Pituitary Apoplexy: Large Surgical Series with Grading System

David H. Jho[1], Beverly M. K. Biller[2], Pankaj K. Agarwalla[3], Brooke Swearingen[3]

Key words
- Hemorrhagic macroadenoma
- Pituitary adenoma
- Pituitary apoplexy
- Transsphenoidal surgery

Abbreviations and Acronyms
GCS: Glasgow Coma Scale
INR: International normalized ratio
KPS: Karnofsky performance status
MRI: Magnetic resonance imaging
NFA: nonfunctioning pituitary adenoma

From the [1]Neurosurgery and Neuroendoscopy Departments, Allegheny General Hospital, Pittsburgh, Pennsylvania; and [2]Neuroendocrine Unit and [3]Neurosurgery Service, Massachusetts General Hospital, Boston, Massachusetts, USA

To whom correspondence should be addressed: Brooke Swearingen, M.D. [E-mail: bswearingen@partners.org]

Citation: World Neurosurg. (2014) 82, 5:781-790. http://dx.doi.org/10.1016/j.wneu.2014.06.005

Journal homepage: www.WORLDNEUROSURGERY.org

Available online: www.sciencedirect.com

BACKGROUND: **Pituitary apoplexy is an infrequent occurrence that can require timely treatment. The term "pituitary apoplexy" as used in the literature describes a heterogeneous spectrum. There is controversy about which subsets require urgent as opposed to elective surgical treatment or even medical treatment alone. We present a retrospective series of 109 consecutive cases of pituitary apoplexy from a single institution from 1992–2012 and develop a comprehensive classification system to analyze outcome.**

METHODS: **Surgical and endocrine consult databases were reviewed to analyze patterns of presentation, imaging, treatment, and outcomes.**

RESULTS: **Most of the patients in this series presented clinically with "classic" pituitary apoplexy (97%), had magnetic resonance imaging for evaluation (99%), underwent transsphenoidal surgery as their primary treatment (93%), and were found to have pituitary adenomas on histopathology (90%). We categorized patients into 5 grades based on clinical presentation. Tumor volume, cavernous sinus involvement, suprasellar extension, and need for ongoing endocrine replacement correlated with grade. Long-term endocrine replacement at follow-up was required in 62%–68% of patients with a higher grade compared with 0–23% of patients with a lower grade. Higher grade patients tended to undergo earlier surgery after symptom onset. Symptoms resolved or improved with treatment in 92%–100% of patients across all grades with good general outcomes for visual deficits and ocular motility problems, validating management decisions overall.**

CONCLUSIONS: **We offer a simple yet comprehensive grading system to classify the clinical spectrum of pituitary apoplexy, which has implications for management, outcomes, and categorization for future studies.**

INTRODUCTION

The term "pituitary apoplexy" was coined by Brougham et al. (5) in a case series of 5 patients during the pre–magnetic resonance imaging (MRI) era, although Bailey (2) was previously credited with describing the first case of pituitary tumor with hemorrhage in 1898. Retrospective series of pituitary apoplexy have since been described in the literature, but there is still disagreement about the definition and optimal management (10, 12, 27, 29, 32). Some authors define the term pathologically as hemorrhage or infarction (or both) of the pituitary or sellar tumor. Others focus on the clinical syndrome, defining "classic" or "acute" pituitary apoplexy as characterized by sudden-onset headache, vomiting, visual problems, and decreased consciousness (20). Asymptomatic pituitary tumor hemorrhage or infarction has been called "subclinical" or "subacute" apoplexy and may be found by MRI, intraoperatively, or histopathologically; this is a controversial subset of patients (approximately 25% quoted frequency) that many authors do not consider as having true pituitary apoplexy (4, 15, 19). Optimal management is also controversial; some authors advocate for early surgical intervention, whereas others identify subsets for conservative management (7, 27, 30).

We define "pituitary apoplexy" both clinically and radiographically, with a spectrum that can be subcategorized by a clinical grading system. This grading system defines pituitary apoplexy radiographically as a sellar mass lesion with suspected hemorrhage or necrosis and categorizes patients into 5 grades of increasing clinical severity based on the most common presenting symptoms. Grade 1 patients are asymptomatic and correspond to "subclinical" apoplexy (described in previous paragraph), grade 2 patients have symptoms attributable only to endocrinopathy, grade 3 patients have headache, grade 4 patients have ocular paresis, and grade 5 patients have visual deficits or a low Glasgow Coma Scale (GCS) score such that vision cannot be assessed. Patients are placed into the highest grade for which they meet symptom criteria. We also discuss 3 clinical subgroups: patients with 1) prolactinomas, 2) hemorrhagic Rathke cleft cysts, and 3) significant comorbidities. The presence of any of these 3 conditions may favor medical treatment. Patients with a higher grade

require timely surgical management, and patients with a lower grade may be treated with elective surgery or even conservative management (Figure 1).

METHODS

We retrospectively screened the institutional pituitary surgical database (2339 cases) and general endocrine consult database (emergency department and inpatient consultations) over a 20-year period from 1992–2012 at Massachusetts General Hospital. Record review was approved by the institutional review board. Patients were included if they had MRI findings consistent with a sellar mass with suspected hemorrhage or infarction; surgical or pathologic confirmation was noted in operative cases. We identified 139 potential patients, with 109 surgically treated cases included in both databases and 30 medically treated cases with putative apoplexy identified from the consult database only. When further evaluation resulted in a diagnosis other than apoplexy, 22 of the nonoperative patients were excluded. Early in the series, 4 patients were excluded because of incomplete medical records. An additional 4 patients were excluded because they had postoperative hemorrhage as a surgical complication rather than as their initial presentation. The final group included 109 patients, with 101 surgically treated and 8 medically treated cases.

Endocrine Testing

Pretreatment hormone testing was performed whenever possible and was available for 106 patients. For patient safety, hypoadrenalism was assumed in the absence of formalized testing, and stress dose corticosteroids were empirically given if early surgery was required. All patients underwent endocrine evaluation in the initial postoperative period and again at 6 weeks. For the purposes of this study, hormone insufficiency at follow-up was assumed based on the prescription of replacement therapy at the time of follow-up testing. Because many of these patients were not ultimately followed at the neuroendocrine clinic, the results of detailed postoperative testing were frequently unavailable, and replacement therapy data were used in lieu of biochemical data.

Radiographic Analysis

All patients were assessed with MRI except for 1 patient who underwent computed tomography angiography because MRI was contraindicated. Both MRI and computed tomography were performed in 67 patients. The maximal tumor diameters in the X, Y, and Z dimensions were recorded for 78 patients with available electronic imaging allowing magnification for measurements. Similar measurements were made for hemorrhage-necrosis diameters for 60 patients who had discrete regions of hemorrhage or necrosis allowing such measurements. The average of X, Y, and Z plane measurements was calculated to obtain the mean tumor and hemorrhage-necrosis diameters. Tumor and hemorrhage-necrosis volumes were calculated using the ABC/2 formula extrapolated from methods used to calculate intracerebral hemorrhage volumes (13).

Surgical and Pathologic Findings

Intraoperative findings were obtained from operative reports, and histopathologic findings were acquired from pathology reports.

Statistical Analysis

Two-tailed t test with graphs and SEM were done using Microsoft Excel (Microsoft Corporation, Redmond, Washington, USA).

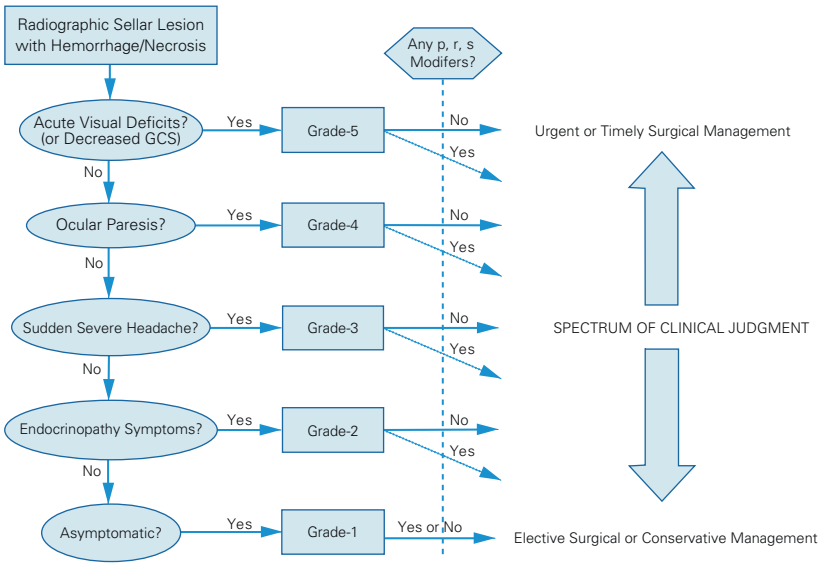

Figure 1. Flow chart illustrating assessment using the Pituitary Apoplexy Grading System. GCS, Glasgow Coma Scale; p modifier, prolactinoma; r modifier, hemorrhagic Rathke cleft cyst; s modifier, significant comorbidities.

RESULTS

Demographics

We identified 109 cases over a 20-year period (1992–2012). Age range was 18–87 years (mean, 51 years; median, 52 years); there were 69 men (63%) and 40 women (37%). Most patients underwent surgery as primary treatment (93%; n = 101 of 109), which accounted for 4.3% (n = 101 of 2339) of the institutional pituitary procedures during that period. In 8 patients, pituitary tumors were known to be present before hemorrhage or infarction, whereas the remaining patients (93%; n = 101 of 109) had pituitary apoplexy as the initial presentation. Median clinical follow-up was 35 months (range, 0–201 months), and median radiographic follow-up was 13 months (range, 0–189 months).

Symptomatic Presentation

Across all groups, 95 patients presented with headaches; 43, with visual acuity or field deficits; 39, with ocular paresis; 36, with vomiting; 14, with reduced GCS score; 8 with meningismus; and 2, with fever (Table 1).

Radiographic Findings

MRI was performed preoperatively in 99% (n = 108 of 109) of cases. The single grade 1 and both grade 2 cases were grouped