CLINICAL VIGNETTE

Pituitary Apoplexy Presenting as Acute Meningitis

Michael Polisky, MD and Jeong-hee Ku, MD

Division of Endocrinology, Department of Medicine, University of California Los Angeles

Case Presentation

A 32-year-old male presented to local emergency department with acutely worsening headache. Past medical history included viral meningitis and probable migraine headaches. He was in his usual state of good health until the day of presentation. ED CT scan showed a two-centimeter pituitary mass. Labs were unremarkable including a sodium of 139 mmol/L. He was discharged with prescriptions for headache and nausea and to follow up with his primary care physician to evaluate the mass. Over the subsequent two days, his headache worsened, with increasing nausea and neck stiffness. The neck stiffness was similar to viral meningitis symptoms as a child. His primary care physician recommended he return to the emergency room. Repeat CT did not show any acute change. Sodium was 129 mmol/L (ref range 136-145mmol/L). Nasal swab was positive for rhinovirus. He developed a fever of 38.7ºC without hypotension or tachycardia. Lumbar puncture confirmed the suspicion of meningitis with presence of red cells and white cells, xanthochromia, and elevated protein. West Nile IgG from CSF was positive, while IgM was negative. All other microbiological CSF studies were negative, including culture. He was admitted with a diagnosis of seronegative meningitis and started on IV antibiotics and anti-herpetic medications.

On hospital day three, serum sodium dropped to 124 mmol/L and further decreased to 114 mmol/L the following morning. Nephrology was consulted and started tolvaptan. Head MRI showed a markedly heterogeneous pituitary mass with suprasellar extension, evidence of interval intratumoral bleeding, with significant mass effect. The optic chiasm had swelling of bilateral optic tracts, left worse than right (Figure 1).

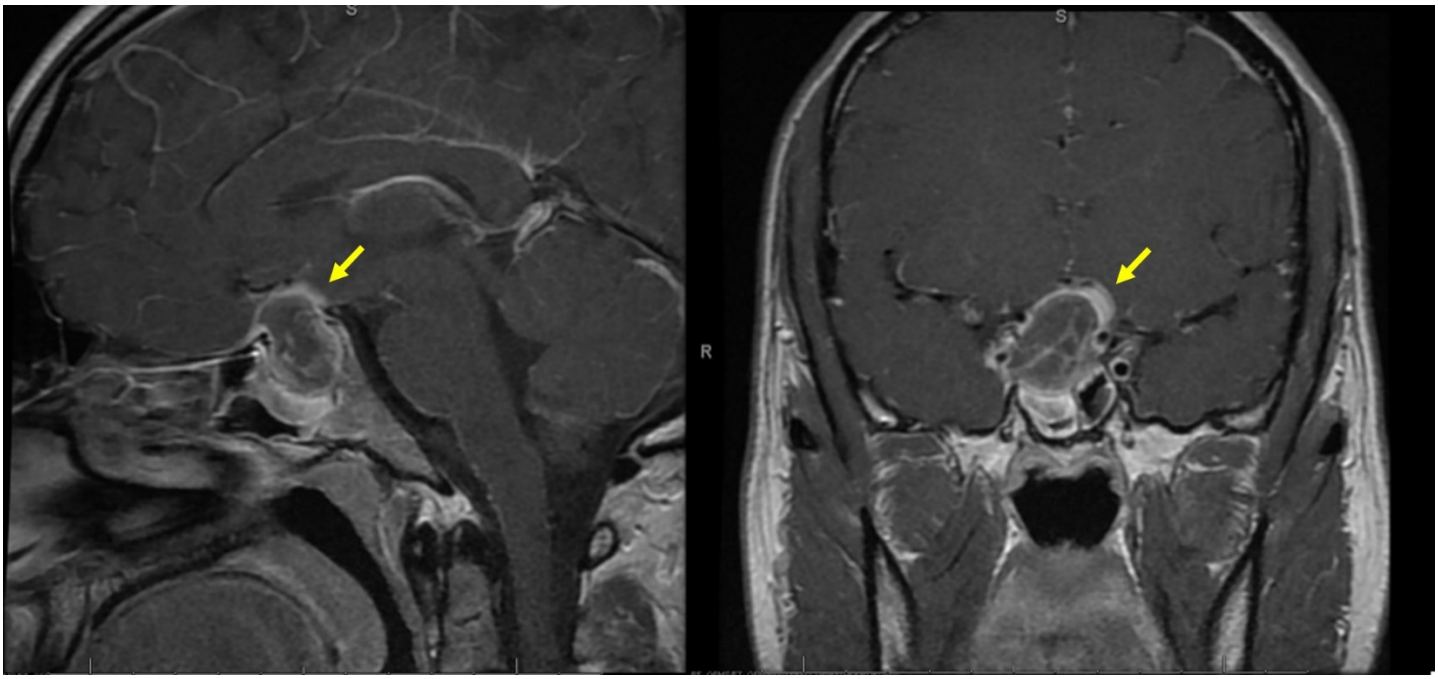

Figure 1. Pituitary MRI showing bilobed shaped pituitary mass with suprasellar extension, also abutting right carvernous ICA and mass effect noted on optic chiasm.

Neurosurgery and endocrine service were consulted, and pituitary labs were checked in evening. Cortisol level was 2 mcg/dL, testosterone was undetectable, TSH was 0.05 mIU/L (ref range, 0.55-4.78mIU/mL), Total T4 was 8.7mcg/dL (ref range, 4.5-10.9 mcg/dL), prolactin was 5.5 ng/mL (ref range 2.1-17.7ng/mL), and IGF-1 was 194 ng/mL (ref range, 95-

290ng/dL). Sodium decreased to 110 mmol/L that evening before correcting to 121 mmol/L overnight and 127 mmol/L the next morning. In the morning cortisol was 13 mcg/dL with ACTH of 23.5 pg/mL (ref range, 7.2-63.3pg/mL). Dexamethasone was started, 4 mg twice daily. Interval physical exam showed significant reduction in left visual field. With addition of the tolvaptan and dexamethasone, sodium levels normalized to 140 mmol/L and the patient stabilized clinically. His headache improved and he began to feel better overall. Neurosurgery concurred that he was stable for discharge with monitoring sodium levels and neurosurgical follow-up for transsphenoidal pituitary tumor resection.

Discussion

Pituitary apoplexy can represent both an endocrine and a surgical emergency. It often occurs when a pituitary macroadenoma, usually previously undiagnosed, develops internal hemorrhage or infarction.[1] Acute bleeding into or necrosis of pituitary gland in a confined space leads to a rapid expansion in pituitary volume, usually impinging on the optic chiasm and placing pressure on the CSF outlet between the third and fourth ventricles. It also exerts pressure on the normal cells of the pituitary that can lead to a rapid functional impairment.[2] This frequently manifests as acute panhypopituitarism, with emergent adrenal impairment, which can lead to adrenal crisis. Most patients with pituitary apoplexy present with classic "mule-kick to the head" sudden onset headache, vision loss, diplopia along with hypopituitarism symptoms. Hyponatremia is commonly reported in up to 40% of patients.[3] A handful of reports[4,5] show pituitary apoplexy patients presenting with symptoms and samples of meningeal irritation. These include fever, headache, neck stiffness, vomiting which are clinically indistinguishable from infectious meningitis. It is speculated that leakage of blood or necrotic tissue into subarachnoid space induces a cytokine-mediated inflammatory response with meningeal irritation and sterile meningitis.[2,4,5] Adrenal insufficiency can also cause increase in temperature[2,6] additionally confounding the diagnosis. Unfortunately, due to presenting clinical signs mimicking other neurologic emergencies such as subarachnoid hemorrhage, bacterial meningitis or cerebral ischemia, diagnosis of pituitary apoplexy can be challenging and delayed as illustrated in our case.[1,3]

Patients require rapid adrenocorticosteroid replacement and evaluation by neurosurgery. Delayed recognition of this endocrine emergency can significantly increase morbidity.[7] Definitive treatment for pituitary apoplexy is surgical decompression of constricted cavernous and suprasellar structures.[2] Expedited surgery is recommended for patient presenting with visual compromise and diminished level of consciousness.[2,8] Most patients with pituitary apoplexy have excellent outcomes with timely diagnosis and appropriate treatment.[8] This diagnosis is more common than suspected. Ezzat et al. estimated that 16.7% have an undiagnosed pituitary adenoma, and 1 in 600 have a macroadenoma.[9] This case highlights importance of including pituitary apoplexy in the differential diagnosis for patient presenting with acute onset severe headache, especially in presence of known pituitary adenoma.

REFERENCES

1. **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. doi: 10.1111/j.1365-2265.2010.03913.x. PMID: 21044119.
2. **Verrees M, Arafah BM, Selman WR**. Pituitary tumor apoplexy: characteristics, treatment, and outcomes. *Neurosurg Focus*. 2004 Apr 15;16(4):E6. doi: 10.3171/foc.2004.16.4.7. PMID: 15191335.
3. **Albani A, Ferraù F, Angileri FF, Esposito F, Granata F, Ferreri F, Cannavò S**. Multidisciplinary Management of Pituitary Apoplexy. *Int J Endocrinol*. 2016;2016: 7951536. doi: 10.1155/2016/7951536. Epub 2016 Dec 15. PMID: 28074095; PMCID: PMC5198093.
4. **Oh K, Kim JH, Choi JW, Kang JK, Kim SH**. Pituitary apoplexy mimicking meningitis. *Brain Tumor Res Treat*. 2013 Oct;1(2):111-5. doi: 10.14791/btrt.2013.1.2.111. Epub 2013 Oct 31. PMID: 24904903; PMCID: PMC4027104.
5. **Myla M, Lewis J, Beach A, Sylejmani G, Burge MR**. A Perplexing Case of Pituitary Apoplexy Masquerading as Recurrent Meningitis. *J Investig Med High Impact Case Rep*. 2018 Nov 15;6:2324709618811370. doi: 10.1177/2324709618811370. PMID: 30480002; PMCID: PMC6243406.
6. **Jang W, Sohn Y, Park JH, Pai H, Kim DS, Kim B**. Clinical Characteristics of Patients with Adrenal Insufficiency and Fever. *J Korean Med Sci*. 2021 Jun 14;36(23):e152. doi: 10.3346/jkms.2021.36.e152. PMID: 34128594; PMCID: PMC8203850.
7. **da Motta LA, de Mello PA, de Lacerda CM, Neto AP, da Motta LD, Filho MF**. Pituitary apoplexy. Clinical course, endocrine evaluations and treatment analysis. *J Neurosurg Sci*. 1999 Mar;43(1):25-36. PMID: 10494663.
8. **Singh TD, Valizadeh N, Meyer FB, Atkinson JL, Erickson D, Rabinstein AA**. Management and outcomes of pituitary apoplexy. *J Neurosurg*. 2015 Jun;122(6):1450-7. doi: 10.3171/2014.10.JNS141204. Epub 2015 Apr 10. PMID: 25859804.
9. **Ezzat S, Asa SL, Couldwell WT, Barr CE, Dodge WE, Vance ML, McCutcheon IE**. The prevalence of pituitary adenomas: a systematic review. *Cancer*. 2004 Aug 1; 101(3):613-9. doi: 10.1002/cncr.20412. PMID: 15274075.