Management and outcomes of pituitary apoplexy

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OBJECT This study was undertaken to analyze the predisposing factors, clinical presentation, therapeutic management, and clinical recovery in patients with pituitary apoplexy, with an emphasis on the long-term visual, endocrine, and functional outcomes.

METHODS The authors performed a retrospective analysis of consecutive cases involving patients treated at Mayo Clinic between 1992 and 2013. Patients were included in the study only if they had 1) abrupt onset of severe headache or visual disturbance in the presence of a pituitary adenoma and 2) radiological or surgical confirmation of a pituitary mass. The primary endpoints of analysis were the visual (ocular motility, visual fields, and visual acuity), endocrine, and functional outcomes (using the modified Rankin Scale).

RESULTS Eighty-seven patients were identified (57 males and 30 females, mean age 50.9 years, range 15–91 years). Twenty-two patients (25.3%) had a known pituitary adenoma. Hypertension was the most common associated factor (39%). Headache was the most frequent presenting symptom (89.7%), followed by visual abnormalities (47.1%). Cranial nerve palsies were present in 39% and visual field defects in 34.1%. MRI detected hemorrhage in 89% patients, as compared with 42% detected by CT scan. Sixty-one patients (70.1%) underwent surgery during acute hospitalization (median time from apoplexy 5 days, IQR 3–10 days), 8 (9.2%) had delayed surgery, and 18 (20.7%) were treated conservatively. Histopathological examination revealed adenoma with pure necrosis in 18 (30%), pure hemorrhage in 4 (6.7%), and both in 6 (10%) patients. Four patients died during hospitalization. The average duration of follow-up was 44.2 ± 43.8 months. All survivors were independent and had complete resolution or substantial improvement in eye movements and visual fields at the last follow-up. Many patients needed long-term hormonal replacement with levothyroxine (62.7%) and cortisol (60%). Daily desmopressin was needed in 23% of all surgical patients at 3 months (versus none of the medically treated) and this requirement decreased slightly over time. Regrowth of pituitary adenoma was seen in 7 patients (8.6%). There were no statistically significant differences in any of the outcome measures across the treatment groups.

CONCLUSIONS The outcome of most patients with pituitary apoplexy is excellent. Selected patients can be managed conservatively, and patients with severe neuro-ophthalmological deficits treated with early surgery can achieve an excellent recovery.

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KEY WORDS pituitary apoplexy; pituitary surgery; visual; endocrine; outcomes

PITUITARY apoplexy (derived from the Greek word *apoplēxia* meaning “to cripple by a stroke”) refers to a constellation of symptoms characterized by sudden onset of severe headache, visual impairment, vomiting, ophthalmoplegia, and altered consciousness.^{11,35} It is an uncommon but a well-established clinical entity that occurs due to a rapid expansion of the contents of the sella

turcica, mostly caused by hemorrhage or infarction of a preexisting adenoma.^{11,12}

The first case of pituitary apoplexy was described by Bailey in 1898.⁶ The term pituitary apoplexy was first used by Brougham et al. in 1950 when describing 5 cases of this clinical entity.¹¹ Since then there have been many case series and case reports describing the spectrum of pituitary

ABBREVIATIONS ACTH = adrenocorticotrophic hormone; CN = cranial nerve; mRS = modified Rankin Scale.

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apoplexy. It occurs in 2%–7% of patients with pituitary adenoma.³⁰ With the advent of CT and particularly MRI scans, it is being increasingly detected that subclinical or minimally symptomatic hemorrhage is much more common, occurring in up to 25% of adenomas;^{10,26} however, the term apoplexy should be reserved for cases with abrupt onset of symptoms.¹²

Resection was traditionally considered the optimal treatment for patients with pituitary apoplexy.^{8,12,13,31,34} However, more recent case series have reported good outcomes with conservative medical therapy.^{9,21,23,24} No randomized studies have been conducted to compare the two management strategies, and guidelines propose individualizing therapy depending on the severity of presentation.³⁰

Most of the literature on pituitary apoplexy consists of relatively small case series. Very few series have included more than 50 patients and presented a long-term follow-up.³³ In this study, we retrospectively analyzed the clinical presentation, predisposing factors, therapeutic management, and clinical recovery of a large series of pituitary apoplexy patients treated at our institutions over a period of 22 years, with an emphasis on the long-term visual, endocrine, and functional outcomes.

Methods

The study was approved by our institutional review board. All included patients had signed a general informed consent form allowing their medical records to be used for research purposes. We retrospectively reviewed the records of pituitary apoplexy patients treated from 1992 to 2013. Cases with diagnosis of pituitary apoplexy were identified using our electronic data search system. Patients were included in the study only if they satisfied the following criteria: 1) abrupt onset of severe headache or visual disturbance in the presence of a pituitary adenoma, and 2) radiological or surgical confirmation of a pituitary mass. Patients were included regardless of whether treatment was surgical or conservative. Only the first episode of apoplexy was included in the analysis.

Information on predisposing factors, clinical presentation, diagnostic investigations, management, and follow-up was obtained from the medical records. Upon admission, all patients were examined by a neurosurgeon, most were also examined by a neurologist, all but 5 were evaluated by an endocrinologist, and 81 were assessed by an ophthalmologist. All patients underwent either CT or MRI scanning of the brain. The results were compared with previous CT and MRI scans in patients with a pre-existing diagnosis of a pituitary adenoma. In patients who underwent surgery, a neuropathological examination was performed on the excised tissue, and the tissue was stained immunohistochemically to determine the tumor type.

Patients were categorized into 3 groups on the basis of their treatment: 1) acute surgery, corresponding to those who had surgery during the same hospitalization; 2) delayed surgery, for those who had a planned surgery at a later time after stabilization of their symptoms; and 3) medical management.

The primary endpoints of our analysis were the visual (ocular motility, visual fields, and visual acuity), endo-

crine, and functional outcomes. A complete recovery of visual acuity was defined as 20/20 vision or return to the baseline before the onset of apoplexy. Formal campimetry testing was used to measure visual field outcomes. The modified Rankin Scale (mRS) was used to measure the patient's functional status. Visual, endocrine, and functional status measures were collected at the time of discharge, 3-month, 1-year, and at their last follow-up.

Data are presented using the basic descriptive statistics. Fisher's exact test and chi-square tests were used to compare outcomes across the treatment groups.

Results

We identified 87 patients (57 [65.5%] males and 30 [34.5%] females, mean age of 50.9 years [range 15–91 years]) who fulfilled the above criteria for pituitary apoplexy diagnosis during the study period. The average duration of follow-up was 44.2 ± 43.8 months (median 36 months, IQR 12–60 months).

Coexistent Factors

Hypertension (39%) was the most common comorbidity, followed closely by dyslipidemia (34.5%) and obesity (27.5%). Only a small proportion of the patients had diabetes mellitus (12.6%). Twelve patients (14.8%) were active smokers, and 22 (27.2%) were previous smokers. Two patients developed apoplexy after major surgery (cardiothoracic operations in both cases). Only 10.3% of the patients were receiving anticoagulant therapy with either heparin (22.2%) or warfarin (77.8%), and 17 (19.5%) were being treated with antiplatelet drugs. Among the women, only 1 was pregnant and 3 were in the postpartum period when they presented with pituitary apoplexy.

Presentation

The most common presenting symptom was sudden onset of severe headache, which was most commonly described as frontal or retro-orbital. Around half of the patients (47.1%) had visual abnormalities in addition to the headache; blurred vision (20%) was the most common visual complaint. Five patients presented with polyuria and polydipsia suggestive of diabetes insipidus. Thirty-nine percent had cranial nerve (CN) palsies, and unilateral CN III palsy was present in 67.6% of these cases. Visual field defects were detected in 29 patients (34.1%), with a predominance of bitemporal hemianopsia (59.3%). Eight patients (9.2%) had an associated weakness, with facial weakness being the most common (62.5%).

Prior to the apoplectic event, 22 patients (25.3%) had a known pituitary adenoma. Twelve had an endocrinologically active tumor (prolactinoma in 9, ACTH-secreting tumor in 2, and gonadotrophic tumor in 1), whereas the tumor was nonfunctional in the other 10.

Diagnostic Investigations

All patients had radiological confirmation of a sellar mass. Sixty-nine patients (79.3%) had a CT scan of the head, and a sellar mass was noted in 63 of these 69 cases. A mass was seen in all patients evaluated with MRI of the brain (n = 82, 94%). Hemorrhage was detected twice as frequently with MRI as with CT scan (Table 1).

Eighty-two patients (94.3%) had an endocrinological evaluation done at the time of presentation, and baseline pituitary functions were obtained in these cases. Of these 82 patients, 35 (45.5%) had abnormally low cortisol levels, and 60% of the men had low testosterone concentrations. One-third of the patients had low ACTH levels. The detailed hormone profile is summarized in Table 2.

Treatment

Most of the patients (92%) were admitted, and 7 patients were treated on an outpatient basis because their acute symptoms subsided rapidly and it was decided to treat them conservatively under close ambulatory supervision. Thirty-eight patients (44.7%) required admission to the intensive care unit. During the acute hospitalization, 72 patients (83.7%) were given corticosteroids, 21 (24.4%) received insulin, 31 (35.6%) received levothyroxine, 7 (8%) received desmopressin, and 4 (4.6%) received bromocriptine. The median length of hospital stay was 5 days (IQR 3–9 days, mean 7.2 ± 6.1 days).

Sixty-one patients (70.1%) underwent surgery with a median time of 5 days (IQR 3–10 days) from symptom onset, whereas 8 patients (9.2%) underwent scheduled surgery after a median of 126 days (IQR 64–776 days) following the acute presentation and medical stabilization. All patients treated with surgery underwent transsphenoidal resection. Eighteen cases (20.7%) were managed conservatively with medical treatment. Of the 79 patients with evidence of hemorrhage on MRI, 59 (80.8%) underwent surgery, and of the 7 with MRI evidence of infarct, 6 (85.7%) underwent surgery (Table 3). Visual deficits (decreased field or acuity) and oculomotor abnormalities were more common in the surgery group than in the conservative management group (47 [68.1%] 69 vs 8 [44.4%] 18), although the difference did not reach statistical significance ($p = 0.06$).

Histopathological examination of the resected tissue revealed an adenoma in 64 cases and Rathke cleft cyst in 4 cases. Frank necrotic tissue was present in 10 cases (16.7%), while pituitary adenoma with pure necrosis was present in 18 (30%), pure hemorrhage in 4 (6.7%), and a mixture of both in 6 (10%). Null cell adenoma was identified in 18 cases and prolactinoma in 8; other types of adenoma were even less common.

Outcomes

The endocrinological outcomes categorized by therapeutic strategy are presented in Table 2, functional and radiological outcomes in Table 4, and ophthalmological outcomes in Table 5. Improvement was noted during the acute hospitalization but continued over time. There were no statistically significant differences in any of the outcome measures across the treatment groups. The patients who had reduced consciousness at presentation (14.9%) recovered favorably. Four patients (4.6%) died during the acute hospitalization (2 who were treated conservatively and 2 who underwent early surgery): 1) an 89-year-old patient who had a massive frontal hemorrhage along with pituitary apoplexy; 2) a 67-year-old patient with multiple comorbidities precluding safe surgery; 3) a 77-year-old patient with an amyloid cardiomyopathy who developed

TABLE 1. Radiological findings

Modality & Finding	Value*
CT	69 (79.3)
Mass	63 (91.3)
Median size of mass in mm (IQR)	22 (20–28)
Hemorrhage	29 (42)
MRI	82 (94.3)
Mass	82 (100)
Size of mass (mm)	
Median	25.5
IQR	20–30
Hemorrhage	73 (89)
Mass increase	21 (25.6)
Infarct	7 (8.5)
Optic chiasm involvement	51 (62.2)
Cavernous sinus involvement	34 (41.5)

* Values represent numbers of patients (%) unless otherwise indicated.

massive hypotension after surgery and was then transitioned to palliative care according to family wishes; and 4) an 89-year-old patient who developed airway complications after surgery and was transitioned to palliative care by family request. Postoperative complications were present in 3 patients who had transient postoperative CSF leaks (without any cases of meningitis), while 3 had severe headache controlled with narcotics, and 1 had postoperative urinary retention.

At last follow-up, all survivors were independent and had minimal or no symptoms. Limitations in eye movements improved in all cases and most often resolved early. A very small minority of patients had no improvement (3 cases) of peripheral vision, all in the early surgical group. Long-term hormonal replacement with levothyroxine was needed in nearly half of the patients, glucocorticosteroids in two-thirds of the patients, and testosterone in close to half of the men. The rates of requiring replacement of anterior pituitary hormones were not significantly different between surgical and medical treatment groups. Daily desmopressin was needed in 23% of all surgical patients at 3 months (vs none of the medically treated patients), and this requirement decreased slightly over time. Regrowth of the pituitary adenoma was seen in 7 (8.6%) patients, all after surgery; repeat surgery was done in 1, radiotherapy in 4 patients, and the other 2 were only monitored as they remained asymptomatic. There were no cases of pituitary apoplexy recurrence.

Discussion

Our study of a large series of patients with pituitary apoplexy, one of the largest collected to date, highlights that this severe condition typically has excellent outcomes with adequate therapy. Early surgery remains the mainstay of treatment, but selected patients can recover very well with a delayed, planned resection or solely with medical therapy. Neurological and ophthalmological symptoms improve early after treatment and fully resolve in most cases over time. Long-term replacement of anterior pitu-

TABLE 2. Endocrinological status at presentation and follow-up categorized by treatment strategy*

Time Point & Variable	Conservative Management (n = 18)	Early Surgery (n = 61)	Delayed Surgery (n = 8)
Abnormal findings at presentation			
Low thyroid-stimulating hormone	15 (88.2%)	16 (30.2%)	1 (12.5%)
Low testosterone	4 (44.4%)	20 (64.5%)	3 (60%)
Low cortisol	8 (47.1%)	23 (44.2%)	4 (50%)
Low ACTH	3 (27.3%)	12 (41.4%)	0
Low prolactin	3 (17.6%)	19 (35.2%)	2 (28.6%)
High prolactin	5 (29.4%)	6 (11.1%)	2 (28.6%)
Low luteinizing hormone	5 (38.5%)	18 (40.9%)	1 (14.3%)
Low follicle-stimulating hormone	3 (27.3%)	6 (15.8%)	0
Low growth hormone	1 (20%)	4 (26.7%)	0
Low insulin-like growth factor-1	6 (50%)	13 (37.1%)	1 (25%)
Replacement therapy at 3-mo follow-up			
Levothyroxine	14 (87.5%)	57 (96.6%)	7 (87.5%)
Cortisone	5 (35.7%)	27 (47.4%)	3 (42.9%)
Testosterone	7 (50%)	42 (73.7%)	3 (42.9%)
Estradiol	1 (12.5%)	21 (50%)	2 (40%)
Progesterone	4 (40%)	3 (20%)	0
Growth hormone	2 (20%)	2 (13.3%)	0
Dopamine antagonist	0	0	0
Desmopressin	1 (7.1%)	4 (7%)	0
Replacement therapy at 1-yr follow-up			
Levothyroxine	0	10 (17.5%)	2 (28.6%)
Cortisone	11 (68.7%)	37 (62.7%)	5 (62.5%)
Testosterone	5 (41.7%)	22 (59.5%)	3 (60%)
Estradiol	4 (33.3%)	26 (70.3%)	3 (60%)
Progesterone	1 (33.3%)	20 (66.7%)	2 (66.7%)
Growth hormone	4 (50%)	2 (28.6%)	0
Dopamine antagonist	2 (25%)	2 (28.6%)	0
Desmopressin	0	1 (2.7%)	1 (20%)
Replacement therapy at last follow-up			
Levothyroxine	9 (56.3%)	25 (42.4%)	6 (75%)
Cortisone	4 (44.4%)	24 (66.7%)	4 (66.7%)
Testosterone	4 (44.4%)	22 (62.9%)	4 (66.7%)
Estradiol	2 (100%)	18 (64.3%)	3 (75%)
Progesterone	5 (71.4%)	2 (25%)	1 (50%)
Growth hormone	2 (28.6%)	2 (25%)	1 (50%)
Dopamine antagonist	0	1 (2.9%)	1 (16.7%)
Desmopressin	1 (11.1%)	4 (11.4%)	2 (33.3%)
	0	3 (8.6%)	1 (16.7%)

* Median amount of time from initial presentation to last follow-up: 36 months (interquartile range [IQR] 24–54 months) for the conservative management group, 48 months (IQR 27–69 months) for the early surgery group, and 48 months (IQR 21.2–99 months) for the delayed surgery group.

itary hormones (particularly glucocorticosteroids) is necessary in more than half of patients, but only a minority require desmopressin after the acute phase.

Multiple precipitating or predisposing factors have been noted in the literature,⁹ including hypertension,³² major surgery,^{1,2} hypotension,¹⁵ closed head trauma,¹⁸ head radiation,³⁶ anticoagulation or intrinsic coagulopathy,^{27,37} pregnancy/postpartum state,^{7,14,32} dynamic pituitary test-

ing,^{4,21,22} and bromocriptine initiation or withdrawal.¹⁹ However, none of these factors is likely to be solely responsible for the occurrence of apoplexy. In our cohort, hypertension was the most common coexistent condition (39%), followed by treatment with anticoagulant or antiplatelet medication (29.8%). Major surgery and pregnancy/postpartum state were uncommon occurrences. None of the other factors previously reported as predisposing to pi-

TABLE 3. Patient characteristics at baseline categorized by treatment strategy

Characteristic	Conservative Management (n = 18)	Early Surgery (n = 61)	Delayed Surgery (n = 8)	p Value
Age (yrs)				0.4364
Median	55.5	54	44.5	
IQR	38–82	42–67.5	33–62	
History of hypertension	7 (38.9%)	25 (41%)	2 (25%)	0.6701
Known adenoma	4 (22.2%)	14 (23%)	4 (50%)	0.2847
No visual complaints	12 (75%)	28 (46%)	5 (62.5%)	0.0904
Reduced consciousness	6 (33.3%)	7 (11.5%)	0	0.0304
Compression of optic chiasm on MRI	4 (33.3%)	43 (79.6%)	4 (50%)	0.0046

pituitary apoplexy were present in our patients. Around 75% of our patients had an undiagnosed pituitary adenoma at the time of presentation, which is consistent with previous reports.³⁰ Infarction in the pituitary adenomas was present in 33 cases (55%), while 10 (16.7%) showed only necrotic tissue, which is also similar to previous series.²⁴

The most common and earliest symptom of pituitary apoplexy is a sudden, severe, retro-orbital or frontal headache, often accompanied by visual abnormalities.³⁴ The cause of visual problems is the lateral compression of the contents of the cavernous sinus or the optic chiasm. In our study, headache was present in nearly 90% of patients and was associated with nausea/vomiting in nearly 40%. Visual alteration was reported by almost half of our patients, with ophthalmoparesis present in 39% and visual field restriction in one-third. These rates of ophthalmological abnormalities are quite similar to those reported in contemporary series but lower than in older series,^{28,34} likely because of more delayed diagnosis before the advent of MRI.

There has been a radical change in the radiological investigations used to diagnose apoplexy in the last 2 decades. Initially, CT scanning was used to diagnose the presence of hemorrhage in the adenoma.³⁶ In our cohort of patients, CT was very effective in identifying the presence of pituitary mass, but it could only identify hemorrhage in 42% of patients. Instead, MRI was extremely sensitive for the detection of hemorrhage into the pituitary mass; the rate of MRI-detected hemorrhage in our study (89%) is comparable to that reported for other smaller modern series.^{20,29,31,33} MRI can also be used to assess the tissue surrounding the pituitary mass and hence may alter the eventual management of the patients. In our study, optic chiasm compression was seen in 62.2% and extension of the tumor into the cavernous sinus was seen in 41.5% patients. Nearly 80% of the patients who were treated surgically had visible compression of the optic chiasm. Hence, it is now clear that MRI should be the diagnostic imaging of choice in patients with suspected pituitary apoplexy.

The acute management of pituitary apoplexy consists of stabilizing the physiological state of the patient with

TABLE 4. Functional and radiological outcomes categorized by treatment strategy

Variable	Conservative Management (n = 18)	Early Surgery (n = 61)	Delayed Surgery (n = 8)
Functional outcome			
Death before 3 months	2 (11.1%)	2 (3.3%)	0
mRS at 3 months			
0	9 (56%)	33 (55.9%)	3 (42.9%)
1	5 (31.3%)	24 (40.6%)	4 (57.1%)
2	0	1 (1.6%)	0
6	2 (12.7%)	1 (1.6%)	0
mRS at 1 year			
0	7 (53.8%)	28 (75.7%)	5 (100%)
1	5 (38.5%)	8 (21.6%)	0
2	1 (7.7%)	0	0
4	0	1 (2.7%)	0
mRS score at last follow-up*			
0	5 (55.6%)	22 (66.7%)	6 (100%)
1	3 (33.3%)	8 (24.2%)	0
6	1 (11.1%)	3 (9%)	0
Radiological†			
Follow-up at 3 months			
Stable size	6 (46.2%)	44 (80%)	6 (75%)
Reduced size	7 (53.8%)	11 (20%)	2 (25%)
Increased size	0	0	0
Follow-up at 1 year			
Stable size	8 (61.5%)	36 (90%)	5 (100%)
Reduced size	5 (38.5%)	1 (2.5%)	0
Increased size	0	3 (7.5%)	0
Last follow-up‡			
Stable size	12 (92.3%)	27 (87.1%)	3 (75%)
Reduced size	1 (7.7%)	1 (3.2%)	0
Increased size	0	3 (9.7%)	1 (25%)

* Median amount of time from initial presentation to last follow-up: 24 months (IQR 24–54 months) for the conservative management group, 36 months (IQR 24–60 months) for the early surgery group, and 48 months (IQR 21.3–75 months) for the delayed surgery group.

† The imaging findings were compared to the postoperative CT/MRI in the surgical patients and to the last in-hospital CT/MRI in the nonsurgical patients.

‡ Median amount of time from initial presentation to last follow-up: 24 months (IQR 24–48 months) for the conservative management group, 48 months (IQR 36–72 months) for the early surgery group, and 42 months (IQR 15.8–78 months) for the delayed surgery group.

the supplementation of corticosteroids and other deficient hormones and maintaining electrolyte balance. Traditionally, most patients with apoplexy were treated surgically after this initial stabilization.^{3,8,13,16,31} However, more recent series have repeatedly reported good outcomes in selected patients treated conservatively with medical therapy only.^{5,9,13,17,21,23,25,31} In our study, 70% of the patients were treated with early resection, but the rest were treated with a delayed, planned surgical intervention (9%) or solely with medical treatment (21%). Treatment outcomes

TABLE 5. Ophthalmological status at presentation and follow-up categorized by treatment strategy

Time Point & Variable	Conservative Management (n = 18)	Early Surgery (n = 61)	Delayed Surgery (n = 8)
At presentation			
Visual field defects	3 (16.7%)	23 (39%)	3 (37.5%)
Unilateral right upper quadrant	2 (11.1%)	0	1 (12.5%)
Unilateral right lower quadrant	0	1 (1.7%)	1 (12.5%)
Unilateral left upper quadrant	1 (5.6%)	0	0
Unilateral left lower quadrant	0	0	0
Bitemporal hemianopia	0	16 (27.1%)	1 (12.5%)
Unilateral hemianopia	0	2 (3.4%)	0
Bilateral inferior	0	2 (3.4%)	0
Unilateral total & contralateral temporal	0	2 (3.4%)	0
Decreased visual acuity	5 (31.3%)	28 (45.9%)	5 (62.5%)
Eye movement disorder	6 (33.3%)	40 (65.6%)	1 (12.5%)
Unilateral CN III	2 (11.1%)	21 (34.4%)	0
Unilateral CN IV	0	4 (6.6%)	0
Unilateral CN VI	1 (5.6%)	8 (13.1%)	1 (12.5%)
Bilateral CN III	1 (5.6%)	2 (3.3%)	0
Bilateral CN IV	1 (5.6%)	0	0
Bilateral CN VI	1 (5.6%)	0	0
Unilateral ophthalmoplegia	0	4 (6.6%)	0
Bilateral ophthalmoplegia	0	1 (1.6%)	0
Follow-up at 3 months	14 (87.5%)	54 (90%)	8 (100%)
Visual fields			
Normal	13 (92.8%)	45 (83.3%)	6 (75%)
Total improvement*	2 (66.7%)	12 (57.1%)	1 (33.3%)
Partial improvement*	1 (33.3%)	7 (33.3%)	2 (66.7%)
No improvement*	0	2 (9.6%)	0
Worsened*	0	0	0
Visual acuity			
Normal	13 (92.8%)	49 (90.7%)	7 (87.5%)
Total improvement*	4 (80%)	21 (80.8%)	4 (80%)
Partial improvement*	1 (20%)	4 (15.4%)	1 (20%)
No improvement*	0	1 (3.8%)	0
Eye movements			
Normal	14 (100%)	50 (92.6%)	7 (87.5%)
Total improvement*	4 (100%)	23 (85.2%)	0
Partial improvement*	0	4 (14.8%)	1 (100%)
No improvement*	0	0	0
Follow-up at 1 year	13 (81.3%)	35 (61.4%)	5 (62.5%)
Visual fields			
Normal	12 (92.3%)	30 (85.7%)	4 (80%)
Total improvement*	1 (50%)	31 (86.1%)	1 (50%)

(continued)

TABLE 5. Ophthalmological status at presentation and follow-up categorized by treatment strategy (continued)

Time Point & Variable	Conservative Management (n = 18)	Early Surgery (n = 61)	Delayed Surgery (n = 8)
Follow-up at 1 year (continued)			
Visual fields (continued)			
Partial improvement*	1 (50%)	3 (8.3%)	1 (50%)
No improvement*	0	2 (5.6%)	0
Visual acuity			
Normal	12 (92.3%)	34 (97.1%)	5 (100%)
Total improvement*	3 (75%)	14 (93.3%)	4 (100%)
Partial improvement*	1 (25%)	0	0
No improvement*	0	1 (6.7%)	0
Eye movements			
Normal	13 (100%)	34 (97.1%)	5 (100%)
Total improvement*	4 (100%)	16 (94.1%)	1 (100%)
Partial improvement*	0	1 (5.9%)	0
No improvement*	0	0	0
Maximum follow-up†			
Visual fields			
Normal	9 (90%)	29 (90.6%)	4 (80%)
Total improvement*	0	29 (90.6%)	2 (66.7%)
Partial improvement*	1 (100%)	2 (6.3%)	1 (33.3%)
No improvement*	0	1 (3.1%)	0
Visual acuity			
Normal	8 (80%)	30 (93.8%)	5 (100%)
Total improvement*	3 (75%)	10 (90.9%)	5 (100%)
Partial improvement*	1 (25%)	0	0
No improvement*	0	1 (9.1%)	0
Eye movements			
Normal	10 (100%)	32 (100%)	5 (100%)
Total improvement*	3 (100%)	14 (100%)	1 (100%)
Partial improvement*	0	0	0
No improvement*	0	0	0

* In patients with abnormalities at presentation.

† Median amount of time from initial presentation to last follow-up: 24 months (IQR 22.5–45 months) for the conservative management group, 36 months (IQR 24–60 months) for the early surgery group, and 36 months (IQR 21.25–66 months) for the delayed surgery group.

were similarly favorable with all treatment approaches. However, it is important to bear in mind that treatment selection was decided by the neurosurgeon in collaboration with members of the multidisciplinary clinical team and patients treated with early surgery were more likely to have neuro-ophthalmological deficits at presentation. This selection bias, whereby more severe cases are treated surgically while milder presentations are managed conservatively, has been previously noted by others.^{5,23} Nonetheless, it is worth noticing that one-third of the patients treated conservatively in our series had presented with reduced level of consciousness and despite this severe presentation most of them (4 of 6) had an excellent recovery. Therefore, conservative management is a valid strategy for patients

TABLE 6. Comparison of Mayo Clinic experience with the treatment of pituitary apoplexy for the periods 1975–1991 and 1992–2013

Variable	Bills et al.	Present Study
Time period	1975–1991	1992–2013
No. of patients	37	87
Male/female	25/12	57/30
Mean age (years)	56.6	53.6
Average follow-up (years)	2.8	4.1
Presenting symptoms/signs		
Headaches (%)	95	89.7
Ocular paresis (%)	78	39
CN III	57	76.4
CN IV	13	14.7
CN VI	30	8.9
Reduction in visual field (%)	64	33.3
Reduction of visual acuity (%)	52	43.7
Altered consciousness (%)	8	15
Radiological findings		
CT scan (%)	94.6	79.3
Pituitary tumor (%)	94	91.3
Pituitary hemorrhage (%)	46	42
Management		
No surgery (%)	2.7	29.9
Interval between onset & surgery (days)	16.8	6.8
Adenoma type		
Null cell (%)	52	29.5
Prolactinoma (%)	17	13.2
Gonadotrophic (%)	13	1.6
Corticotrophic (%)	9	9.8
Postoperative visual outcomes		
Visual acuity improvement (%)	88	94.4
Visual field deficits (%)	95	93.3
Ocular paresis (%)	100	100
Hormone deficiency		
Hypoadrenalism (%)	82	60
Hypothyroidism (%)	89	62.7
Hypotestosteronism (%)	64	63.6
Diabetes insipidus (%)	11	10

without severe neuro-ophthalmological deficits and for those who respond quickly to early medical therapy

We compared our current results (for the period between 1992 and 2013) with our previous experience between 1975 and 1991⁸ (Table 6). The main difference is a greater number of patients treated conservatively in the more recent past. As previously mentioned, the lower rates of ophthalmoparesis and visual field deficits in the current series can be explained by earlier diagnosis enabled by MRI. Outcomes were generally excellent in both series. Yet, there has been a small decline in the rates of long-term hypoadrenalism and hypothyroidism.

The main strengths of our study are the relatively large size of our cohort and the detailed and prolonged follow-up. However, it also has limitations. Treatment selection bias affects the comparison between conservative and surgical therapy groups, a limitation that our study shares with all previous ones, as no randomized studies of medical versus surgical treatment of pituitary apoplexy have ever been conducted. Also, not all patients had neurological, endocrinological, and ophthalmological evaluations at every time point of follow-up. Lastly, it is possible that we may have missed very mild cases of pituitary apoplexy that were treated in the ambulatory setting and were not called apoplexy by their treating physician.

Conclusions

We conclude that pituitary apoplexy is an eminently treatable condition that is generally characterized by a very favorable outcome when adequate treatment is provided in a timely manner. Selected cases can be managed conservatively, but surgery is associated with excellent outcomes and a very low risk of complications in experienced hands. Patients with pituitary apoplexy may need long-term hormone replacement, but they can be informed that the prognosis is otherwise excellent in the vast majority of cases, even among those presenting with neuro-ophthalmological deficits.

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