

Hemorrhage Within Pituitary Adenomas: How Often Associated with Pituitary Apoplexy Syndrome?

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To determine the clinical significance and specificity of suspected intratumoral hemorrhage in pituitary adenomas, we reviewed the clinical presentations, CT results, and findings at surgery in 12 patients who had hyperintense signal within intrasellar and suprasellar masses on short TR/TE spin-echo MR pulse sequences. Eight of the cases were confirmed at surgery. In seven of the operated cases, hemorrhage was found within pituitary adenomas and in the eighth case there was hemorrhage but no identifiable adenomatous tissue. Nine of the 12 patients had CT scans; three had focal areas of increased attenuation, four had focal areas of decreased attenuation, and two had uniform hypoattenuation. All nine of these CT abnormalities correlated with areas of hemorrhage on MR. Three patients had clinical apoplexy; in two there was increased attenuation on CT and in one it was decreased.

We found that intratumoral hemorrhage may be seen without clinical evidence of pituitary apoplexy, and that the areas of hemorrhage can appear as low attenuation on CT. CT may be better for visualizing intratumoral hemorrhage within the first few days, but MR is more sensitive in detecting and following the hemorrhage in the subacute stage.

Clinical pituitary apoplexy is the sudden infarction, either bland or hemorrhagic, within a normal or neoplastic pituitary gland. The gland suddenly enlarges and may cause compression of structures adjacent to the sella. This can lead to a number of signs and symptoms, including sudden loss of visual acuity with a chiasmal field loss, oculomotor palsies, and severe headache. In addition, the patient may experience decreased sensorium, hypopituitarism, and subarachnoid irritation, the latter being secondary to hemorrhage [1]. Proper clinical management may not only save the patient's vision but also the patient's life. CT has been used to diagnose bland and hemorrhagic infarction within pituitary adenomas [2]. CT can visualize acute (approximately first 3 days) hemorrhage within the adenoma, but subacute (approximately 4 days to 1 month) and chronic (older than 1 month) hemorrhage may be confused with cystic degeneration, abscesses, and bland infarction, as these all have lower absorption coefficients [2]. MR has been shown to be a sensitive method for detecting hematomas within the brain, especially in the subacute and chronic stages [3], and has been used to study pituitary adenomas [4-10]. Subacute hemorrhage within pituitary adenomas can be recognized as an area of hyperintensity on short TR/TE spin-echo pulse sequences. The purpose of this study was to determine whether patients with MR evidence of intratumoral hemorrhage had clinical evidence of pituitary apoplexy, and to correlate the MR findings with surgery and CT.

Subjects and Methods

Twelve patients (10 females, 2 males) 15-73 years old (mean, 38 years) were studied by MR imaging because of symptoms referable to a pituitary mass, including headaches, bitemporal hemianopsia, galactorrhea, amenorrhea, oculomotor palsies, subarachnoid hem-

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orrhage, epistaxis, and seizures. Since the case material was obtained from three medical centers, varying CT and MR scanners were used. High-resolution CT scanners were used with 1.5- to 3.0-mm-thick sections, taken in the coronal and/or axial planes through the sella with and without IV contrast material. Three patients had contrast-enhanced scans only and three patients did not have CT. Because this was both a retrospective and prospective study and

was carried out at three institutions, a variety of TRs, TEs, and excitations were used. Multiple-plane MR studies were performed on 0.5-, 1.0-, and 1.5-T units with TRs of 250–2000 msec, TEs of 16–140 msec, and 5-mm or smaller sections. All patients had T1-weighted, 250–800/13–40 (TR/TE), and T2-weighted, 2000–3000/60–140, studies. The time interval between the intrasellar hemorrhage and the MR scan in those nine patients who did not have an abrupt

TABLE 1: Summary of Patients with MR Evidence of Intratumoral Hemorrhage

Case No.	Age	Gender	Clinical Findings	CT Findings	T1-weighted MR Findings	Time from MR to Surgery	Findings at Surgery
1	24	F	Headaches; bitemporal hemianopsia; galactorrhea	Hypodense	Increased intensity throughout	3 months	Hemorrhage into pituitary adenoma
2	36	M	Acute decreased vision, right eye; sixth nerve palsy; diagnosis: apoplexy	Focal area of increased density	Focal area of increased intensity	10 days	Hemorrhage into pituitary adenoma
3	62	F	Bitemporal hemianopsia	None	Focal area of increased intensity	6 weeks	Hemorrhage into pituitary adenoma
4	15	F	Headaches; small stature; hypopituitarism; no menarche; normal visual field	Focal area of low density	Focal area of increased intensity	1 month	Hemorrhage into pituitary adenoma
5	50	F	Epistaxis	No focal areas of density abnormality but erosion of skull base	Two areas of increased intensity	No surgery; bromocriptine	—
6	73	F	Subarachnoid hemorrhage; diagnosis: apoplexy	(Contrast-enhanced study only); decreased density, left gland; enhancement, right gland	Increased intensity, left gland	3 days	Hemorrhage into pituitary adenoma
7	29	M	Decreased vision	(Contrast-enhanced study only); areas of increased density	Increased intensity	1 day	Hemorrhage into pituitary adenoma
8	22	F	Amenorrhea-galactorrhea; elevated prolactin	(Contrast-enhanced study only); decreased density, left gland	Increased intensity, left gland	Lost to follow-up	—
9	30	F	Elevated prolactin	None	Increased intensity	5 days	Hemorrhage into pituitary adenoma
10	41	F	Panhypopituitarism 10 years before; bitemporal hemianopsia; headache	Peripheral Ca ⁺⁺ ; decreased density	Increased intensity	6 months	Hemorrhage; no tumor at surgery; presumed old adenoma
11	49	F	Status post-adenoma resection 6 years before with recurrence; bitemporal hemianopsia	No recent CT study (last CT in 1983)	Increased intensity; follow-up: decreased intensity	No surgery	—
12	29	F	Severe, sudden headaches; bitemporal hemianopsia in last 2 weeks of pregnancy; diagnosis: apoplexy	Increased density	Increased intensity; fluid level	No surgery; bromocriptine	—

onset of clinical symptoms is unknown. In the three patients with pituitary apoplexy, however, MR scans were obtained between 5 days and 1 month after the onset of the apoplectic event.

Results

Twelve patients had MR evidence of intrasellar hemorrhage (Table 1). These patients had focal areas of increased signal intensity on short TR/TE pulse sequences that remained as high signal intensity on long TR/TE sequences, correlating with the presence of methemoglobin in subacute hematomas [3]. Eight of the 12 patients had surgical confirmation of intrasellar hematomas, with seven of these hematomas found within pituitary macroadenomas (Fig. 1). One surgical patient had no evidence of adenomatous tissue but did have a hematoma. This patient had a presumed pituitary adenoma 10 years earlier (Fig. 2). Of the four patients who had no surgery, one (Fig. 3) had a presumed recurrence of a pituitary

adenoma that had been resected 6 years earlier, one (Fig. 4) had hemorrhage into a presumed adenoma and was treated with bromocriptine, another (case 5) was treated with bromocriptine alone, and one (case 8) was lost to follow-up.

Nine of the 12 patients had recent CT scans. Three patients had focal areas of increased density (Fig. 5) and four patients had focal areas of decreased attenuation (Fig. 6). Both of these patterns correlated with MR evidence of hemorrhage. Two patients had no focal areas of increased or decreased density but had homogeneous-appearing adenomas, one being diffusely slightly hypodense (Fig. 1) and the other a slightly enhancing adenoma eroding the skull base. Three patients had contrast-enhanced CT scans only; one of these had focal areas of increased density (Fig. 7) and two had decreased attenuation on the left side of the adenoma and enhancement on the right side (Fig. 8).

Three patients had clinical evidence of pituitary apoplexy, while the other nine patients had no clinical evidence of this

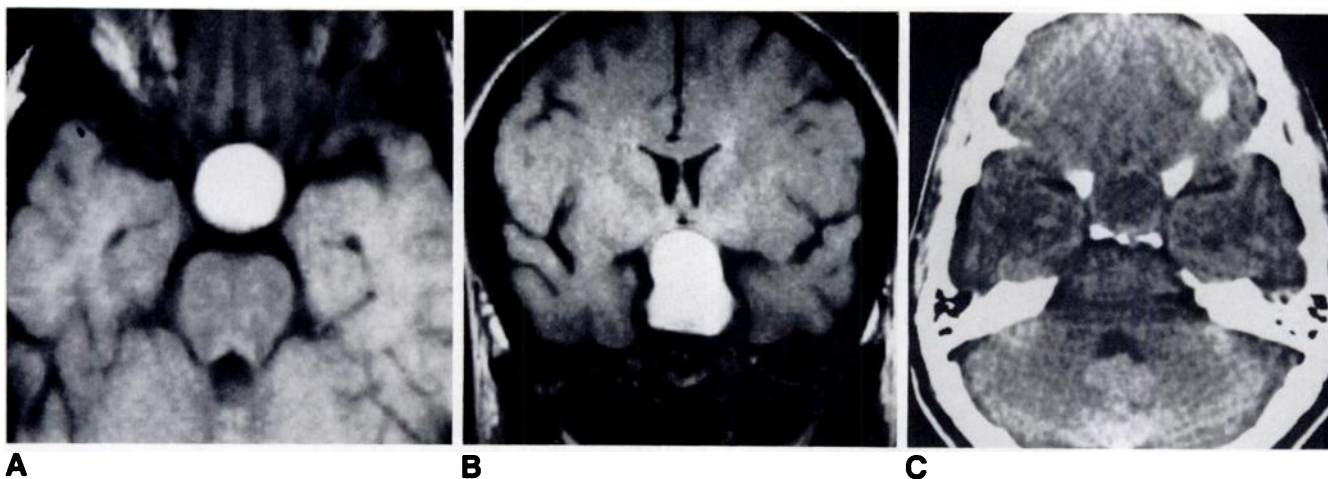
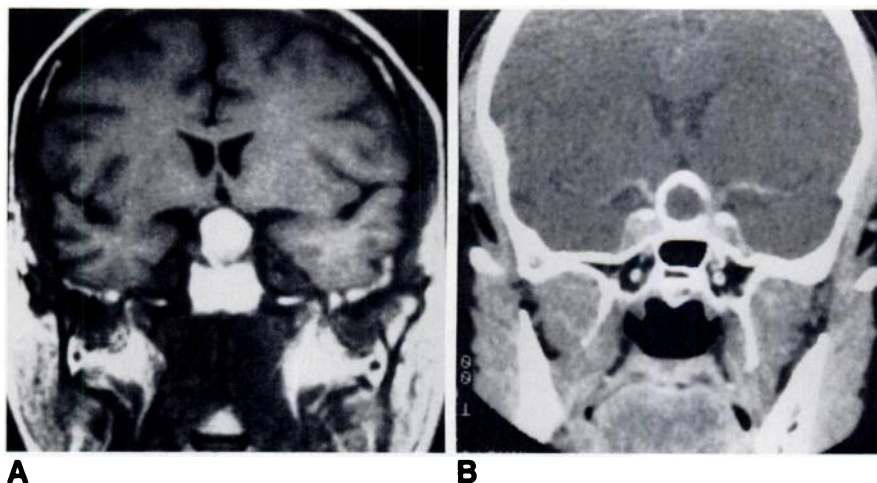


Fig. 1.—Case 1.
A and B, Axial (A) and coronal (B) MR images (795/40) show homogeneous increased signal intensity throughout adenoma. Note compression of optic chiasm by suprasellar extension of mass.
C, Axial noncontrast CT scan shows slightly hypodense adenoma. Hematoma within tumor would not be suspected from this CT scan.

Fig. 2.—Case 10.

A, Coronal MR image (500/30) shows homogeneous increased signal intensity of intra- and suprasellar mass with compression of optic chiasm and inferior third ventricle.

B, Coronal contrast-enhanced CT scan shows hypodense sellar and suprasellar mass at approximately same plane as MR. Peripheral rim of increased density was also present on non-enhanced CT scan, compatible with rim of calcification.



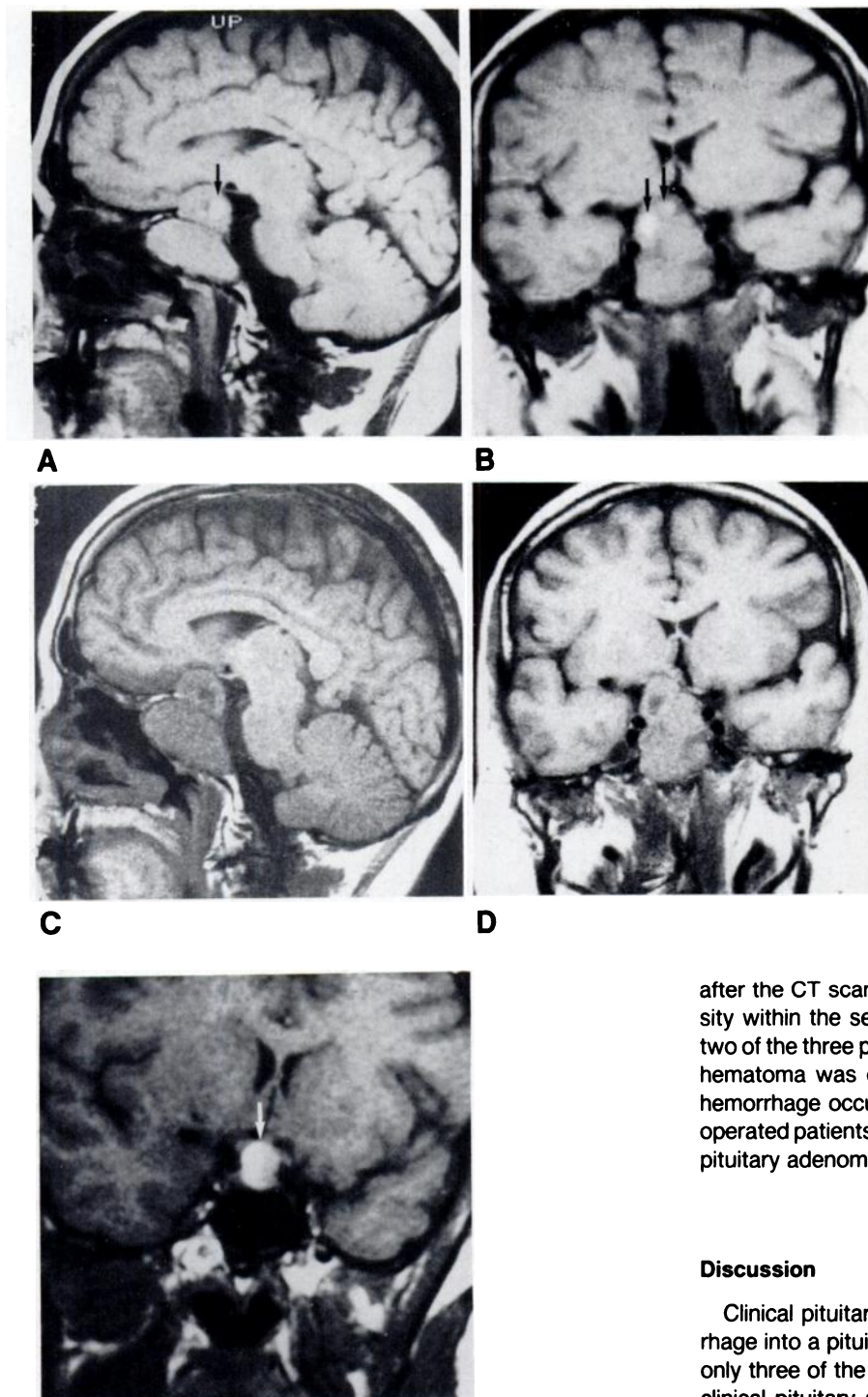


Fig. 3.—Case 11.

A and B, Sagittal (A) and coronal (B) MR images (700/300) show large recurrent pituitary adenoma with suprasellar extension and growth into sphenoid sinus. Note focal areas of increased signal intensity (arrows).

C and D, 7 months later. Sagittal (C) and coronal (D) MR images (500/17) show focal areas of decreased signal intensity where hyperintense abnormalities were in A and B.

Fig. 4.—Case 12.
Coronal MR study (800/20) with patient in right lateral decubitus position shows methemoglobin-fluid level (arrow).

(Table 1). Two patients had CT scans within 1 week of the apoplectic event, and had increased attenuation within the pituitary adenomas compatible with hemorrhage. The earliest MR studies in these two patients were 5 days and 1 month

after the CT scans and demonstrated increased signal intensity within the sella corresponding to high density on CT. In two of the three patients with pituitary apoplexy, the intrasellar hematoma was confirmed at surgery; in these patients the hemorrhage occurred in pituitary adenomas. The other non-operated patients were presumed to have hemorrhages within pituitary adenomas.

Discussion

Clinical pituitary apoplexy is not synonymous with hemorrhage into a pituitary adenoma. As can be seen in this study, only three of the 12 patients with intrasellar hemorrhage had clinical pituitary apoplexy (cases 2, 6, and 12). Intratumoral hemorrhage can vary from small focal hematomas (Figs. 3 and 6) to diffuse hemorrhage throughout the adenoma (Figs. 1 and 7). One side of the gland can even be predominantly affected by hemorrhage (Figs. 5 and 8). Pituitary apoplexy is caused by the sudden expansion of a normal or neoplastic gland secondary to bland or hemorrhagic infarction. This study was concerned with hemorrhagic infarction, but bland infarction can be another cause of pituitary apoplexy, as demonstrated in Figure 9. In this patient, all but the periphery

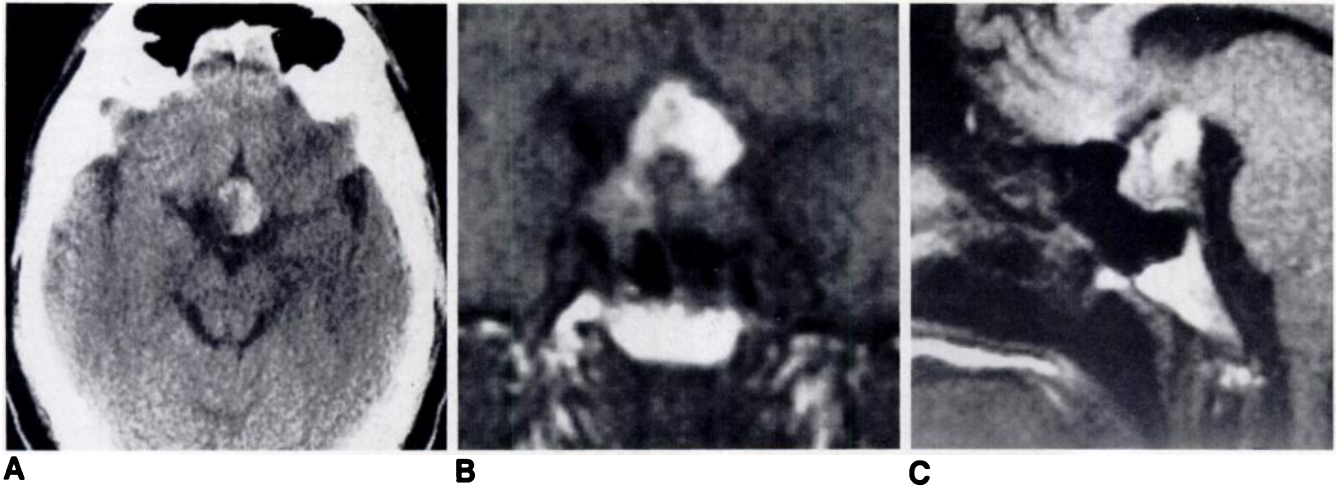


Fig. 5.—Case 2.

A, Axial nonenhanced CT scan shows areas of increased density within adenoma, mostly superiorly on left. **B** and **C**, Coronal, 250/20 (**B**), and sagittal, 600/20 (**C**), MR images 5 days after CT show areas of increased signal intensity, mostly superiorly and to left.

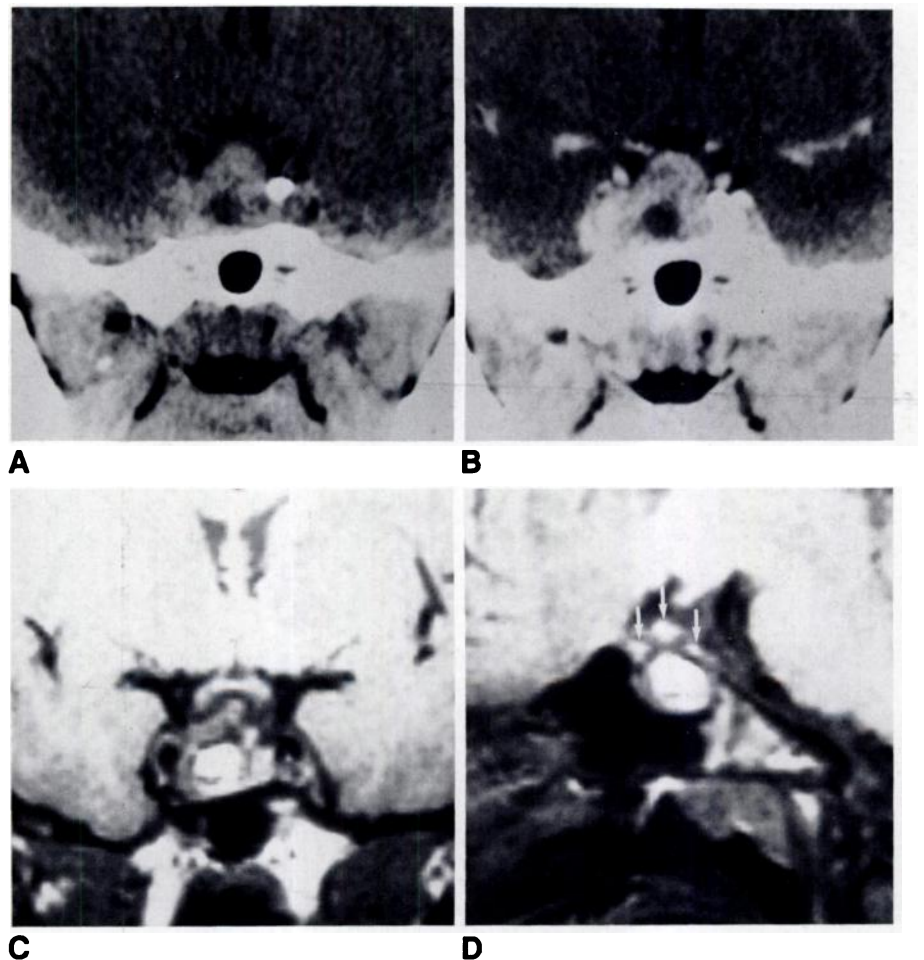


Fig. 6.—Case 4.

A and **B**, Coronal CT scans without (**A**) and with (**B**) contrast material show enhancing adenoma with large central area of low density.

C, Coronal MR image (800/26) 8 days after CT shows focal central area of increased intensity corresponding to low-intensity area on CT. Remainder of gland is inhomogeneous, with low intensity (presumed hemosiderin) and intermediate signal intensities.

D, Sagittal MR image (800/26) shows three focal areas of increased intensity (arrows) superior to central focal area of increased signal intensity.

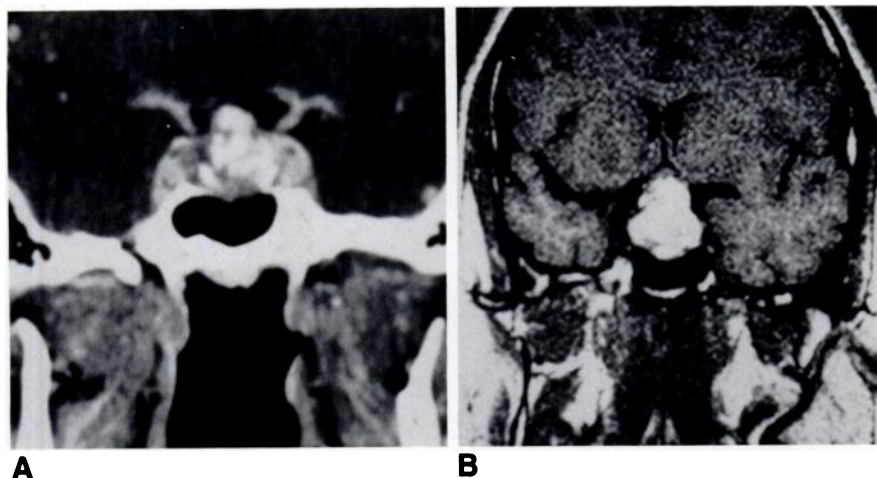


Fig. 7.—Case 7.

A, Coronal contrast-enhanced CT scan shows multiple focal areas of increased intensity (non-enhanced CT study was not done).

B, Coronal MR image (500/30) 1 month after CT shows increased signal throughout most of intra- and suprasellar adenoma.

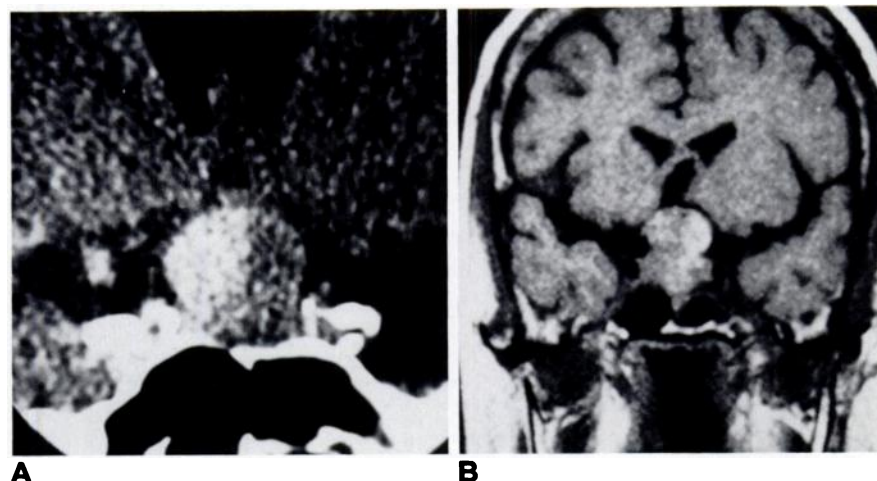


Fig. 8.—Case 6.

A, Contrast-enhanced coronal CT scan with enhancement of right side of adenoma and slightly decreased density on left side.

B, Coronal MR image (500/30) 1 day after CT shows small areas of increased intensity scattered throughout adenoma, more confluent on left. Note compression of inferior third ventricle.

of the adenoma was isointense relative to brain on a short TR/TE (500/16) pulse sequence. At a longer TR/TE (2000/35), the adenoma was hyperintense relative to the brain, indicating increased water content within the adenoma secondary to the infarct. CT showed only rim enhancement of an isodense macroadenoma.

CT of pituitary adenomas cannot differentiate necrosis with cystic changes within adenomas from old hemorrhage [11]. However, our results indicate that MR can make this differentiation. By using short TR/TE spin-echo pulse sequences, cystic areas tend to be hypointense to slightly hyperintense, depending on the protein content of the fluid, and increase in intensity with longer TR/TE sequences, having higher intensity than CSF [12]. In Figure 10, the focal area of low density within the left side of the adenoma on CT could have been secondary to necrosis or to old hemorrhage, but the MR shows no clear-cut hyperintensity on the shorter TR/TE image but does show increasing signal intensity within the focal area on the left side of the tumor with increasing TR/TE, indicating nonhemorrhagic fluid within this portion of the tumor, compatible with a protein-containing cyst [12]. A subacute he-

matoma would have had higher signal intensity on the spin-echo 1200/26 sequence.

The high signal intensity of subacute and chronic hematomas on short TR/TE spin-echo MR sequences has been well described [3, 13, 14]. This phenomenon is commonly thought of as being related to T1 shortening of the hematoma secondary to methemoglobin; however, Hackney et al. [15] believe that T1 shortening does not explain the high signal intensity of subacute and chronic hemorrhage on spin-echo MR images. They believe that the main contribution to the contrast difference between hemorrhage and white matter appears to be secondary to proton-density differences with some T2 component and almost no T1 component. Whatever the explanation, subacute hemorrhage is seen as hyperintensity on short TR/TE sequences. High intensity on short TR/TE pulse sequences can also indicate "high liquid cholesterol content" [16], as in craniopharyngiomas, or can be secondary to high protein content within cysts [12].

Bromocriptine has been used in the medical treatment of prolactin-secreting and growth-hormone-secreting adenomas. Signal changes on MR when using spin-echo pulse

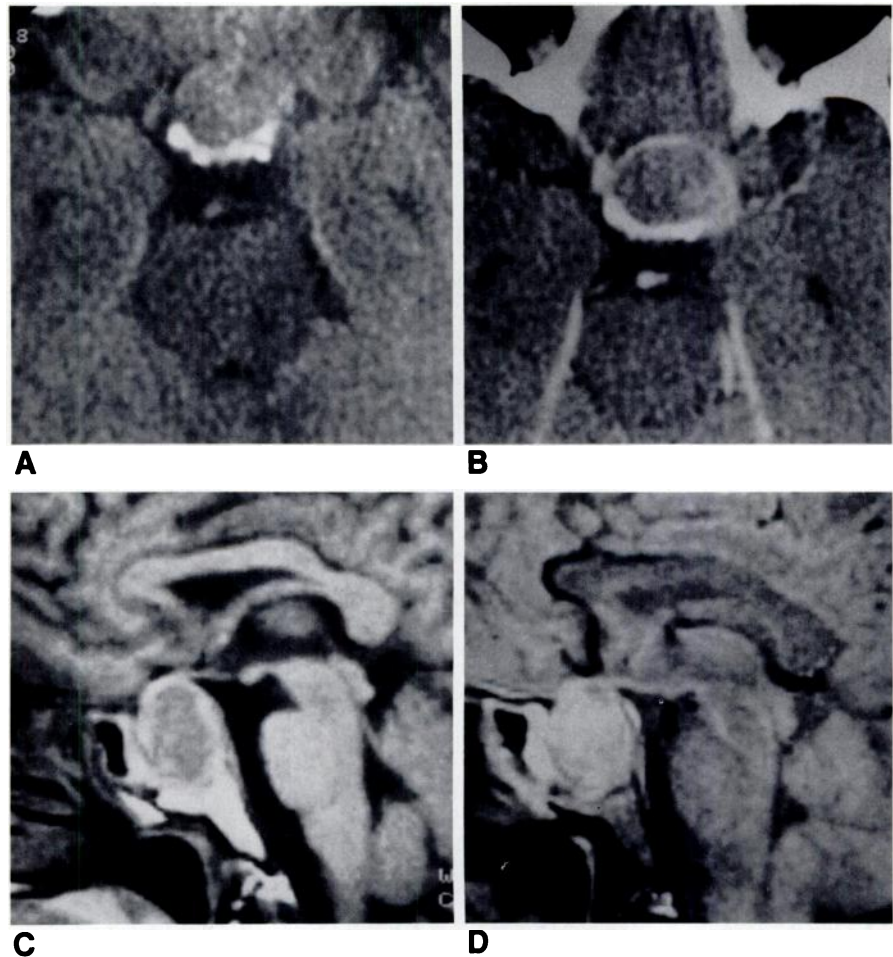
Fig. 9.—49-year-old man with diplopia and headache who developed a right third nerve palsy, bilateral sixth nerve palsy, and bitemporal hemianopsia.

A and B, Axial CT scans show isodense pituitary macroadenoma (**A**) with rim enhancement (**B**).

C, Sagittal MR image (500/16) shows isointense adenoma with rim of increased intensity.

D, MR (2000/35) shows confluent areas of increased signal intensity throughout adenoma, indicating increased water content within adenoma secondary to infarction.

At surgery, a nonhemorrhagic infarcted pituitary adenoma was found. There was no pathologic evidence of hemorrhage. Rim of hyperintense signal in **C** probably relates to increased protein content of extracellular space in periphery of tumor. Note that this increased signal is relatively less intense compared with that in proved intratumoral hemorrhage (e.g., Fig. 1).



sequences have been observed within these pituitary adenomas; some were of increased intensity on short TR/TE sequences and others were of increased or decreased intensity on long TR/TE pulse sequences [17]. Pojunas et al. [18] reported a patient with a microadenoma on bromocriptine who had a focal area of increased intensity on a short TR sequence and decreased signal on a long TR sequence. They stated it is possible that changes in the prolactinoma cell ultrastructure can result in altered MR signals and ventured that "bromocriptine does not usually cause necrosis or infarction of pituitary tissue but inhibits protein synthesis in prolactin-secreting cells" [18]. Weissbuch [17] wrote that "rarely, if ever, are areas of hemorrhage or infarction observed" in prolactinomas treated short term (6 weeks) with bromocriptine. Figure 7 shows CT and MR images of a patient who was undergoing treatment of his pituitary adenoma with bromocriptine and stopped his medication. After he stopped taking the bromocriptine, the adenoma began to enlarge and bitemporal hemianopsia developed. The coronal contrast-enhanced CT scan (noncontrast CT was not performed) showed multiple punctate areas of increased attenuation within the adenoma. Coronal MR (500/30), performed 1 month after CT, showed increased signal intensity throughout

most of the adenoma, proved at surgery to be hemorrhage. It is unclear whether the intratumoral hemorrhage occurred during or after the cessation of bromocriptine therapy, but the possibility exists that patients who stop bromocriptine therapy before adequate tumor involution may be at risk for developing intratumoral hemorrhage.

Figure 2 shows diffuse intrasellar hemorrhage in a patient with a 10-year history of hypopituitarism. On CT, note that there is a calcified rim to the lesion. It is possible that this patient had a pituitary adenoma in the past that degenerated over time and the periphery of the lesion calcified, "walling off" the degenerated tumor. Although no tumor was found at surgery, there was old hemorrhage. Subacute or chronic hemorrhage that has been isolated from the systemic circulation may be detectable by MR years after the hemorrhagic event.

In summary, we found that hemorrhage within pituitary adenomas may be seen without clinical evidence of pituitary apoplexy, and we believe that these patients can be differentiated from patients with cystic necrosis and bland infarction by MR. MR is sensitive in detecting intrasellar hemorrhage in the subacute and chronic stages, while CT is most valuable in the acute stage of pituitary hemorrhage, particularly within

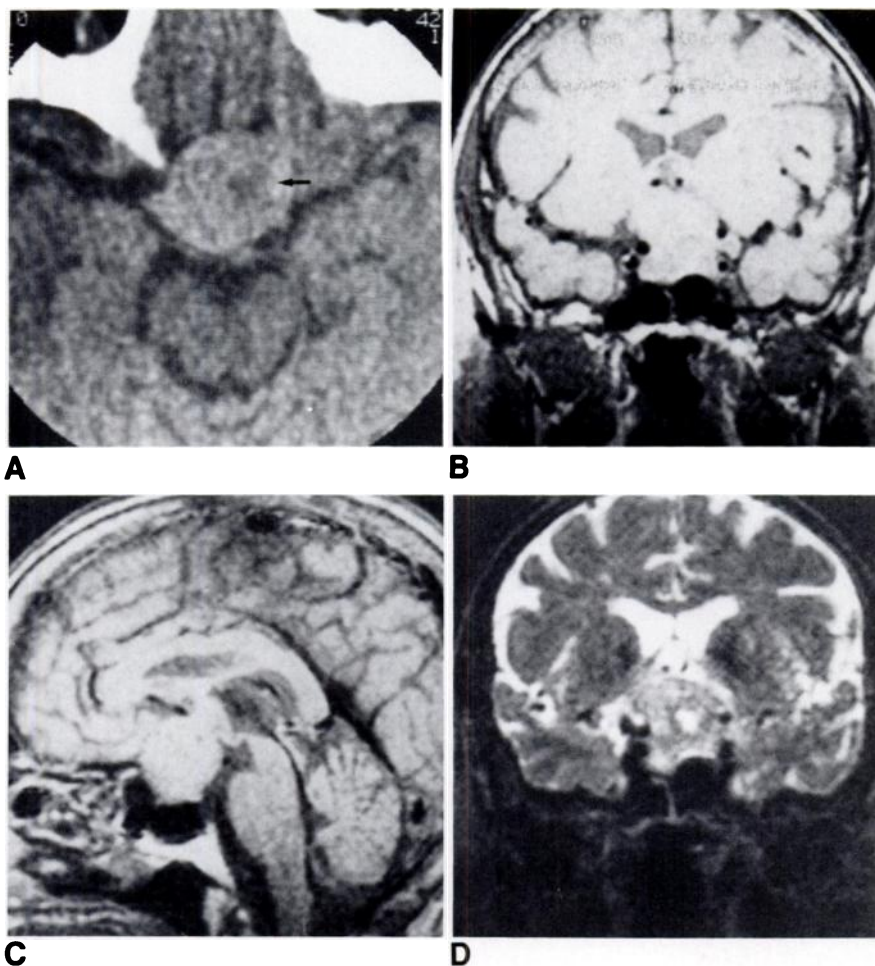


Fig. 10.—70-year-old woman with right temporal and left nasal visual field defect.

A, Noncontrast axial CT scan reveals focal area of decreased density to left of midline within macroadenoma (arrow).

B and C, Coronal MR, 1200/26 (B), and sagittal MR, 1000/26 (C), show isointense homogeneous macroadenoma.

D, Coronal MR image (3000/140) shows focal area of increased signal intensity to left of midline within adenoma; signal intensity is similar to that of CSF, compatible with focal areas of necrosis.

At surgery, focal area of necrosis within adenoma was found. There was no pathologic evidence of hemorrhage.

the first 24–48 hr. CT can demonstrate hemorrhage within the tumor, and from a clinical standpoint this diagnosis is important in patient management. Some pituitary macroadenomas with “cystic” areas on CT may actually have areas of hemorrhage within them and can be detected by MR. On the other hand, many cysts in macroadenomas are possibly caused by focal areas of previous bland infarction.

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