

Central diabetes insipidus emerging after steroid replacement in pituitary apoplexy

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A healthy 50-year-old woman presented with acute onset of the worst headache of her life. She characterized the headache as constant, pulsating and over her entire head. It was associated with photophobia and fever without visual changes and neck stiffness. On examination, the patient was febrile (38.3°C) with stable hemodynamics (heart rate 70–90 beats/min and blood pressure 120–140/60–80 mm Hg). She was somnolent, requiring voice to arouse, but able to participate; she had no other abnormal examination findings. Cranial imaging with computed tomography (CT) and magnetic resonance imaging (MRI) showed a 2.3-cm hemorrhagic pituitary macroadenoma without suprasellar extension and compression of the optic chiasm (Figure 1).

Bedside lumbar puncture showed no xanthochromia; the cerebrospinal fluid had a normal glucose level and mild protein elevation. Given the initial concern of meningitis, the patient was started on broad-spectrum antibiotics and acyclovir, but these were stopped after culture testing returned without growth. Laboratory tests showed low random serum cortisol at 33 (normal range 165–579) nmol/L with normal adrenocorticotropic hormone. The remainder of the pituitary panel was normal. After discussion with neurosurgical and endocrinology colleagues, we managed the patient conservatively with high-dose glucocorticoids, given absence of visual symptoms and altered mentation.

KEY POINTS

- The diagnosis of pituitary apoplexy can be challenging, as its presentation can mimic other neurologic conditions.
- All patients with pituitary apoplexy should undergo immediate pituitary testing and empiric high-dose glucocorticoid replacement.
- Central diabetes insipidus is an uncommon, but life-threatening complication of pituitary apoplexy, most often emerging after steroid replacement.
- An interdisciplinary approach with endocrinology, ophthalmology and neurosurgery is needed.

About 8 hours after we began steroid replacement, the patient developed substantial polyuria with a urine output of 0.5 to 1 L/h. She became hypernatremic to 151 (normal range 137–147) mmol/L with dilute urine osmolality of 118 (normal range 300–900) mOsm/kg. She received hypotonic crystalloid solution and 1 dose of oral 100 µg desmopressin. After 3 hours, serial urine analysis and basic metabolic panels showed stable improvement in the patient’s fluid status and output. Repeat brain imaging showed that pituitary macroadenoma size remained unchanged.

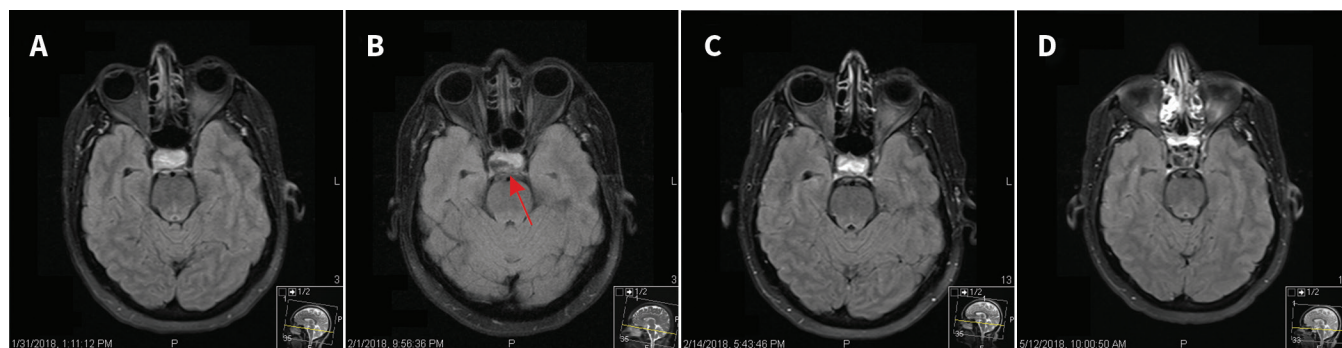


Figure 1: Axial sellar magnetic resonance imaging fluid-attenuated inversion recovery (FLAIR) sequences throughout the clinical course of a 50-year-old woman with pituitary apoplexy. L = left side. (A) Initial presentation showing FLAIR hyperintense 2.3 × 1.3 cm lesion in sella turcica suggestive of acute to subacute pituitary macroadenoma hemorrhage without suprasellar extension or optic chiasm compression. (B) After development of central diabetes insipidus. Stable lesion size with evolving blood products. Additionally, the suprasellar component may have thinned the optic chiasm on the left (arrow). (C) At time of new visual field deficits, before emergent surgery. Again, overall stable mass size without new acute appreciable hemorrhage and radiographically stable compression of optic chiasm on left. (D) Postoperative images after transsphenoidal pituitary resection.

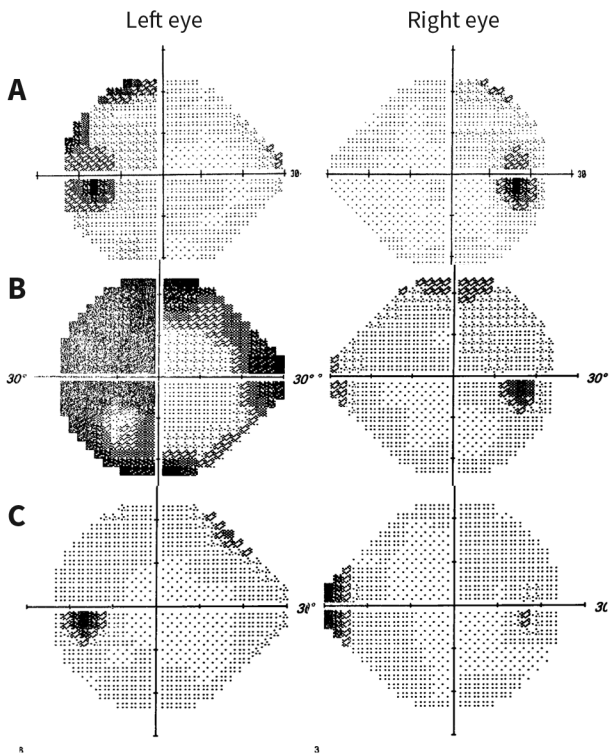


Figure 2: Humphrey visual field testing in a 50-year-old woman. Humphrey visual field 24–2 grayscale images with visual field deficits in darker areas showing (A) initial evaluation at presentation of mild bilateral, but predominantly left, superotemporal quadrantanopia; (B) subsequent testing with acute, dense left temporal hemianopia prompting emergent pituitary resection; (C) postoperative visual fields showing dramatic resolution of deficits.

Three days after admission, the patient had formal visual testing, which showed mild bilateral, but predominantly left, superotemporal quadrantanopia (Figure 2A); she was subsequently discharged with a steroid taper, thyroid hormone replacement for new secondary hypothyroidism, and close endocrine and neurosurgical follow-up for anticipated elective transsphenoidal pituitary resection. However, 2 weeks after the initial onset, at her endocrine appointment, she reported a new left visual field deficit, confirmed on visual field testing to be new left temporal hemianopia (Figure 2B). Repeat MRI showed no new vascular event, but possibly increased edema in a left-ecentric mass and new compression of the optic chiasm (Figure 3). The patient underwent urgent endoscopic endonasal pituitary resection with resolution of hemianopia by postoperative day 2 (Figure 2C). She did not have any new pituitary dysfunction during her second admission to hospital. Outpatient testing showed ongoing adrenal insufficiency, but she remains well on oral hydrocortisone and levothyroxine.

Discussion

Pituitary apoplexy is an uncommon clinical syndrome caused by abrupt pituitary hemorrhage, infarction or both, often into an unrecognized, nonfunctioning pituitary adenomas.¹ Sparse epidemiologic data suggest that prevalence of pituitary apoplexy is about 6.2 per 100 000 people, with most occurring in nonfunctioning pituitary adenomas,^{2,3} but endocrine assessment often followed acute pituitary damage, raising the possibility of missed prior functioning adenomas. In these reports, pituitary apoplexy had a male preponderance and was diagnosed mostly in the fifth or sixth decade.

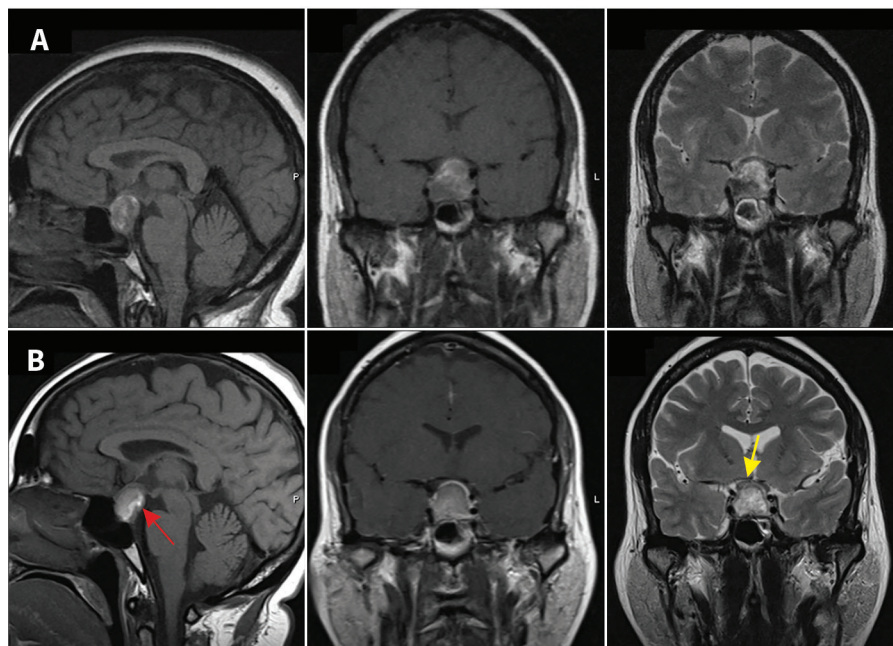


Figure 3: Sellar magnetic resonance imaging of a 50-year-old woman at initial presentation and worsened left temporal hemianopsia. Row (A) represents initial presentation and Row (B) shows new left temporal hemianopsia. Within each row, from left to right: sagittal T_1 -weighted, coronal T_1 -weighted and coronal T_2 -weighted images. The pituitary hemorrhage in row B is more T_1 hyperintense, compatible with evolving subacute blood products, and the infundibulum is displaced and compressed posteriorly (red arrow). Compression of the optic chiasm is possibly more pronounced (yellow arrow).

The exact pathophysiology of pituitary apoplexy is unknown. Undetected, nonphenotypic (asymptomatic) macroadenomas may be larger, with higher metabolic demand and limited blood supply conferring susceptibility to vascular events. Therefore, several precipitants are possible: acute hypoperfusion or hyperperfusion, gland stimulation, and medications including anti-coagulants, dopamine agonists and estrogen therapy.⁴ Many cases do not have an attributable cause and possibly occur spontaneously,³ as was likely the situation in our patient.

Diagnosis

The course of pituitary apoplexy is variable, as patients may recover spontaneously with or without sequelae, or clinically deteriorate to coma or death. Thus, prompt diagnosis of pituitary apoplexy is essential but can be challenging in a patient without a known pituitary lesion because it can mimic subarachnoid hemorrhage or bacterial meningitis.⁵ Diagnosis relies on clinical manifestations and sellar imaging. Sudden onset of headache, followed by visual disturbances, are the most common presenting

symptoms, owing to acute enlargement of the mass. Meningeal irritation from extravasation of blood or necrotic tissue into sub-arachnoid space may cause nausea, vomiting, photophobia, fever, meningism or altered consciousness, which can be misleading.^{3,4,6} Consequentially, lumbar puncture may not help in differentiating subarachnoid hemorrhage and bacterial meningitis from pituitary apoplexy, apart from cerebrospinal fluid cultures.⁵ Further, CT may regularly miss pituitary hemorrhage; thus, pituitary MRI may be necessary.⁶

Hypopituitarism after apoplexy

Hypopituitarism is a major manifestation of pituitary apoplexy. Corticotrophic deficiency has been observed in up to 70% of cases and is the most life-threatening consequence, owing to hemodynamic instability and hyponatremia.^{3,7} Therefore, all patients with suspected pituitary apoplexy should have pituitary function testing followed by immediate, empiric administration of high-dose glucocorticoids.⁵ Patients may also have thyrotropic, gonadotropic or multiple acute endocrine insufficiencies.

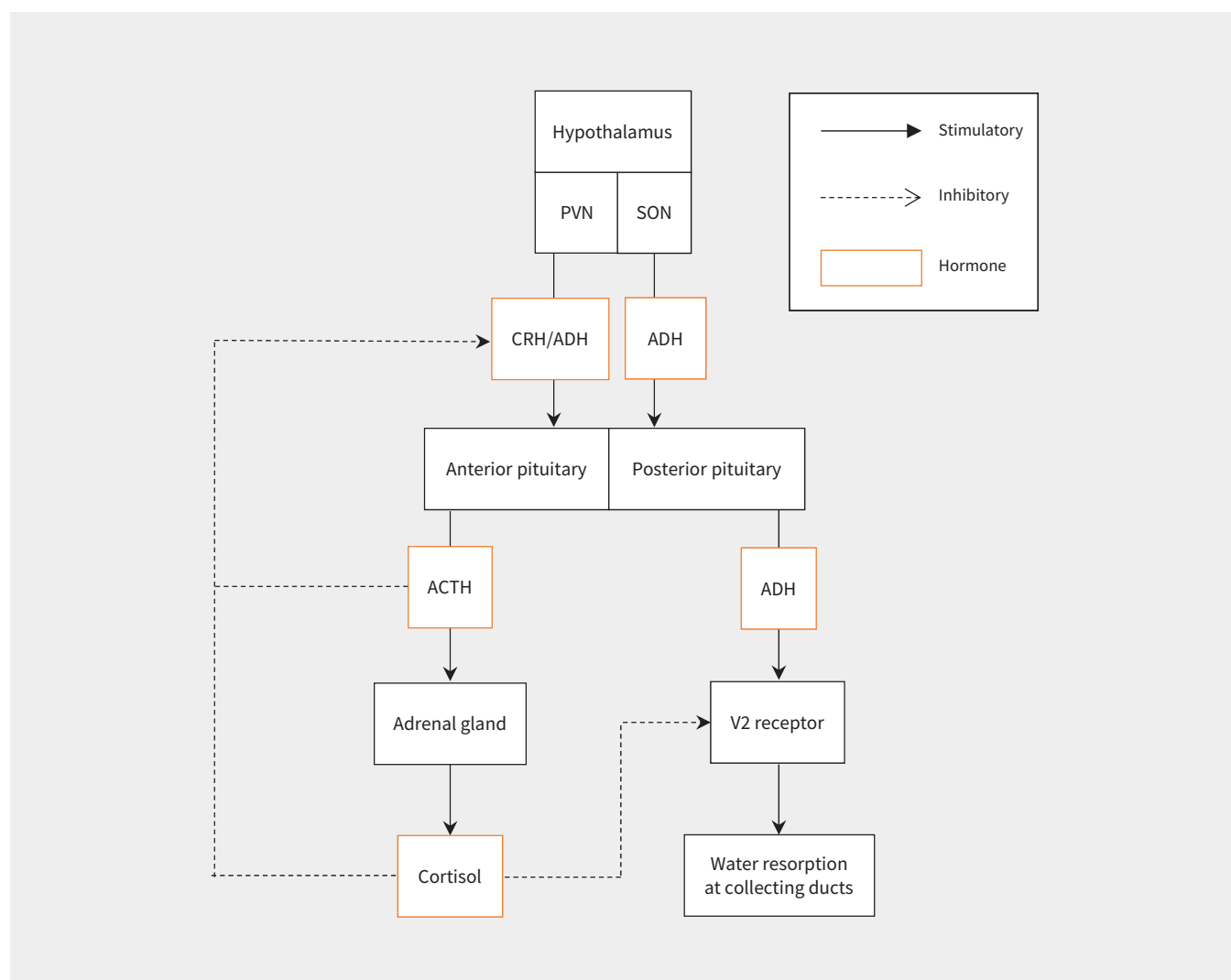


Figure 4: Hypothalamic–pituitary–adrenal axis and antidiuretic hormone (ADH) pathway showing steroid inhibition of ADH secretion and effects.¹⁰ Note: ACTH = adrenocorticotropic hormone, CRH = corticotropin-releasing hormone, PVN = paraventricular nucleus, SON = supraoptic nucleus, V2 = vasopressin 2.

Central diabetes insipidus is a rare complication of pituitary apoplexy, presenting in, it is estimated, less than 5% of cases, and is usually transient.⁸ In some cases, it emerges after steroid replacement or postoperatively from pituitary resection.^{3,7,9} The hypothalamus produces antidiuretic hormone, which migrates to the posterior pituitary gland with several sites above the gland involved in secretion of antidiuretic hormone. Therefore, damage to the posterior pituitary gland typically causes only temporary central diabetes insipidus. Pituitary apoplexy more often involves only the anterior pituitary gland; the posterior gland or pituitary stalk may be involved if substantial mass effect or interruption in blood supply is present.⁸

Glucocorticoid replacement may precipitate diabetes insipidus in the setting of adrenal insufficiency (Figure 4). Low cortisol levels will stimulate the release of antidiuretic hormone, increasing water reabsorption in the kidney, which can be inhibited by exogenous steroids, thereby rapidly manifesting diabetes insipidus;¹⁰ this was likely the situation in this patient's course.

Choosing medical or surgical management

Controversy surrounds the role and timing of surgical management. No randomized controlled trials examining neurosurgical decompression versus conservative approach exist, given the rarity of pituitary apoplexy. Some patients with oculomotor deficits may spontaneously recover without surgery, but surgical intervention may provide a protective effect on visual acuity and pituitary function recovery.¹¹ Given the surgical risks of meningitis, diabetes insipidus and cerebrospinal fluid leak, conservative management may be preferred in patients with nonsevere visual deterioration. In those with severely reduced and persistent visual field deficits or altered level of consciousness, surgical management should be considered.⁵ Thus, many advocate for an

interdisciplinary approach to evaluate severity of symptoms, although at present, it is unclear what criteria define substantial or severe neuro-ophthalmic deficits.⁴

Conclusion

This case highlights a challenging diagnosis of life-threatening pituitary dysfunction that required prompt recognition and close monitoring, on an interdisciplinary basis, for life-threatening complications.

References

1. Wildenberg LE, Glezer A, Bronstein MD, et al. Apoplexy in nonfunctioning pituitary adenomas. *Pituitary* 2018;21:138-44.
2. Fernandez A, Karavitaki N, Wass JAH. Prevalence of pituitary adenomas: a community-based, cross-sectional study in Banbury (Oxfordshire, UK). *Clin Endocrinol (Oxf)* 2010;72:377-82.
3. 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.
4. Rajasekaran S, Vanderpump M, Baldeweg S, et al. UK guidelines for the management of pituitary apoplexy. *Clin Endocrinol (Oxf)* 2011;74:9-20.
5. Capatina C, Inder W, Karavitaki N, et al. Management of endocrine disease: pituitary tumour apoplexy. *Eur J Endocrinol* 2015;172:R179-90.
6. Randeve HS, Schoebel J, Byrne J, et al. Classical pituitary apoplexy: clinical features, management and outcome. *Clin Endocrinol (Oxf)* 1999;51:181-8.
7. Sibal L, Ball SG, Connolly V, et al. Pituitary apoplexy: a review of clinical presentation, management and outcome in 45 cases. *Pituitary* 2004;7:157-63.
8. Silva CM, Lima GA, Machado EO, et al. Transient central diabetes insipidus followed by pituitary apoplexy treated in a conservative way. *Arq Neuropsiquiatr* 2008;66:415-7.
9. Sweeney AT, Blake MA, Adelman LS, et al. Pituitary apoplexy precipitating diabetes insipidus. *Endocr Pract* 2004;10:135-8.
10. Patel H, Augustine P, Fremont R. Unmasking of central diabetes insipidus in a patient after steroid treatment. *Chest* 2012;142(Suppl):324A. doi: 10.1378/chest.1387937.
11. Tu M, Lu Q, Zhu P, et al. Surgical versus non-surgical treatment for pituitary apoplexy: a systemic review and meta-analysis. *J Neurol Sci* 2016;370:258-62.

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