Peritumoral cysts associated with pituitary macroadenoma

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OBJECT Peritumoral cysts are benign nonneoplastic cysts that are found adjacent to extraaxial brain tumors such as meningiomas, schwannomas, craniopharyngiomas, and esthesioneuroblastomas. Peritumoral cysts associated with pituitary macroadenomas have not been previously described in the literature. The authors report 6 cases of giant macroadenoma-associated peritumoral cysts and delineate their imaging spectrum.

METHODS The authors retrospectively reviewed the records of 179 patients diagnosed with pituitary macroadenomas who underwent tumor resection at their institution and had preoperative MRI scans available for review. The patients were evaluated for the presence of associated peritumoral cysts. Clinical presentation, histopathology, follow-up time, tumor and peritumoral cyst dimensions were recorded. Signal intensity on T1-weighted, T2-weighted, diffusion-weighted, and FLAIR sequences, as well as pre- and postcontrast appearance, were determined.

RESULTS Six patients (3.4%) with associated peritumoral cysts were identified in our cohort of 179 patients with pituitary macroadenoma. Twelve patients in the cohort had giant macroadenomas (≥ 4.0 cm), and 50% of these tumors had associated peritumoral cysts with significant extrasellar extension of the macroadenoma. Only tumors with craniocaudal, transverse, and anteroposterior diameters of $3.6 \times 3.4 \times 4.2$ cm to $7.0 \times 7.4 \times 6.8$ cm (mean $5.3 \times 5.1 \times 5.6$ cm), respectively, had associated peritumoral cysts. The growth pattern in all tumors was suprasellar, with predominant anterior and lateral extension.

Cysts showed T1-weighted, T2-weighted, and FLAIR hyperintensity in 67%, 67%, and 60% of patients, respectively. There was no contrast enhancement of the cyst wall or fluid contents in any patient. Postoperatively, cysts had completely resolved (4 of 5) or significantly decreased in size (1 of 5). One patient was lost to follow-up.

CONCLUSIONS Macroadenoma-associated peritumoral cysts are rare, benign, and likely nonneoplastic fluid collections that do not represent neoplasm. These cysts display a predictable pattern of hyperintensity on T1-weighted, T2-weighted, and FLAIR sequences and do not enhance. They most likely represent proteinaceous CSF in a sulcus or cistern that becomes trapped (encysted) by anterolateral extension of unusually large macroadenomas. Peritumoral cysts may facilitate resection of the associated macroadenoma by providing a cleavage plane.

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KEY WORDS peritumoral cyst; intracranial cyst; macroadenoma; tumor-associated cyst; nonneoplastic cyst; pituitary surgery

PERITUMORAL cysts are benign nonneoplastic cysts that have been reported in association with extraaxial brain tumors including meningioma, schwannoma, craniopharyngioma, and esthesioneuroblastoma.^{1,16} Peritumoral cysts occurring with pituitary macroadenomas are occasionally observed on imaging, at surgery or on autopsy (Fig. 1), but have not been previously described in the literature. We report 6 cases of juxtatumoral cysts associated with giant macroadenomas and delineate their imaging spectrum.

Methods

In this institutional review board–approved retrospective study, we reviewed the records of patients who underwent resection for pituitary macroadenoma in our institution from January 2001 through August 2013 for whom pre- and postoperative imaging was available for review. One hundred seventy-nine patients diagnosed with pituitary macroadenoma (defined as a pituitary adenoma ≥ 1 cm in maximum diameter) were identified. Preoperative

ABBREVIATIONS AP = anteroposterior; CC = craniocaudal; DWI = diffusion-weighted imaging; T = transverse.

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FIG. 1. Case 2. Preoperative imaging demonstrating both intratumoral and peritumoral cysts. **Left:** Axial precontrast T2-weighted MR image showing a large lobulated macroadenoma with presence of a common, intratumoral cyst (*hollow arrow*) and rare, peritumoral cysts resulting from obstruction of the left sylvian fissure and right olfactory sulcus (*arrows*). Also present is an obstructed temporal horn of the left lateral ventricle. **Right:** Coronal T1-weighted MR image also showing an intratumoral cyst (*hollow arrow*) and peritumoral cyst located in left sylvian fissure (*arrow*).

imaging was initially reviewed for size in each case to confirm a diagnosis of pituitary macroadenoma. Age at initial diagnosis, sex, histopathology, and clinical presentation were tabulated.

Preoperative MRI scans were reviewed by a neuroradiologist holding certification of added qualifications for the presence or absence of associated peritumoral cyst(s). Imaging findings were analyzed for tumor size measured in 3 dimensions (craniocaudal [CC], transverse [T], and anteroposterior [AP]), presence and direction of tumor extrasellar extension, tumor shape, presence of intratumoral hemorrhage, and restriction on diffusion-weighted imaging (DWI). Tumor volume was approximated by a modified ellipsoid volume formula ($CC \times T \times AP/2$). Peritumoral cysts were examined for signal hyperintensity on T1- and T2-weighted MR images in addition to FLAIR sequences by comparing the measured point value of cyst fluid to CSF within the ventricles. Cyst margins and contents were also evaluated for the presence of enhancement on postcontrast T1-weighted MRI scans. Where available, postoperative MRI scans were also reviewed for resolution of cysts and other postoperative changes. The length of follow-up was determined from clinical records and was defined as time from resection to when the last documented MRI study was performed.

Results

Clinical and Histopathological Findings

Twelve patients were identified with giant macroadenomas (≥ 4.0 cm in maximum diameter); 6 patients (3.4%) had macroadenoma-associated peritumoral cysts within our cohort of 179 patients with pituitary macroadenoma. There were 3 female and 3 male patients. Mean age at diagnosis was 39 years (range 25–57 years). All patients were symptomatic at presentation. Four patients presented with symptoms of visual loss, although none had classic bitemporal hemianopsia. Cognitive decline was present in 3 patients, with incontinence secondary to hydrocephalus presenting concomitantly in the single patient with symp-

tomatic hydrocephalus. Two patients presented with headache as a primary symptom. One patient presented with endocrine abnormalities, and 1 patient presented with a CSF leak (Table 1).

Three of the 6 patients had null cell adenomas on histopathological analysis. One patient had a mixed adenoma of the lactotrophic/somatotrophic (prolactinoma/growth hormone-secreting) subtype, 1 had a lactotrophic adenoma, and 1 had a mixed gangliocytoma/somatotrophic adenoma, a rare 2-cell type of tumor. Two patients had transsphenoidal resections, whereas 4 patients underwent both transsphenoidal and transcranial procedures. The mean follow-up time was 4.1 years (range 0.5–8.9 years), with 1 patient lost to follow-up (Table 1).

Imaging Findings

All 6 macroadenomas were multilobular in shape and exhibited suprasellar extension; 4 (67%), 5 (83%), and 3 (50%) of the macroadenomas also displayed inferior, anterior, and posterior growth patterns, respectively. Mean CC, T, and AP tumor dimensions were 5.3 cm (range 3.6–7.0 cm), 5.1 cm (range 3.4–7.4 cm), and 5.6 cm (range 4.2–6.8 cm), respectively. Mean tumor volume was 77.3 cm³ (range 41.6–138.6 cm³). Associated peritumoral cysts had a mean diameter of 2.9 cm (range 0.6–5.8 cm). On imaging, all 6 macroadenomas obstructed or trapped adjacent sulci and fissures, leading to peritumoral cyst formation. Four patients had cysts involving the sylvian fissure, 3 involving the olfactory sulcus, and 1 each involving the suprasellar cistern and interhemispheric fissure. Three pa-

TABLE 1. Demographic and clinical characteristics of patients with pituitary macroadenoma

Characteristic	Value*
Total group	6 (100%)
Sex	
M	3 (50%)
F	3 (50%)
Mean age at diagnosis in yrs (range)	39 (25–57)
Clinical presentation†	
Visual loss	4 (67%)
Cognitive decline	3 (50%)
Headache	2 (33%)
Incontinence (hydrocephalus)	1 (17%)
Endocrine abnormalities	1 (17%)
CSF leak	1 (17%)
Pituitary adenoma types	
Null cell	3 (50%)
Lactotrophic	1 (17%)
Mixed (somato-/lactotrophic)	1 (17%)
Mixed gangliocytoma/somatotrophic adenoma	1 (17%)
Resection	
Transsphenoidal	2 (33%)
Transsphenoidal and transcranial	4 (67%)
Follow-up time in yrs (range)	4.1 (0.5–8.9)

* Number of patients (%) unless otherwise indicated.

† Several patients presented with more than 1 chief complaint.

tients had solitary peritumoral cysts while the other 3 had 2 or more cysts associated with their tumor (Table 2).

In 4 (67%) of the 6 patients, cyst fluid was hyperintense relative to CSF on T1- and T2-weighted MRI sequences (Fig. 2). One patient with pituitary apoplexy had hemorrhage into the peritumoral cyst. Five of 6 patients had available FLAIR sequence data; 3 (60%) of 5 patients had hyperintense cystic lesions. In 2 patients, cyst fluid was isointense with CSF on all sequences. None of the peritumoral cyst walls or fluid enhanced with contrast. DWI sequences were available for review in 3 patients, and 1 patient demonstrated restricted diffusion (Table 3).

Postoperative MRI scans were available in 5 of 6 patients. The peritumoral cysts had completely resolved in 4 patients (80%) and had significantly decreased in size in 1 patient (20%). There were no recurrences or new hyperintensities in any patient (Table 3).

Discussion

There are 2 types of cysts associated with extraaxial CNS neoplasms (e.g., meningioma, schwannoma, cranio-pharyngioma, and esthesioneuroblastoma): peritumoral and intratumoral. Peritumoral cysts (i.e., tumor-associated cysts) are nonneoplastic cysts that develop at tumor margins. Intratumoral cysts develop within the tumor itself and are usually due to microcystic degeneration, ischemic necrosis, or hemorrhage within the tumor.^{1,5,16,22} The pathogenesis of peritumoral cysts is thought to be quite different. Proposed mechanisms include reactive gliosis, peritumoral edema, or trapping of CSF within the cleft between the expanding tumor and adjacent brain.^{2,9,12,15,20,21} The latter mechanism is the most likely etiology of the cysts in our study.

TABLE 2. Macroadenoma and peritumoral cyst characteristics

Characteristic	Value*
Tumor shape	
Multilobular	6 (100%)
Tumor growth pattern	
Superior	6 (100%)
Inferior	4 (67%)
Anterior	5 (83%)
Posterior	3 (50%)
Tumor dimensions (range)	
CC in cm	5.3 (3.6–7.0)
T in cm	5.1 (3.4–7.4)
AP in cm	5.6 (4.2–6.8)
Volume in cm ³	77.3 (41.6–138.6)
Associated cyst diameter in cm (range)	2.9 (0.6–5.8)
Cyst locations†	
Sylvian fissure	4 (67%)
Olfactory sulcus	3 (50%)
Suprasellar cistern	1 (17%)
Interhemispheric fissure	1 (17%)

* Number of patients (%) unless otherwise indicated.

† Three of 6 patients had 2 or more peritumoral cysts.

Elevated protein concentrations (relative to CSF) have been found in the fluid of peritumoral cysts in several studies.^{6,9–11} We did not evaluate the biochemical composition of peritumoral cystic fluid associated with pituitary macroadenoma and the operating surgeon did not notice a proteinaceous or xanthochromic fluid during the course of resection. All macroadenomas were resected transphenoidally, either as primary resection or in the initial

FIG. 2. Case 4. Preoperative and postoperative imaging. **A:** Preoperative sagittal precontrast T1-weighted MR image showing a large lobulated macroadenoma with significant suprasellar extension (arrow). The left lateral ventricle is obstructed and enlarged. A peritumoral cyst can be seen just anterior to the tumor. Cyst fluid identified by the asterisk (*) is moderately hyperintense to CSF in the trapped ventricle. **B:** Preoperative axial T2-weighted MR image showing the lobulated tumor (arrows) and a large unilocular peritumoral cyst almost completely surrounding the macroadenoma. The cyst fluid measured moderately hyperintense relative to CSF. **C:** Preoperative axial FLAIR image showing that the cyst fluid (indicated by asterisk) is significantly hyperintense relative to CSF and does not suppress. **D:** Preoperative axial postcontrast, fat-saturated T1-weighted MR image showing that the lobulated macroadenoma enhances intensely. The cyst wall (arrows) and cyst fluid (indicated by asterisk) do not enhance. **E:** Preoperative coronal postcontrast T1-weighted MR image showing the superolateral extension of the macroadenoma. The juxtatumoral cyst wall (arrow) does not enhance. **F:** Axial precontrast T1-weighted MR image showing postoperative collapse of peritumoral cyst (arrow) that is communicating with the right lateral ventricle.

TABLE 3. Preoperative peritumoral cyst MRI characteristics and postoperative outcome

Case No.	Hyperintensity Pattern			Contrast Enhancement	DWI Restriction	Prominent Perivascular Spaces	Hemorrhage	Postop Cyst Resolution
	T1	T2	FLAIR					
1	+	+	NA†	–	NA†	–	–	Complete
2	+	+	+	–	–	–	+	Partial
3	–	–	–	–	NA†	–	–	Complete
4	+	+	+	–	NA†	–	–	Complete
5	+	+	+	–	–	–	–	NA
6	–	–	–	–	+	–	–	Complete
Total‡	4 (67%)	4 (67%)	3 (60%)	0	1 (33%)	0	1 (17%)	

NA = not available; +/- = pattern observed/not observed.
* Cysts were isointense to slightly hyperintense on T2-weighted MRI.
† Designated sequence was not performed.
‡ Total number of patients and (%) calculated as a total of patients who had the designated MRI sequence.

approach, so observation of the surrounding peritumoral cysts and the response to surgical decompression was not possible. The walls of the cysts were not specifically sampled at the time of surgery; drainage of cysts occurred at the time of the resection as verified on postoperative imaging. The preoperative MRI findings in our cases, however, are consistent with elevated protein concentrations within most of the peritumoral cysts, which were hyperintense on T1-weighted and FLAIR imaging sequences in the majority of our patients.^{7,13} The high prevalence of hyperintensity on T2-weighted images is also consistent with cystic lesions and peritumoral edema.^{4,9} We also observed in the 2 cases with isointense cystic fluid that the CSF flow within these spaces was not completely obstructed, and they continued to communicate to some extent with the ventricles and subarachnoid space. None of our 6 cases showed enhancement on postcontrast MRI scans, which is consistent with previously reported findings and indicates that neither blood-brain barrier disruption nor the tumor itself is the source of the peritumoral cysts.^{8,9} Thus, it is likely that as a juxtatumoral cleft becomes completely trapped, it begins to become more proteinaceous relative to CSF.

In previous studies, entrapment or loculation of CSF was criticized as an improbable mechanism of peritumoral cyst formation in extraaxial tumors,^{3,9,14} although these studies did not evaluate cysts associated with pituitary macroadenoma. Each tumor in our study demonstrated an anatomical relationship to the surrounding fissures and sulci, indicating that the expanding tumor likely traps CSF in the adjacent cleft. We observed that peritumoral cysts were only associated with macroadenomas that grew to a diameter of at least 4.2 cm in the AP direction. The only macroadenoma less than 4.0 cm in either the CC or T diameters also had reached the maximal AP diameter, 6.8 cm, achieved by any tumor in our study. During our investigation, we identified only 12 patients (7%) with giant macroadenomas (defined as a tumor ≥ 4.0 cm) that were ≥ 4.2 cm in any dimension, the minimum diameter we observed in patients with cysts (data not shown). Six of these patients did not develop cysts, which was likely because of the primarily suprasellar growth pattern with T or AP diameters less than 4.2 cm (Fig. 3). The 6 cases included in our study also had exclusively multilobular macroadenoma shapes, whereas the other 6 patients had either rounded or “snowman”-shaped tumors. The size and growth pat-

FIG. 3. Images obtained in 1 of 6 patients with giant macroadenoma (dimensions of 5.1 × 2.8 × 2.5 cm in the CC, T, and AP diameters, respectively) who did not develop associated peritumoral cysts. **A:** Coronal T1-weighted precontrast MR image showing predominantly CC growth pattern without associated peritumoral cyst. **B:** Axial T2-weighted MR image showing a lobulated macroadenoma with T extension toward left sylvian fissure but without obstruction (arrow). **C:** Sagittal T1-weighted MR image also demonstrating predominant suprasellar growth pattern of macroadenoma (asterisks) with minimal AP growth.

tern correlation in our study supports a primary etiology of CSF obstruction in peritumoral cysts associated with pituitary macroadenoma.

It is generally believed that resection of the associated neoplasm with evacuation of cyst fluid will decompress and resolve the peritumoral cyst;⁹ however, some authors have shown persistence of the cyst despite this method and have postulated that there may be neoplastic meningothelial cells within the cyst wall.^{8,19} Others have reported that cyst walls consist of glial cell proliferation as confirmed by the presence of glial fibrillary acidic protein.^{17,18} In our study, we did not observe any evidence of a cystic capsule, and with no recurrences, it is unlikely that glia play a role in peritumoral cyst formation associated with pituitary macroadenoma. Thus, the cyst itself does not need to be resected or drained if the associated tumor is sufficiently resected to relieve the obstruction. The cyst may actually aid in tumor resection by providing an enhanced cleavage plane to spare normal brain.

Conclusions

Peritumoral cysts associated with pituitary macroadenoma are uncommon and previously undescribed in the literature. These cysts are likely nonneoplastic, occur outside of the tumor margins, and should not be mistaken for neoplasm. Here, we report 6 cases that were associated with large macroadenomas that demonstrated extensive anterolateral growth resulting in obstruction of CSF in adjacent brain fissures or sulci. These cysts do not appear to recur or increase in size after surgical decompression and resection of the associated macroadenoma. Peritumoral cysts may aid in resection by functioning as a cleavage plane while resection of the cysts themselves is likely unnecessary.

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