PITUITARY APOPLEXY

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Updated August 11, 2022

CLINICAL RECOGNITION

Insult to the pituitary can be in the form of hemorrhage, infarction, or both. When abrupt and sometimes catastrophic hemorrhagic infarction occurs in the pituitary it is defined as apoplexy. The constellation of headache, vomiting, visual impairment (Apoplexy Triad), and altered consciousness with hemodynamic instability, although not specific for pituitary apoplexy, are reasons to consider the diagnosis (Table 1). Often the presentation in this dramatic fashion is the first time the patient is aware that he/she harbors a pituitary tumor. Asymptomatic hemorrhage and infarct into a pituitary tumor can occur in 10-25% of patients, however true apoplexy (the constellation of symptoms noted above) occurs in 2-10% of pituitary tumor patients.

Table 1. Signs and Symptoms of Pituitary Apoplexy

Symptom	Incidence
Headache	95%
Vomiting	70%
Vision Defects: Visual field defect Decreased visual acuity Diplopia (CN III, IV, V and VI)	 64% 52% 78%
Hemiplegia	Rare
Meningismus	Rare
Hypotension (cardiovascular collapse)	95%

The most common presenting complaint, headache, can present variably from retroorbital to unilateral to bilateral temporal headaches. These are the symptoms during the acute phase of apoplexy. As the hemorrhagic infarct resolves often times the patient is left with hypopituitarism (refer to section on Hypopituitarism).

Certain conditions will predispose a patient to the catastrophe of pituitary apoplexy. (Table 2). While all large pituitary tumors are at risk for hemorrhagic infarction, certain functional pituitary tumors such as those in Cushing's disease or acromegaly may be particularly prone. Nearly 25% of all patients with apoplexy have inadequately treated hypertension.

Table 2. Predisposing Conditions Associated with Pituitary Apoplexy
Pituitary Tumor
Non-functioning pituitary macroadenoma
Certain functional tumors
Hypertension and/or hypotension
Surgery
Cardiac surgery (heart lung bypass; coronary artery grafts)
Major orthopedic procedures
Drugs
Endocrine stimulation tests (Thyrotropin releasing hormone stimulation; insulin tolerance test)
Anticoagulants
Estrogen
Head Trauma
Pregnancy and Delivery
Infections
Dengue fever
Hypophyisitis
Radiation therapy

PATHOPHYSIOLOGY

It is thought that alterations in blood flow to pituitary adenomas coupled with high metabolic demands lead to apoplexy. The main symptoms and consequences of apoplexy are due to the increased pressure present within the bony walls of the sella turcica in which the pituitary resides. A sudden increase in the sella contents due to blood and edema results in increased pressure. This increased pressure and meningeal irritation are responsible for the neurologic symptoms described in Table 1, including the increased pressure in the cavernous sinus and the cranial nerve palsies as well as bitemporal-hemianopsia. Extravasation of blood into the subarachnoid space causes meningeal irritation.

DIAGNOSIS AND DIFFERENTIAL

Physicians must promptly recognize that patients presenting with the triad of headache, vomiting, and visual disturbances may have any one of several diagnoses that require urgent attention to prevent death or irreversible neurologic impairment.

Clinical Evaluation

Evaluation of the patient should begin with a thorough history, from the patient if sufficiently conscious to give one, or from family members. A history of a pituitary tumor should raise the suspicion for apoplexy. More subtle abnormalities associated with pituitary dysfunction (hypothyroidism, adrenal insufficiency, or

hypogonadism) may be helpful (see section on Hypopituitarism).

Radiologic and Laboratory Evaluation (Table 3)

The cornerstone for diagnosis of patients presenting with the Apoplexy Triad is urgent radiologic assessment. MRI T2 weighted images are the test of choice and should be performed emergently in all patients with visual symptoms. A CT scan can be useful when an MRI is neither available or possible.

Urgent measurement of blood chemistries, including electrolytes, kidney function, liver function, complete blood count with platelets, and prothrombin time can be useful. Since more than 80% of patients will have endocrine dysfunction, urgent measurement of free T4, TSH, prolactin, ACTH, and a random cortisol can be helpful and usually is readily available. Less rapidly available and helpful (and less important in the initial diagnosis and management) are other pituitary hormones such as LH, FSH, estradiol or testosterone, growth hormone, and IGF I.

Examination of cerebral spinal fluid is usually not diagnostic, and unnecessary if the diagnosis of apoplexy is certain. However, if there is bleeding into the CSF as a result of the apoplexy, red blood cells as well as elevated protein and xanthochromia can be seen.

Table 3. Useful Tests in the Diagnosis of Pituitary Apoplexy

TEST	Expected Result in Apoplexy
MRI pituitary	Hemorrhagic infarct in region of pituitary
Electrolytes	Hyponatremia,
Complete Blood Count	Anemia, thrombocytopenia
Prothrombin time	Possibly prolonged
FT4/TSH	Low/Low or normal
Prolactin	Low (< 1 ng/dl)
Cortisol, random	Usually < 5 ug/dl
Other tests of the endocrine axes	See section on Hypopituitarism
Visual Field Testing	Defect

The differential diagnosis of pituitary apoplexy should include other conditions that result in the symptoms of headache, vomiting, visual disturbances, and hemodynamic instability (Table 4). Each of these conditions is itself a medical emergency that requires specific treatment.

Table 4. Differential Diagnosis of Pituitary Apoplexy
Subarachnoid hemorrhage (can be distinguished from apoplexy by MRI with MR angiogram)
Infectious meningitis
Cavernous sinus thrombosis
Migraine
Rathke cyst hemorrhage
Hyperemesis gravidarum
Stroke

TREATMENT

The key to successful management of patients with pituitary apoplexy is a team approach including critical care neurologists, neurosurgeons, neuro-ophthalmologists, and endocrinologists. Together each of these specialists provide needed expertise in the management and ongoing care of these patients. Acute secondary adrenal insufficiency is seen in approximately two-thirds of patients and is the major source of mortality associated with this condition. Prompt glucocorticoid replacement is there for mandatory and should not be delayed for confirmatory testing. The initial management is stabilization of the hemodynamic status with IV 0.9% NaCl boluses to maintain normal tissue perfusion, and usually high dose parenteral glucocorticoids (100 mg hydrocortisone q 8h intravenous). Unless significant cerebral edema is present, hydrocortisone rather than dexamethasone is favored.

Although there is a general consensus that patients with pituitary apoplexy and significant neuro-ophthalmic signs or reduced level of consciousness should have surgical decompression, there is significant controversy in the best timing for the surgical procedure due to lack of good quality outcomes data. (see figure 1 for a suggested management approach).

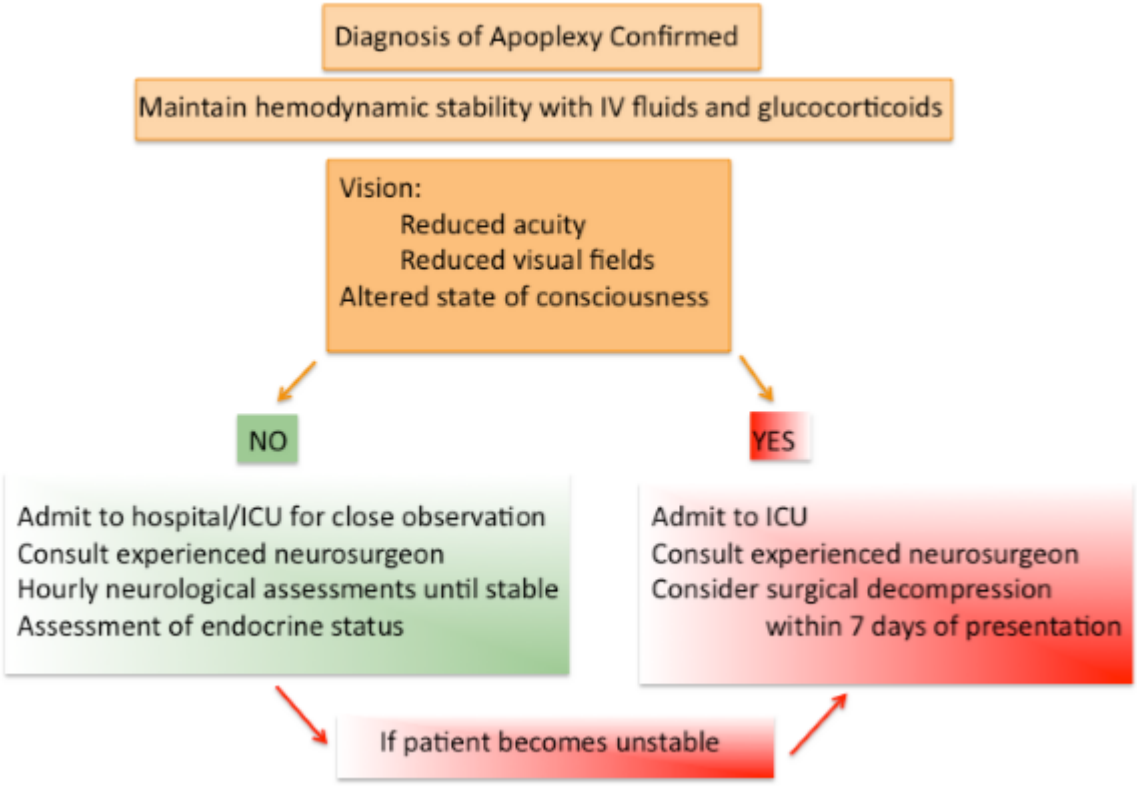

Figure 1. Treatment of Pituitary Apoplexy.

FOLLOWUP

While 80% of patients have residual hypopituitarism following apoplexy (with or without surgical decompression) some patients do not display immediate evidence of hypopituitarism. In addition, recurrent apoplexy and tumor regrowth has been reported to occur. MRI of the pituitary should be obtained at 3–6-month intervals until the anatomy is stable and then yearly for 5 years. A month after discharge from the hospital and recovery from the acute event, if necessary, patients are subject to repeat endocrine testing to determine if the endocrine defects persist. Repeat testing will confirm whether the patient needs to remain on life-long hormone replacement therapy.

GUIDELINE

Rajasekaran, S., Vanderpump, M., Baldeweg, S., Drake, W., Reddy, N., Lanyon, M., Markey A., Plant, G., Powell, M., Sinha, S., Wass, J. UK guidelines for the management of pituitary apoplexy. Clin Endocrinol (Oxf) 2011 Jan 74(1);9-20. PMID 21044119 http://www.ncbi.nlm.nih.gov/pubmed/21044119

REFERENCES

1. Chung TT, Koch CA, Monson JP. Hypopituitarism. In: Feingold KR, Anawalt B, Boyce A, Chrousos G, Dungan K, Grossman A, Hershman JM, Kaltsas G, Koch C, Kopp P, Korbonits M, McLachlan R, Morley JE, New M, Perreault L, Purnell J, Rebar R, Singer F, Trence DL, Vinik A, Wilson DP, editors. Endotext [Internet]. South Dartmouth (MA): MDText.com, Inc.; 2000-2018 Jul 25
2. Vanderpump M1, Higgens C, Wass JA. UK guidelines for the management of pituitary apoplexy a rare but potentially fatal medical emergency. Emerg Med J. 2011 Jul;28(7):550-1.
3. Donegan D, Erickson D. Revisiting Pituitary Apoplexy. J Endocr Soc. 2022 Jul 26;6(9):bvac113. doi: 10.1210/jendso/bvac113. eCollection 2022 Sep 1. PMID: 35928242