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Hemorrhagic and nonhemorrhagic Rathke cleft cysts mimicking pituitary apoplexy

Mandy J. Binning, M.D.,[1] James K. Liu, M.D.,[2] John Gannon, B.S.,[1] Anne G. Osborn, M.D.,[3] and William T. Couldwell, M.D., Ph.D.[1]

Departments of [1]Neurosurgery and [3]Radiology, University of Utah, Salt Lake City, Utah; and [2]Department of Neurological Surgery, Northwestern University Feinberg School of Medicine, Evanston Northwestern Healthcare, Evanston, Illinois

Object. Rathke cleft cysts (RCCs) are infrequently symptomatic, and apoplexy is one of the most unusual presentations. Only a few cases of apoplexy associated with RCCs have been reported, and their clinical, imaging, surgical, and pathological features are poorly understood. In the cases that have been reported, intracystic hemorrhage has been a consistent finding. The authors report 6 cases of RCCs in which the presenting clinical and imaging features indicated pituitary apoplexy, both with and without intracystic hemorrhage.

Methods. The authors retrospectively reviewed charts and magnetic resonance (MR) imaging studies obtained in patients who underwent transsphenoidal surgery for RCC. Six patients were identified who presented with symptoms and MR imaging characteristics consistent with pituitary apoplexy but were found intraoperatively to have an RCC. All 6 patients presented with a sudden headache, 2 with visual loss, and 1 with diplopia. Review of the preoperative MR images demonstrated mixed signal intensities in the sellar masses suggestive of a hemorrhagic pituitary tumor. In all patients there was a presumed clinical diagnosis of pituitary tumor apoplexy and an imaging-documented diagnosis of hemorrhagic pituitary tumor.

Results. All 6 patients underwent transsphenoidal resection to treat the suspected pituitary apoplexy. Intraoperative and histopathological findings were consistent with the diagnosis of an RCC in all cases. Only 2 cases showed evidence of hemorrhage intraoperatively. In all cases, an intracystic nodule was found within the RCC at surgery, and this intracystic nodule was present on the initial MR imaging when retrospectively reviewed. The imaging characteristics of the intracystic nodules were similar to those of acute hemorrhage seen in cases of pituitary apoplexy.

Conclusions. The clinical and imaging features of RCCs appear similar to those of hemorrhagic pituitary tumors, making them often indistinguishable from pituitary apoplexy. *(DOI: 10.3171/JNS/2008/108/01/0003)*

Key Words • pituitary apoplexy • pituitary tumor • Rathke cleft cyst • transsphenoidal surgery

Rathke cleft cysts are nonneoplastic sellar and suprasellar lesions derived from remnants of the Rathke pouch. They are often asymptomatic and are often found incidentally because they are not typically large enough to cause compression or a mass effect on surrounding structures. When an RCC is symptomatic, the patient can present with headaches or symptoms due to compression of the optic chiasm, cavernous sinus, hypothalamus, or pituitary gland.[5,7,14,16–18,21] Rarely, RCCs can present in a manner similar to pituitary apoplexy, with acute-onset headaches, nausea and vomiting, meningismus, visual field and acuity loss, oculomotor palsies, and, less commonly, hypothalamic dysfunction.[9,14,16–18] Although the authors of recent reports have described the neuroimaging characteristics of RCCs,[9,14,16–18] it can be difficult to distinguish the characteristic intracystic nodule of an RCC from acute hemorrhage seen in pituitary apoplexy. In addition, intracystic hemorrhage has been a consistent feature in the reported cases of RCC apoplexy, making a diagnosis even more difficult to establish. Nonhemorrhagic RCC apoplexy has not been reported in the literature but is a distinct clinical entity. We present an interesting series of patients with RCCs who presented with symptoms of pituitary apoplexy both in the presence and absence of hemorrhage.

In this report, we detail 6 patients with RCCs (2 hemorrhagic and 4 nonhemorrhagic) who presented with clinical pituitary apoplexy and neuroimaging characteristics similar to those of hemorrhagic pituitary tumors.

Abbreviations used in this paper: MR = magnetic resonance; RCC = Rathke cleft cyst.

Clinical Material and Methods

The OpCoder operative database at the University of Utah was searched to generate a list of patients who underwent transsphenoidal surgery and were found to have an RCC at the time of surgery. The hospital charts of these patients were then reviewed to determine whether the patients had presented with any of the following clinical symptoms consistent with pituitary apoplexy: sudden onset of a headache, nausea/vomiting, meningismus, visual field or acuity

loss, or diplopia from oculomotor palsies. The clinic notes and preoperative notes were screened to establish whether "pituitary apoplexy" was documented in the differential diagnosis. The records of identified patients were reviewed further to establish the clinical, imaging, surgical, and pathological features of these cases of RCC apoplexy.

The preoperative MR imaging studies obtained in all identified patients were reviewed for the presence of hemorrhage, suprasellar optic compression, lateral compression of the cavernous sinus, and sphenoid sinus mucosal thickening and enhancement. All MR images were reviewed to determine whether either "hemorrhagic pituitary tumor" or "pituitary apoplexy" was documented in the differential diagnosis by the radiologist. The MR images were also reviewed to see whether an intracystic nodule of RCC was present.

All patients had undergone transsphenoidal surgery for a presumed clinical and imaging diagnosis of pituitary apoplexy. The operative reports were reviewed to determine the presence or absence of hemorrhage or an intracystic nodule. All available pathology reports were also reviewed to confirm the diagnosis of RCC.

This retrospective review was approved by the Institutional Review Board. All data acquisition and chart reviews were in compliance with the Health Insurance Portability and Accountability Act of 1996 and regulations determined by the University of Utah Institutional Review Board.

Results

Clinical Presentation

Chart review and search of the operative database yielded 6 cases in which initial clinical presentation and neuroimaging characteristics raised suspicion of pituitary apoplexy and in which the patients were ultimately identified as having an RCC (Table 1).

All 6 patients (4 women and 2 men) had a diagnosis of presumed pituitary apoplexy documented in the chart before surgery. The mean age of these patients was 32 years (range 20–54 years). All patients presented with a sudden-onset headache (including 3 in whom headache was the only symptom), 2 (33%) presented with additional visual acuity or field loss, and 1 (17%) presented with additional diplopia due to oculomotor palsy. All patients underwent preoperative endocrinological testing. One patient had mildly decreased testosterone levels, 1 had slightly decreased thyroid hormone levels (free T4 and T3), and 1 had a mildly elevated prolactin level from stalk effect.

Neuroimaging Studies

On preoperative MR imaging, in all 6 patients we observed a sellar/suprasellar mass with cystic features and mixed signal intensities. These findings were suggestive of a hemorrhagic pituitary tumor. Similarly, in all 6 patients, pituitary apoplexy or hemorrhagic pituitary adenoma was documented as part of differential diagnosis on the imaging report. Specifically, MR imaging consistently revealed an area within the cystic mass that exhibited T1-weighted hyperintensity, T2-weighted hypointensity, and no contrast enhancement; however, in retrospect, it was clear that these signal characteristics were also consistent with an intracystic nodule found in the RCC, which was observed on a second review of the MR images. Four patients had imaging evidence of optic nerve compression, and 2 of these patients presented with subjective and objective evidence of visual acuity and field loss. In 5 patients there was imaging evidence of lateral compression on the cavernous sinus and in only 1 was there clinical evidence of diplopia due to oculomotor palsy. In 3 patients, imaging demonstrated evidence of sphenoid sinus mucosal thickening and enhancement.

Operative Findings

All patients underwent transsphenoidal surgery for presumed pituitary apoplexy. Intraoperative and histopathological findings were consistent with the diagnosis of RCC in all cases, and marsupialization of the RCC was performed. In only 2 cases was there intraoperative evidence of hemorrhage; the remainder of the lesions were nonhemorrhagic and had typical proteinaceous mucoid material found in RCCs. An intracystic nodule was found intraoperatively in all 6 patients.

Illustrative Cases

Case 1

This 20-year-old man presented to an outside facility with acute headaches, nausea, vomiting, and diplopia. Initial MR imaging demonstrated a sellar mass of mixed signal intensity (Fig. 1A and B). The patient elected to receive conservative therapy, and his headaches and diplopia eventually resolved. He was referred to our clinic 3 months after his apoplectic event when he requested further counseling regarding the mass. Repeated MR imaging (Fig. 1C–E) revealed a decrease in the size of the mass with persistent mixed signal intensity suggestive of hemorrhagic products. Preoperative endocrine findings were all normal except for a low testosterone level of 134 ng/dl (reference range 350–890 ng/dl at our institution). The patient underwent transsphenoidal resection, and a nonhemorrhagic RCC with an intracystic nodule was found. In retrospect, we saw that the intracystic nodule was present on the MR imaging; it appeared hyperintense on T1-weighted images (Fig. 1A and C) and hypointense on T2-weighted images (Fig. 1D). This is a most interesting case in that the RCC diminished in size on the follow-up images, without evidence of previous hemorrhage at surgery.

Case 2

This 23-year-old woman presented with acute headaches and bitemporal hemianopsia. Magnetic resonance imaging demonstrated a sellar mass with suprasellar extension of heterogeneous intensity with peripheral enhancement suggestive of a hemorrhagic pituitary adenoma (Fig. 2A–D, *arrow* in panel E). There was sphenoid sinus mucosal thickening and enhancement (Fig. 2D, *small arrow*). The results of the preoperative endocrine workup were normal except for a mildly elevated prolactin of 34.5 ng/ml (reference range 2.8–26 ng/ml), likely due to stalk effect. The patient underwent transsphenoidal decompression for presumed pituitary apoplexy. At surgery, an RCC with an intracystic nodule was identified; there was no evidence of

TABLE 1

*Summary of clinical presentation, imaging characteristics, intraoperative findings, and outcomes in patients with RCC apoplexy in this series and case reports in the literature**

Case No./ Author & Year	Age (yrs), Sex	Presentation	Apoplexy Grade†	SSMT	Location/ Finding	Preop Endocrine Findings	Intracystic Nodule		Hemorrhage at Surgery	Postop Endocrine Results	Postop Neurological Outcome
							On MRI	At Surgery			
1	20, M	HA, nausea, vomiting, diplopia	II	no	S, CC	decreased testosterone	yes	yes	no	testosterone HRT	normal
2	23, F	HA, visual loss	II	yes	S, CC, OC	mild PRL elevation	yes	yes	no	normal	normal
3	49, M	HA	I	no	S	normal	yes	yes	no	normal	normal
4	21, F	HA	I	yes	S, CC, OC	decreased T4, normal TSH	yes	yes	no	thyroid HRT	normal
5	24, F	HA	I	no	S, CC, OC	normal	yes	yes	yes	normal	normal
6	54, F	HA, visual loss, meningismus	II	yes	S, CC, OC	normal	yes	yes	yes	normal	normal
Onesti et al., 1990	25, F	HA	I	no	S, OC	normal	no	not mentioned	yes	normal	normal
Kurisaka et al., 1998	8, F	HA	I	no	S, OC	normal	mixed intensity	yes, based on description	yes	normal	normal
Nishioka et al., 1999	46, F	HA, visual loss	II	no	S, OC	normal	mixed intensity	not mentioned	yes	normal	normal
Pawar et al., 2002	19, M	HA, blurred vision	II	no	S	normal	no	not mentioned	yes	normal	normal
Rosales et al., 2004	34, M	HA, diplopia	II	no	S, CC, OC	PRL elevation, decreased T4, normal TSH	no	not mentioned	yes	HRT for DI & thyroid	normal

* CC = cavernous sinus compression; DI = diabetes insipidus; HA = headache (acute); HRT = hormone replacement therapy; OC = optic compression; PRL = prolactin; S = sellar; SSMT = sphenoid sinus mucosal thickening; TSH = thyroid stimulating hormone.

† Apoplexy grade based on classification described in Liu and Couldwell.

hemorrhage. In retrospect, we found that the intracystic nodule was present on the MR imaging studies, appearing hyperintense on T1-weighted images (Fig. 2A and B) and hypointense on T2-weighted images (Fig. 2C).

Discussion

Pituitary apoplexy, whether related to hemorrhage or infarction, most commonly occurs in association with pituitary adenomas and thus has been described by some authors as pituitary tumor apoplexy.[20] It is rarely associated with other sellar lesions such as RCCs. Clinically, RCCs are infrequently symptomatic, and apoplexy is one of the most unusual presentations. When symptoms are present, the most common is headache. In addition, patients with RCCs can present with visual deficits, hypopituitarism, and hypothalamic dysfunction. Symptoms in these cases are directly related to the degree of compression on surrounding parasellar structures. To date, few cases of RCC apoplexy have been reported in the literature, and their clinical, imaging, operative, and pathological features are poorly understood.[9,14,16–18] Although the neuroimaging characteristics of RCCs have been extensively reported, it often remains difficult to differentiate RCCs from other cystic sellar or suprasellar lesions, especially in the face of suspected hemorrhagic apoplexy.

Rathke cleft cysts may appear similar to other cystic sellar and suprasellar lesions, such as craniopharyngiomas and pituitary adenomas, and the MR imaging signal intensity is often extremely variable on T1- and T2-weighted images.[3,5,13] Classic attempts at differentiating RCCs from these other pituitary lesions on MR images have been based on signs including smooth contours, the lack of a cyst wall or an extracystic solid component, absence of calcification, homogeneous attenuation, and absence of enhancement.[1,3,6,8,11–13,15,19]

The authors of several recent reports have detailed the imaging characteristics of intracystic nodules associated with RCCs.[2–4] The nodules consistently display low signal intensity on T2-weighted images and high signal intensity on T1-weighted images, with no enhancement after Gd administration. In addition, the nodule is typically well circumscribed and discrete. The detection of intracystic nodules on T1-weighted images can sometimes be more difficult because of similar signal intensities between the surrounding cyst fluid and the nodule. The nodule can often appear isointense to slightly hyperintense to the surrounding cyst fluid on T1-weighted images. In contrast, the nodule is more easily observed on T2-weighted images because most intracystic nodules are hypointense relative to the hyperintense surrounding cyst fluid.

Liu and Couldwell[10] noted the presence of sphenoid sinus mucosal thickening on MR imaging has been reported in up to 79% of patients with pituitary apoplexy. This find-

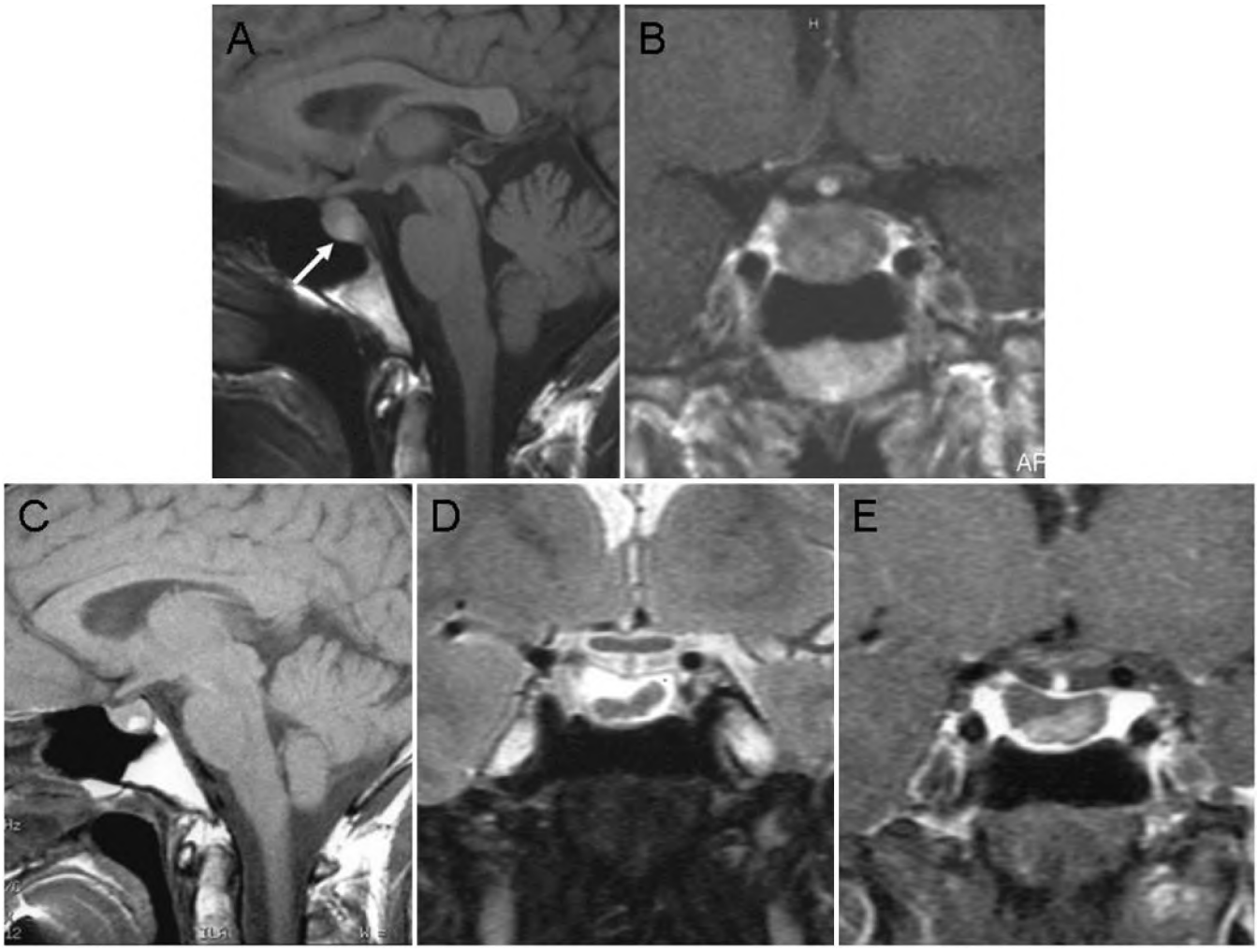

FIG. 1. Case 1. A and B: Initial T1-weighted images. Sagittal unenhanced (A) and coronal contrast-enhanced (B) images showing an intrasellar mass with an area of T1 shortening (A, *arrow*). The mass does not enhance after contrast medium administration. C–E: Follow-up images obtained 3 months later demonstrating interval decrease in the size of both the mass and intracystic lesion. The sagittal T1-weighted image (C) showing that the intracystic nodule appears even more hyperintense. Coronal T2-weighted image (D) demonstrating that the mass is somewhat oblong and isointense with the brain. A coronal T1-weighted image obtained after contrast medium administration (E) showing that the hyperintense intracystic lesion is smaller than it appears in panel B. The lesion itself does not enhance. An RCC with an intracystic nodule and no hemorrhage was found at surgery.

ing, however, is neither specific for nor does its absence exclude the diagnosis of pituitary apoplexy. In our series, sphenoid sinus mucosal thickening was seen in 50% of patients (1 case of Grade I and 2 cases of Grade II apoplexy[10]) (Fig. 2). In 2 of these patients, no intracystic hemorrhage was found at the time of surgery. As noted in Case 1 (Fig. 1), rarely are there changes in the size of the cystic lesion that can be documented commensurate with symptoms or their resolution, suggesting that a simple RCC may be somewhat dynamic in nature. One patient with intracystic hemorrhage did not have mucosal thickening, making this imaging finding unreliable as an indicator of pituitary apoplexy or intracystic hemorrhage.

Apoplexy associated with RCCs has been previously reported.[9,14,16–18] All 6 patients in our series presented with acute onset of severe headache. Of these, 2 presented with visual deficits. Kurisaka et al.[9] reported a case of sudden-onset severe headache in an 8-year-old girl in whom imaging demonstrated hemorrhage into a cystic sellar lesion. At surgery, she was found to have a hemorrhagic RCC. Nishioka et al.[14] described a case of a 46-year-old woman who suffered a clinical apoplectic event, but in whom intraoperatively there was evidence of repeated episodes of hemorrhage. In all of the cases reported in the literature the authors have described patients with documented hemorrhage into an RCC. In contrast, the existence of nonhemorrhagic RCC apoplexy has not been described. The clinical and imaging features of nonhemorrhagic RCC apoplexy were indistinguishable from those of patients with hemorrhagic RCC apoplexy in our patients, all of whom had a presumed clinical and imaging diagnosis of pituitary apoplexy preoperatively. In addition, no reference is made in the literature to the existence of intracystic nodules either on preoperative MR imaging or intraoperatively in cases of RCC

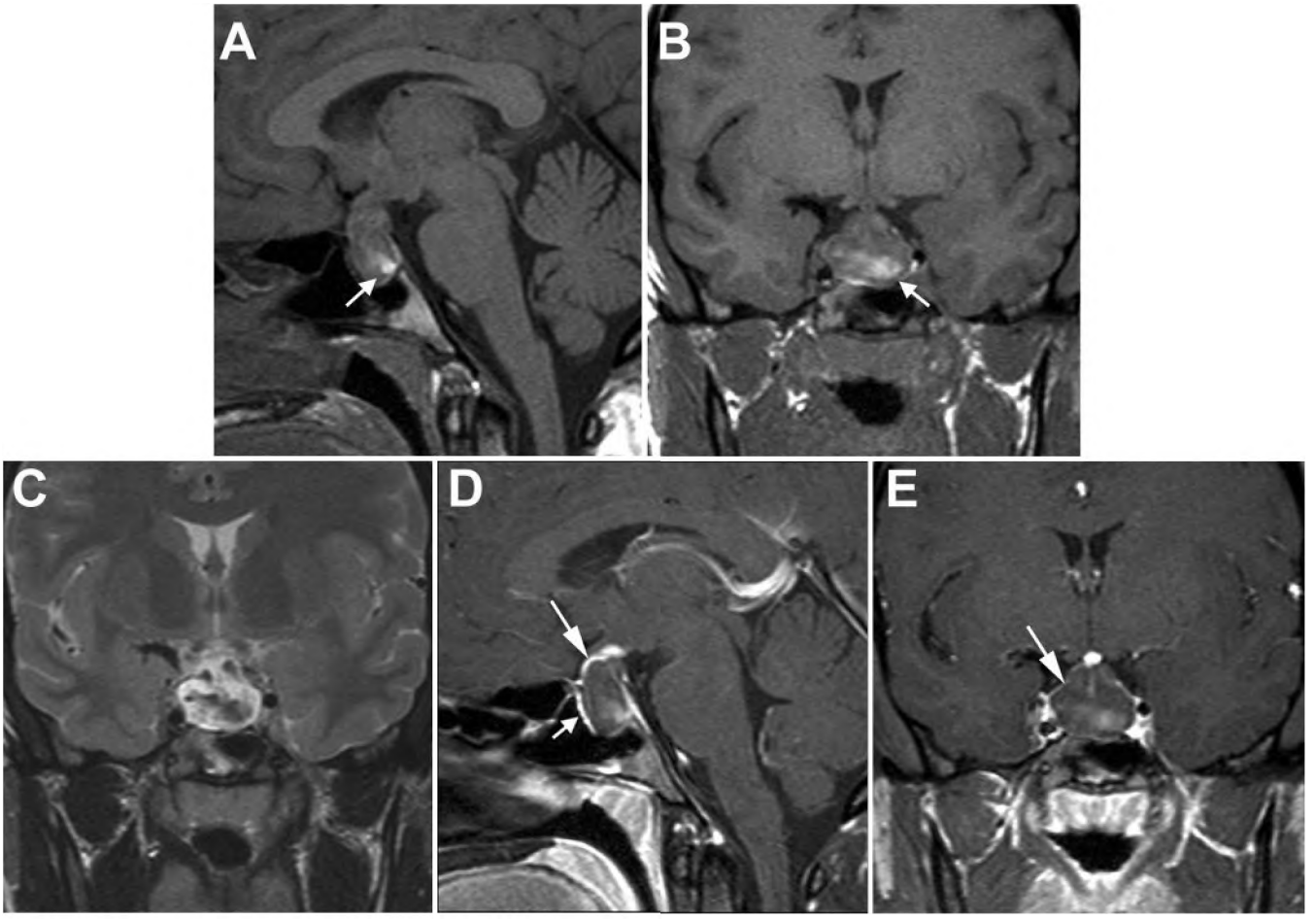

FIG. 2. Case 2. Sagittal (A) and coronal (B) T1-weighted MR images obtained before contrast medium administration, showing an intrasellar mass with suprasellar extension. The mass is predominately isointense with brain and contains some foci with T1 signal shortening *(arrows)*, suggesting subacute hemorrhage. Coronal T2-weighted MR image (C) demonstrating that the lesion is predominantly hyperintense with some central hypointense foci. Sagittal (D) and coronal (E) postcontrast T1-weighted MR images revealing rim enhancement *(large arrows)* around the lesion together with mucosal thickening in the adjacent sphenoid sinus (*small arrow* in D). The preoperative diagnosis in this patient was pituitary apoplexy. At surgery, the presence of an RCC was noted. No hemorrhage was identified, and the intracystic foci were identified as inspissated protein.

apoplexy. Because of similar MR imaging characteristics, these nodules can easily be mistaken for hemorrhage, making the preoperative diagnosis between RCC and pituitary tumor apoplexy problematic. Although gradient-refocused T2*-weighted imaging is helpful in identifying parenchymal brain hemorrhage, this modality is not routinely performed in standard sella/pituitary protocols and was not performed in any of our patients.

The diagnosis of pituitary apoplexy was presumed in all 6 cases on the basis of the clinical syndrome of acute headaches with or without cranial nerve deficits coupled with mixed signal intensity on MR imaging. Hemorrhage was only found, however, in 2 patients at the time of surgery. This can explain the sudden onset of apoplectic symptoms in these patients. In patients without intracystic hemorrhage, the possibility of cyst expansion and encroachment on neighboring structures may provide a possible mechanism for nonhemorrhagic RCC apoplexy.

The surgical management of patients with pituitary apoplexy compared with that of those patients with RCC and apoplectic symptoms depends on the patient's presenting symptoms. Patients with a sellar/suprasellar lesion and visual deficits or endocrine disturbance as well as evidence of mass effect on the optic apparatus, pituitary stalk, or gland, may require transsphenoidal surgery for decompression and resection of the cyst. Patients who present with headache, without cranial nerve deficits, and with no evidence of hemorrhage on gradient-refocused T2*-weighted imaging may be good candidates for symptomatic treatment and observation.

Conclusions

Rathke cleft cyst apoplexy is a very rare clinical entity. It can be either hemorrhagic or nonhemorrhagic in character. Its clinical and imaging features are often difficult to distinguish from those of pituitary tumor apoplexy. Although intracystic nodules in association with RCCs are common

MR imaging findings, it may be difficult to make a distinction between the nodules and hemorrhage because of similar signal intensities on standard imaging sequences. In the presence of apoplectic symptoms, however, it is important to include RCCs in addition to pituitary apoplexy in the differential diagnosis.

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Address correspondence to: William T. Couldwell, M.D., Ph.D., Department of Neurosurgery, University of Utah, 175 North Medical Drive, Salt Lake City, Utah 84132, email: neuropub@hsc.utah.edu.