (n=1), non small cell carcinoma of the lung (n=2), large cell carcinoma of the lung (n=1), squamous cell carcinoma of the lung (n=1), primitive neuroectodermal tumor metastatic from the adrenal gland (n=1), malignant melanoma (n=1), and renal cell carcinoma (n=2). Five patients presented for cyst aspiration after prior treatments that included craniotomy (n=1), fractionated radiation therapy (n=4) or Gamma knife radiosurgery (n=1).

Simultaneous biopsy was performed in six patients. One patient with non small cell carcinoma of the lung, had two cystic lesions: one in the cerebellum and one in the temporal lobe. Both cysts were drained during the same procedure using two different trajectories. Two patients required repeated drainage by subsequent stereotactic aspiration and eventual cyst-reservoir placement. The percentage of calculated cyst volume drainage at the time of initial aspiration varied from 49% to 100% (mean =80%). Nine of 11 patients treated for cystic metastatic tumors showed significant symptomatic improvement in the immediate postoperative period. None deteriorated and no procedure-related morbidity was encountered.

Four patients had Gamma knife radiosurgery the day after cyst aspiration. Fractionated radiation therapy was performed in all seven patients who had not received radiation prior to cyst aspiration. Adjuvant chemotherapy to treat systemic disease was performed in all patients. Two patients underwent craniotomy at one (adenoid cystic carcinoma) and nine months (large cell carcinoma of the lung) after aspiration. Four patients remained alive at seven to 24 months after aspiration. In the remaining patients with metastatic lesions, median survival from initial aspiration and from the time of diagnosis was three months (range 0.5-15) and six months (range 2.5-40) respectively. These patients died of active extracranial disease but were palliated by cyst drainage.

Radiosurgery after cyst aspiration

In this series, radiosurgery was performed within 48 hours of cyst aspiration in seven patients (three glial and four metastatic tumors). Four aspiration procedures were followed by stereotactic radiosurgery within two hours of aspiration. Radiosurgery was performed on the first postaspiration day in the other two patients and on the second postaspiration day in one patient. None of these seven patients were felt to be acceptable candidates for radiosurgery on initial evaluation due to the large target volume in a critical location. All four cystic

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metastatic tumors were situated in lobar locations and caused limb weakness. All three patients with primary brain tumors had tumors in central locations involving the brain stem (Figure 2), hypothalamus, optic chiasm or thalamus. These patients presented with headache, visual field deficit, hemiparesis, or lower cranial nerve dysfunction of long standing duration (range, ten months to four years). In these three patients the location was considered to be critical and primary craniotomy was not believed to be a desirable option.

Discussion

The literature on the management of cystic intracranial tumors is limited. Drainage of cyst fluid is often necessary when tumor cysts produce clinical deterioration and resection is not feasible. Free hand CT-guided and stereotactic techniques have been used to drain benign and malignant cysts and cyst aspiration is associated with prompt relief of acute symptoms caused by the pressure effect of the cyst.[8-11] Unfortunately, simple aspiration alone is often followed by symptomatic cyst recurrence. Complete or even partial tumor excision is often associated with cyst resolution, however, complete tumor excision may not be possible when tumors are in critical brain locations. Alternative treatments to control tumor cysts include repeated stereotactic aspiration, cyst-reservoir placement, and radioactive isotope instillation. Fractionated radiation therapy and adjuvant chemotherapy are also used in order to control the solid tumor growth. Since many patients with cystic brain tumors undergo treatment involving many modalities, the specific effectiveness of any single therapy is difficult to determine. Nevertheless, we found that stereotactic aspiration is sufficient in the majority of patients to improve neurologic symptoms and in several patients, to facilitate additional treatments aimed at control of the solid tumor component.

Low grade cystic gliomas

In children, hemispheric astrocytomas have been reported to be cystic in 55-70%.[12] In a study of such tumors, Mercuri et al[13] reported that 11 of the 17 cystic tumors were pilocytic astrocytomas. Management strategies included cyst evacuation, excision of the tumor nodule and creation of a communication between the ventricular system and the cyst. Regardless of the extent of excision, long-term outcome has been found to be better in cystic tumors in comparison to solid tumors. Tomita et al[14] reported 13 infants and children with cystic low grade glial tumors. In the cases of pilocytic astrocytomas, these authors recommended excision of the mural nodule alone with preservation of the ependymal layer to avoid subdural hygromas. Palma and Guidetti[15] also reported an excellent prognosis in patients with cystic pilocytic astrocytomas of cerebral hemisphere after mural nodule excision and observed that cyst wall removal or radiation therapy did not have any additional benefit. When the tumor is located in central areas such as the optic chiasm, hypothalamus, or thalamus, we believe a more conservative approach should be selected. In the present series, cyst aspiration for tumors of central location followed by other, less invasive management options has resulted in low morbidity and extended survival.

Malignant cysts glioma

Symptomatic cyst formation in anaplastic astrocytomas and GBM has been reported to be less than 10%,[13] although the incidence is probably much higher. Microcyst formation in anaplastic astrocytomas and GBM is quite common. In a large series of glioblastomas, Frankel and German[16] reported microcystic components in 40% of patients. Large cysts however, are found in 8-10% of the cases.[1,13,17] Poisson et al[1] noted a frequency of 5% to 8% of cystic tumors in patients with recurrent malignant gliomas and designated them “pseudocysts”. Afra et al[17] treated seven patients with cystic glial tumors by aspiration. Single aspiration was sufficient in five patients; in two patients re-accumulation necessitated repeated drainage and finally placement of a reservoir or a shunt. They noted prompt relief of symptoms in four patients in whom the evolution of cyst was accompanied by clinical signs of raised intracranial pressure. In a review of 25 cases of supratentorial cystic gliomas by Loftus et al,[18] maximal feasible tumor resection followed by radiation therapy was the most common procedure that led to cyst control. They reported cyst control in 50% of the patients managed with burr hole aspiration alone. In the present series, 12 of 18 patients with malignant cystic tumors improved symptomatically after cyst aspiration. However, seven of 18 ultimately required further tumor excision at a median of three months following cyst aspiration. Cyst aspiration in malignant glioma offers an opportunity for volume reduction that can improve symptoms of mass effect.

Malignant astrocytomas of the brain stem are more commonly cystic than their supratentorial counterparts.[2] Coffey and Lunsford[19] reported 12 patients with malignant glioma of the brain stem; immediate neurological improvement was observed in six patients who underwent aspiration of the cystic component. Hood and McKeever[2] reported multimodality management of 10 brain stem cystic gliomas. They suggested that aspiration and radiation alone did not prevent cyst re-accumulation in most cases and that additional treatments such as re-aspiration and intracavitary irradiation should be considered. In the present series, nine patients had glial tumors involving brain stem, hypothalamus or thalamus; all nine patients showed improvement after cyst aspiration.

Metastatic cystic tumors

Metastatic brain tumors are usually solid. Cyst formation in a metastasis may occur due to central necrosis or intratumoral hemorrhage.[12] Cystic change is most common in lung carcinoma but also occurs in the context of metastatic breast, pancreas, or kidney carcinomas and with melanoma.[20] In the present series, 9 of the 11 patients who had a cystic metastasis experienced symptomatic improvement after cyst drainage; only two required delayed tumor excision.

Cyst aspiration and symptomatic improvement

Stereotactic aspiration of cystic lesions is a safe and minimally invasive method in the armamentarium of management options. No patient experienced worsening symptomatology. In fact 28 of 38 (73.7%) patients improved at the time of initial aspiration. In patients who improved symptomatically, the median percent volume of fluid aspirated was 80%. Cyst location played a significant role. Eleven of 13 patients (77%) with cystic tumors in deep locations (brain stem, hypothalamus, thalamus) noted symptomatic improvement. Of the patients with cysts in a lobar location, 17 of 25 (68%) experienced improvement following cyst aspiration.

Cyst aspiration in preparation for radiosurgery

Radiosurgery is an effective, minimally invasive treatment modality for both glial and metastatic tumors.[21-23] In the present series, radiosurgery was facilitated in seven patients after cyst aspiration because the target volume was considerably reduced. Stereotactic aspiration is a low risk procedure that can be used (in a single frame application) as an adjunct to (prior to) radiosurgery to reduce the target volume specifically for cystic tumors in critical brain locations. This combination approach (stereotactic aspiration followed by radiosurgery in the same frame application) is effective for symptom improvement as well as prevention of cyst recurrence.

Conclusion

Stereotactic cyst aspiration is a low risk procedure designed to provide temporary relief from intracranial mass effect from symptomatic benign and malignant tumors. Because of the likelihood of cyst re-accumulation, it needs to be followed by adjuvant therapies to reduce fluid formation by the cyst wall or tumor nodule. Cyst-reservoir systems are useful in cases of re-accumulation of cyst fluid. After cyst aspiration, radiosurgery may become possible as the target is smaller and more sharply defined. We found this strategy especially useful for cystic tumors involving deep brain locations.

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