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UNCOMMON AND/OR UNUSUAL HEADACHES AND SYNDROMES (J AILANI, SECTION EDITOR)

Presentation and Management of Headache in Pituitary Apoplexy

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Abstract

Purpose of Review Pituitary apoplexy (PA) occurs in the setting of an infarction and/or hemorrhage of a pre-existing adenoma. The most common presenting symptom is a severe, sudden onset headache. However, the characteristics of headache in the setting of PA are varied and can sometimes mimic primary headache disorders. The purpose of this article is to review the various presentations of headache in PA. We also outline treatment options for persistent headaches following PA.

Recent Findings A recent retrospective review of patients undergoing transsphenoidal resection of sellar lesions, including PA, found that gross total resection and short duration of preoperative headache were predictors of improvement in headaches postoperatively. This strengthens the importance of timely recognition of PA as potential etiology of headache.

Summary The most common presentation of PA is thunderclap headache; however, several other primary HA disorders have been described including status migraine, SUNCT, and paroxysmal hemicrania

Keywords Pituitary apoplexy · Headache · Thunderclap headache · Pituitary adenoma

Introduction

Pituitary apoplexy is a rare disorder, with incidence of 0.6 to 7% [1•]. It is typically defined by the acuity of the presenting symptoms including severe acute headache, visual disturbances, nausea, and/or vomiting. If the diagnosis is not considered at the time of patient presentation, the end result can be fatal. Therefore, quick recognition is key. Less common presentations of PA can include a subacute headache that may be clinically indistinguishable from a primary headache disorder.

Pathophysiology

Pituitary apoplexy occurs due to an infarction and/or hemorrhage of an existing pituitary adenoma, most commonly a nonfunctional macroadenoma [2]. It is not well understood why pituitary adenomas are prone to hemorrhage or infarction, but unique vascularization properties likely contribute.

Normal pituitary gland is supported by the capillary network of the hypophysial portal system, whereas pituitary adenomas, by comparison, have a reduced blood supply fed by direct arteries. It is hypothesized that pituitary adenomas are predisposed to hemorrhage because of the rich portal vascularization of the normal gland and the immature and fragile blood vessels that support the adenoma. Pituitary tumor infarction may occur because the adenomas outgrow their blood supply or because expansion of the tumor compresses feeding vessels against the boney sella [3]. It is not uncommon for imaging or pathology to reveal both hemorrhage and ischemic necrosis.

Either of these processes (or both) leads to rapid expansion within the sella and compression of adjacent structures (Fig. 1). The rapid enlargement results in increased pressure of the intrasellar contents. Intrasellar pressure is reportedly higher in patients with headache as a presenting symptom of pituitary adenomas [5, 6]. Headache likely occurs as a result of both dural stretching by mass effect, and extravasation of blood and necrotic tissue into the subarachnoid space causing meningeal irritation [1•, 3].

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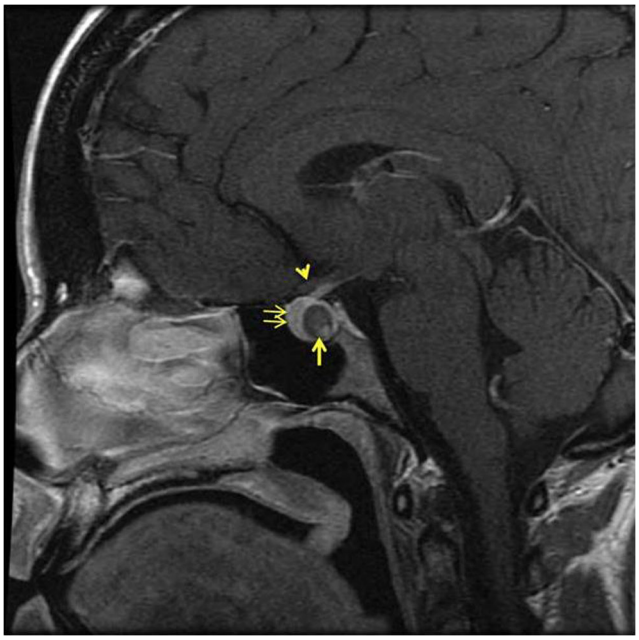

Fig. 1 Pituitary gland with hyper-intensity within the gland signifying ischemia (long arrow), with resulting surrounding hemorrhage (double arrows). Original figure is from Shabas et al. [4]

Presentation

Pituitary apoplexy is rare, with the overall incidence ranging from 0.6 to 7% and rising to 2–12% in patients with a known pituitary adenoma [2]. Retrospective case series of patients with PA report that between 87 and 92% present with acute headache [2, 7•]. Nearly half (45.8%) of subjects in a retrospective series of 60 patients with PA presented with thunderclap headache. Several published case reports and series describe presentation with severe acute headache with maximum intensity at onset [8]. Although the criteria for thunderclap headache in these reports are not defined by strict methodology, it is like the most common sub-type of headache in PA. Therefore, PA should be considered as a potentially life-threatening cause of thunderclap headache along with the better recognized etiologies such as subarachnoid hemorrhage and carotid dissection.

The incidence of presentation of PA with headache phenotypes other than thunderclap is unknown. However, there are several case reports of PA identified in the routine evaluation of patients with subacute or chronic headaches. As reported by Shabas et al., a patient presented with a gradual onset, unremitting headache of several weeks duration. The headache was described as throbbing and associated with nausea, phonophobia, and mild photophobia. The patient was treated for status migrainosus with a short course of steroids and the headache resolved. However, an MRI of the brain subsequently revealed hemorrhagic pituitary apoplexy without mass effect [4].

A history of primary headaches, such as migraine, may also delay recognition of PA. Silvestrini et al. reported a 22-year-old man with a history of migraines with aura who presented with severe headache, followed by double vision and left ptosis, diagnosed as ophthalmoplegic migraine. Following unsuccessful migraine treatment and a nondiagnostic lumbar puncture, MRI of the brain showed hemorrhagic pituitary adenoma [9].

PA is also reported to present with a headache mimicking paroxysmal hemicrania, which is a type of trigeminal autonomic cephalgia. An 83-year-old man with no prior history of headache and was admitted for severe unilateral headaches, up to five attacks per day, associated with ipsilateral ptosis, meiosis, palpebral edema, and watering of the left eye. MRI of the brain revealed recent PA [10].

These presentations highlight the importance of MRI evaluation of patients presenting with new-onset headache disorders as the clinical features of headache in PA may be indistinguishable from a primary headache disorder.

Diagnostic Workup

Pituitary apoplexy is uncommon, but should be considered in any patient who presents with an acute-onset or thunderclap-type headache, with or without any visual complaints. A history of pituitary adenoma is helpful, but not necessary. Only 7% of patients were known to have a pituitary adenoma at presentation, as reported by Bujawansa et al. Other articles offer a complete overview of the diagnostic workup, including hormone evaluation for patients with suspected PA [11].

For patients presenting with headache in the outpatient setting, the screening evaluation for possible subacute PA involves a thoughtful choice of imaging. As with other headaches attributed to the pituitary gland, MRI without contrast of the sella is the imaging modality of choice and has been shown to confirm pituitary apoplexy in > 90% of the patients. Computed tomography scan is an appropriate choice for patients with acute presentation. A CT scan was helpful in identifying a mass in 80% of the patients with pituitary apoplexy; however it was diagnostic in only 21–28% of those cases. In the event that an MRI is not possible or contraindicated, a CT scan of the head with thin cuts, with and without contrast, and with dedicated sagittal and coronal reconstruction is the next best option [1•, 12•].

The timeline of the apoplexy has been reported to be evident on an MRI, as the breakdown of hemoglobin and resultant oxidation of the hemosiderin results in hypointensity, noted specifically on T1- and T2-weighted images. Of note, CT scans can be helpful for hemorrhagic-type apoplexy, as the blood shows up hyperdense. Addition of contrast results in minimal or no enhancement. However, peripheral

enhancement may be noted with contrast in a rare event that an empty sella is present [1•].

Treatment

There are no studies evaluating the incidence or duration of headache following recognition and treatment of PA. The headache in PA likely occurs as a result of both dural stretching by mass effect and extravasation of blood and necrotic tissue into the subarachnoid space causing meningeal irritation [1•, 3]. Thus, alleviation of mass effect and resorption of blood would be expected to predict headache improvement. Consistent with this, a recent retrospective review of patients undergoing transsphenoidal resection of sellar lesions, including PA, found that gross total resection and short duration of preoperative headache were predictors of improvement in headaches postoperatively [13]. However, as seen in subarachnoid hemorrhage, the author's experience is that patients may experience persistent headache despite receiving appropriate acute treatment.

Initial interventions should be conservative and start with acetaminophen. NSAIDs may need to be avoided initially due to inhibition of platelet aggregation potentially increasing risk of further hemorrhage. In the acute setting, Singh reported three patients experienced symptomatic relief with narcotics [14]. However, opioid and butalbital containing medications may potentially confound clinical exams due to their sedative effects.

Given the lack of evidence, we proposed that similar to chronic post traumatic headaches, treatment of chronic headache following PA should be phenotypic.

Case reports indicate this may be an effective strategy. For example, the patient who presented with paroxysmal hemicrania experienced improvement with indomethacin [10]. Therefore, using the same philosophy, it is recommended for providers to treat headaches following PA according to primary headache disorder it most closely resembles.

Conclusion

Pituitary apoplexy due to an infarction or hemorrhage of an existing pituitary adenoma is a rare cause of headache. Although headache is typically thunderclap, it can mimic benign primary headache disorders such as migraine and trigeminal autonomic cephalgias. Therefore, there must be a strong clinical suspicion in patients who are at risk, including patients with a known pituitary adenoma or with history concerning for pituitary hormone dysfunction. The authors propose that headaches following PA should be treated phenotypically.

Compliance with Ethical Standards

Conflict of Interest Himanshu Suri and Carrie Dougherty declare no conflict of interest.

Human and Animal Rights and Informed Consent This article does not contain any studies with human or animal subjects performed by any of the authors.

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