

Clinical Reasoning: A 41-year-old man with thunderclap headache

Scott Grossman, MD, Aaron Rothstein, MD, Jenna Conway, MD, Lindsey Gurin, MD, and Steven Galetta, MD
Neurology® 2018;91:e87-e91. doi:10.1212/WNL.0000000000005738

Correspondence

Dr. Grossman
scott.grossman@nyumc.org

Section 1

A 41-year-old man with a history of low testosterone on androgen therapy presented to the emergency department complaining of acute onset of the worst headache of his life. He reported being well until 6 hours earlier, when he was resting in his hotel room and experienced a thunderclap headache. The headache was initially described as retro-orbital, left-sided, associated with vomiting, and extending to the occiput. It was maximal within moments of onset. There were no associated visual complaints, weakness, numbness, or tingling. On initial examination, he was noted to have preserved mental status. The cranial nerve examination showed intact visual fields, normal extraocular motility, and no evidence of papilledema. Sensorimotor function was intact and symmetric throughout, and his gait was stable and narrow-based. Initial laboratory studies including blood count and metabolic panel were unremarkable. He was administered oxygen via nasal cannula, metoclopramide, and diphenhydramine without improvement.

Questions for consideration:

1. What is the differential diagnosis for thunderclap headache?
2. What further evaluation should be pursued emergently?

GO TO SECTION 2

From the Departments of Neurology (S. Grossman, A.R., J.C., L.G., S. Galetta) and Psychiatry (L.G.), New York University, New York.

Go to Neurology.org/N for full disclosures. Funding information and disclosures deemed relevant by the authors, if any, are provided at the end of the article.

Section 2

Thunderclap headache presents multiple diagnostic possibilities, such as subarachnoid hemorrhage, pituitary apoplexy, reversible cerebral vasoconstriction syndrome (RCVS), meningitis, venous sinus thrombosis, and hemorrhagic or ischemic stroke. In this patient who was on androgen replacement therapy, there was concern for venous sinus thrombosis. Given his history of endocrinologic disturbance, there was also concern about disturbance of his hypothalamic–pituitary axis. Specifically, pituitary adenomas can cause disturbance in testosterone, and such tumors are liable to bleed due to their abnormal blood supply. Therefore, pituitary apoplexy was also a strong consideration. The character of the headache and acute onset to maximum severity also raised concern for subarachnoid or intraparenchymal hemorrhage.

Noncontrast head CT was performed and was normal. CSF examination revealed 50 red blood cells (RBC) and 2 white blood cells (WBC) in tube 1 and 3 RBC and 1 WBC in tube 4 without xanthochromia. Glucose was 83 mg/dL and protein was 48 mg/dL. The patient received dexamethasone 10 mg IV, along with 1 L of normal saline and 2 mg

morphine IV. The headache remained refractory to multiple medications.

Further history revealed a remote history of IV drug abuse 20 years prior. He had no headache history. He was recently evaluated for sexual dysfunction and started on testosterone gel. However, due to insurance issues, he reported taking this medication inconsistently for several months. Prior workup for testosterone deficiency revealed serum testosterone of 324 (normal 270–1,070 ng/dL) and prolactin 8.4 (normal <20 ng/dL). On further examination, he was noted to have prominent prognathia, frontal bossing, large hands and feet, and macroglossia. He and his wife also noted a recent change in his shoe size and coarsening of his facial appearance. His wife noted that he looked different than he did in photographs from 11 years prior. Further, he was found to have a tattoo of a wedding ring, and reported he could not find one large enough to fit his hands.

Questions for consideration:

1. What would be your next choice of imaging given this clinical scenario?
2. What are the most important next steps in management of this case?

GO TO SECTION 3

Section 3

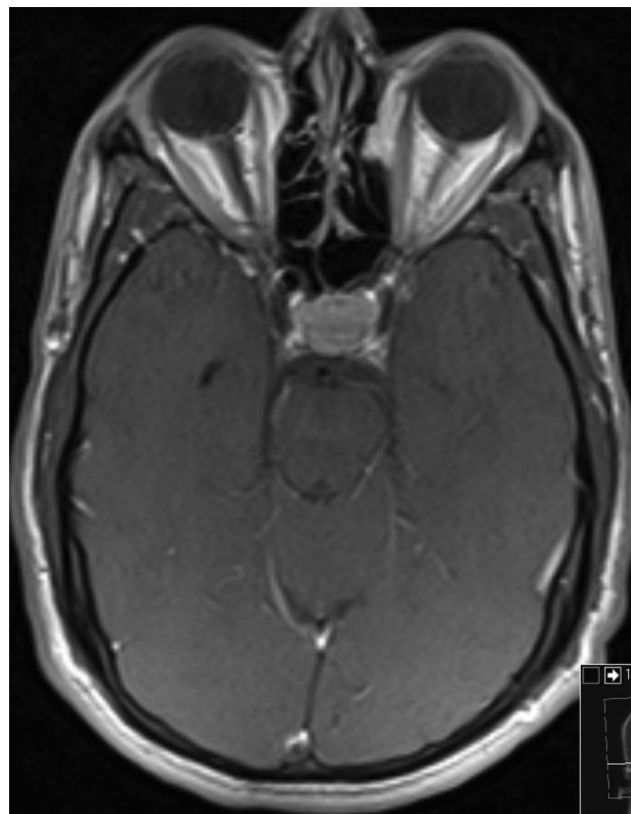
Given concern for a pituitary adenoma causing long-standing acromegalic features with new thunderclap headache, urgent MRI brain with and without gadolinium with focus on the pituitary gland was obtained (figures 1–3). This scan showed mild enlargement of the sella turcica along with a 1.1-cm T1-hyperintense lesion demonstrating mixed T2 signal, including low T2 signal components in the pituitary stalk with deviation to the right and mild suprasellar extension without chiasmatic compression. Magnetic resonance venogram demonstrated patent sinuses without thrombus. RCVS was considered as a diagnostic possibility but angiographic imaging was deferred given clinical concern for pituitary adenoma.

Because of these imaging findings, neurosurgery, ophthalmology, and endocrinology were consulted. Endocrinology recommended starting hydrocortisone 50 mg IV every 6 hours to support the hypothalamic–pituitary axis, as well as a workup for a pituitary adenoma including diluted prolactin, insulin-like growth factor 1 (IGF-1), thyroid-stimulating hormone (TSH), fT4, T3, luteinizing hormone (LH), follicle-stimulating hormone (FSH), HgbA1c, and serum testosterone. Ophthalmologic examination did not detect any visual field deficits. On dilated fundoscopic examination, there was no appreciated disc pallor or edema. Given suspected pituitary hemorrhage, the patient was started on a regimen of IV fluids, metoclopramide, magnesium, and tramadol. This provided some relief and his headache stabilized.

Figure 1 The patient's hand (far) with tattoo of wedding ring and examiner's hand for comparison



Figure 2 Axial precontrast T1-weighted MRI through the pituitary



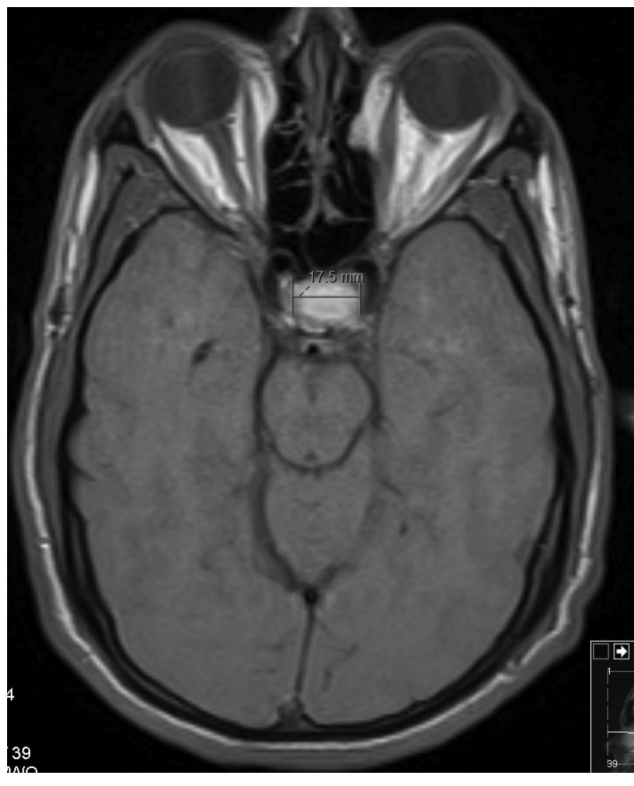
Admission laboratory work ultimately returned notable for IGF-1 elevated at 894 (normal 52–328). Further laboratory studies were within normal limits. Neurosurgery determined that no urgent surgery was indicated. Given the patient's clinical stability, he was discharged under the care of his wife and went on to establish care at a facility near his home in another metropolitan area. On most recent contact, he reported having undergone trans-sphenoidal resection of his pituitary adenoma and was stable.

The natural history of pituitary apoplexy

Pituitary apoplexy occurs in 0.6%–7% of pituitary adenomas, usually in macroadenomas.^{1,2} Its incidence in the general population is 0.17 episodes per 100,000 per year.³ It can happen at any age but is seen most frequently in the fifth or sixth decade of life in men.³

The pathophysiology of pituitary apoplexy is not fully understood. However, there is some suggestion that apoplexy occurs due to the unusual organization of blood supply in the pituitary gland, which is through a portal system. Pituitary adenomas tend to have a more dominant arterial blood supply, which is thought to be more exposed to systemic arterial pressure.⁴ Moreover, the vessels that supply adenomas tend to have ruptured and fragmented basal membranes and may mature incompletely, leading to increased risk of

Figure 3 Axial postcontrast T1-weighted MRI through the pituitary



hemorrhage.⁴ Large adenomas can also outgrow their blood supply.² Pituitary tumors may also become ischemic and then hemorrhage due to compression of the vessels by the expanding mass.³

In some studies, 60%–80% of cases of apoplexy have no clear precipitant.⁴ The most common precipitating factors include major surgery, clotting disorders, estrogen therapy, dopamine agonist therapy, head trauma, pregnancy, and radiotherapy.²

Even without a clear precipitant, pituitary apoplexy often manifests in a recognizable manner. The most frequent symptom is severe sudden headache—usually bifrontal or suboccipital⁵—and it is observed in approximately 80% of patients.³ Visual disturbances occur in more than half of patients and ocular motor palsies affect up to 50%–60% of patients due to damage of cranial nerves III, IV, and VI.³ Because of the superior orientation of CN III within the cavernous sinus, it is most likely to be affected in the acute phase of pituitary apoplexy and thus can mimic the presentation of a posterior communicating artery aneurysm. Other symptoms include nausea, vomiting, photophobia, and altered mental status.² Patients can also present with meningismus due to blood in the suprasellar cisterns that leaks into the subarachnoid space.⁵

Most episodes of apoplexy occur in macroadenomas and thus endocrine symptoms may be discovered before the patient

begins to develop hemorrhage into the gland. Anterior pituitary hormone abnormalities, including LH, FSH, TSH, prolactin, growth hormone, and adrenocorticotropic hormone (ACTH), are present in approximately 80% of patients at presentation. Around 70% of patients have ACTH deficiency leading to hypotension and hyponatremia, requiring acute intervention.² Other pituitary hormone dyscrasias may manifest as acromegaly, a symptom that preceded apoplexy in our patient by many years.

With regard to the diagnostic approach, a noncontrast head CT is usually the first test ordered when patients present to the emergency department with an acute-onset severe headache. A CT scan is an imperfect but occasionally useful initial test. It shows an intrasellar mass in 80% of cases and can demonstrate hemorrhagic components in up to one-third of cases.³ Nevertheless, MRI is the imaging modality of choice as it is more sensitive in detecting tumor and hemorrhage that can be missed by a routine noncontrast CT scan. MRI provides a detailed picture of the surrounding structures that may be affected, including the carotid arteries and the cavernous sinus.³

Approach to therapy and future directions in the management of apoplexy

Treatment of pituitary apoplexy involves medical and surgical management. Medical management includes monitoring vital signs, administering IV corticosteroids to prevent an Addisonian crisis, and checking laboratory values including serum glucose, electrolytes, and pituitary hormone levels. Once medically stabilized, patients should be evaluated for surgical decompression of the pituitary gland. Clinically stable patients, including those with isolated ocular motor palsies, can be managed conservatively with favorable outcomes.^{6,7}

For patients with progression of symptoms, surgery is indicated. Urgent surgical decompression is performed for altered consciousness or severe/progressive impairment of vision including reduced acuity or field loss.⁷ In patients with severe/progressive impairment of vision, trans-sphenoidal surgery within 8 days results in significantly greater improvement in visual acuity and fields than later surgery.^{8,9} Surgical intervention not only improves visual outcomes, but may also improve hypopituitarism, which can remain an ongoing issue with many patients, requiring long-term hormone replacement therapy.⁹ Moreover, given that regrowth of the tumor years after pituitary apoplexy is possible, all patients require long-term surveillance. Despite these guidelines, evidence for optimal management of pituitary apoplexy in the form of randomized controlled trials is lacking.⁷

Author contributions

Scott Grossman: study concept and design, acquisition of data, analysis and interpretation of data, critical revision of manuscript for intellectual content. Aaron Rothstein: study concept and design, acquisition of data, critical revision of manuscript for intellectual content. Jenna Conway: study

concept and design, acquisition of data, critical revision of manuscript for intellectual content. Lindsey Gurin: critical revision of manuscript for intellectual content. Steven Galetta: critical revision of manuscript for intellectual content.

Study funding

No targeted funding reported.

Disclosure

The authors report no disclosures relevant to the manuscript. Go to Neurology.org/N for full disclosures.

References

1. Pearce JMS. On the origins of pituitary apoplexy. *Eur Neurol* 2015;74:18–21.
2. Johnston PC, Hamrahian AH, Weil RJ, Kennedy L. Pituitary tumor apoplexy. *J Clin Neurosci* 2015;22:939–944.
3. Briet C, Salenave S, Bonneville J-F, Laws ER, Chanson P. Pituitary apoplexy. *Endocr Rev* 2015;36:622–645.
4. Nawar RN, AbdelMannan D, Selman WR, Arafah BM. Analytic review: pituitary tumor apoplexy: a review. *J Intens Care Med* 2008;23:75–90.
5. Dubuisson AS, Beckers A, Stevenaert A. Classical pituitary tumour apoplexy: clinical features, management and outcomes in a series of 24 patients. *Clin Neurol Neurosurg* 2007;109:63–70.
6. Haider AS, Rao PJ. A 64-year-old woman with dilated right pupil, nausea, and headache. *Digit J Ophthalmol* 2013;19:1–12.
7. Capatina C, Inder W, Karavitaki N, Wass JA. Management of endocrine disease: pituitary tumour apoplexy. *Eur J Endocrinol* 2015;172:R179–R190.
8. Muthukumar N, Rossette D, Soundaram M, Senthilbabu S, Badrinarayanan T. Blindness following pituitary apoplexy: timing of surgery and neuro-ophthalmic outcome. *J Clin Neurosci* 2008;15:873–879.
9. Randeva HS, Schoebel J, Byrne J, Esiri M, Adams CB, Wass JA. Classical pituitary apoplexy: clinical features, management and outcome. *Clin Endocrinol* 1999;51:181–188.

Neurology®

Clinical Reasoning: A 41-year-old man with thunderclap headache

Scott Grossman, Aaron Rothstein, Jenna Conway, et al.

Neurology 2018;91:e87-e91

DOI 10.1212/WNL.0000000000005738

This information is current as of July 2, 2018

Updated Information & Services	including high resolution figures, can be found at: http://n.neurology.org/content/91/1/e87.full
References	This article cites 9 articles, 1 of which you can access for free at: http://n.neurology.org/content/91/1/e87.full#ref-list-1
Subspecialty Collections	This article, along with others on similar topics, appears in the following collection(s): Endocrine http://n.neurology.org/cgi/collection/endocrine Other cerebrovascular disease/ Stroke http://n.neurology.org/cgi/collection/other_cerebrovascular_disease__stroke Primary brain tumor http://n.neurology.org/cgi/collection/primary_brain_tumor Secondary headache disorders http://n.neurology.org/cgi/collection/secondary_headache_disorders Visual fields http://n.neurology.org/cgi/collection/visual_fields
Permissions & Licensing	Information about reproducing this article in parts (figures, tables) or in its entirety can be found online at: http://www.neurology.org/about/about_the_journal#permissions
Reprints	Information about ordering reprints can be found online: http://n.neurology.org/subscribers/advertise

Neurology® is the official journal of the American Academy of Neurology. Published continuously since 1951, it is now a weekly with 48 issues per year. Copyright © 2018 American Academy of Neurology. All rights reserved. Print ISSN: 0028-3878. Online ISSN: 1526-632X.

