CLINICAL VIGNETTE

A Case of Hypopituitarism Presenting as Failure to Thrive in an Older Adult

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A 77-year-old veteran was living independently with occasional visits from family. He was obese with Type 2 diabetes, hyperlipidemia, and hypertension. He noticed poor appetite and dizziness after starting empagliflozin for better glucose control. Empagliflozin was stopped, but symptoms continued. Liraglutide was stopped a month later without resolution of symptoms. He also noted progressive 20lb unintentional weight loss over the past year and low blood pressures at home, as low as 70/40. Losartan was decreased and stopped. Age appropriate cancer screening was unremarkable, and labs including CBC, CMP, and TSH were normal.

Nine months after onset of symptoms, he presented to an outside hospital with aspiration pneumonia, hypernatremia, and acute kidney injury. He had a complicated hospital stay and was discharged to a nursing home with a stage III decubitus ulcer and a percutaneous gastrostomy tube (PEG) in place due to ongoing poor swallow function during his admission. He tolerated increased oral intake and feeding tube and PEG were discontinued and he was discharged home but remained debilitated and required significant in home assistance.

Six months later he was admitted from the Emergency room after he presented with fatigue, hypotension, and atrial fibrillation. He was found to have a UTI and started on antibiotics. His heart rate was controlled with beta blockers, and he was discharged home on oral antibiotics after 5 days. He presented back to the Emergency Room on the day of discharge with worsening nausea, vomiting, and a new headache. Labs were remarkable for hyponatremia with sodium of 120 which was previously normal on admission. CT brain in the Emergency Room demonstrated a pituitary mass concerning for pituitary apoplexy. MRI of the pituitary demonstrated a pituitary macroadenoma, measuring 17mm by 18mm by 13mm with no sign of pituitary apoplexy. He was re-admitted with Endocrinology consultation. Additional labs included low TSH and free T4, low AM cortisol, low LH and FSH, and normal prolactin. He was started on hydrocortisone and levothyroxine during his admission and was discharged home.

Since discharge he has regained most of his independence.

Discussion

Clinical presentation of hypopituitarism can vary depending on the underlying cause and amount of damage to the pituitary. The factors affecting clinical presentation are rapidity of onset, such as pituitary apoplexy versus slow growing tumor, severity of hormone deficiency, and the number of different hormone-producing cells affected. The hormones affected include TSH, gonadotropins, prolactin, and ACTH.

Epidemiology and Risk Factors

Two cross-sectional surveys of over 146,000 adults in northern Spain reported, prevalence of hypopituitarism in 29 of 100,000 in 1992 and 45.5 of 100,000 in 1999.[1]

A study of 773 adults with hypopituitarism found the following distribution of etiologies[2]: about 50% with nontumoral causes, 44% pituitary tumors, and 7% extra pituitary tumors.

Clinical Presentation

Depending on which cells are affected, clinical presentation can widely vary. This patient was deficient in ACTH, thyrotropin (TSH), and gonadotropins, which present as below.

Symptoms from ACTH deficiency are from cortisol deficiency. Typically, these symptoms include postural hypotension and tachycardia but also can include lassitude, fatigue, weight loss, decreased libido, hypoglycemia, and eosinophilia. There are some notable differences between secondary adrenal insufficiency from hypopituitarism and primary adrenal insufficiency. Hyponatremia such as in this case can be due to inappropriate increase in vasopressin secretion from cortisol deficiency.[3] Notably, ACTH deficiency does not involve deficiency in mineralocorticoids, so the salt wasting and hyperkalemia typically seen in adrenal insufficiency would not be expected. There is also no hyperpigmentation from increased ACTH secretion.[4] Hypoglycemia is also a more prominent symptom in ACTH deficiency than in primary adrenal insufficiency.[5]

Symptoms of TSH deficiency are identical to those of low thyroid hormone from primary thyroid gland failure. These include fatigue, cold intolerance, constipation,[6] facial puffiness, bradycardia,[7,8] delayed relaxation of deep tendon reflexes, anemia,[9,10] and dry skin[11].

Gonadotropins deficiency in males presents as testicular dysfunction which can affect fertility and cause symptoms of low testosterone including low libido and low bone mineral density.[12]

Impaired vision is the most common symptom leading patients with nonfunctioning adenoma to seek medical attention.[13] Other neurologic symptoms of sellar masses that lead patients to seek medical attention include headache from mass expansion of the sella, pituitary apoplexy with excruciating headache and diplopia and cerebrospinal fluid rhinorrhea.

Assessment

Suspicion for deficiencies in pituitary hormone products should be evaluated with lab testing. Testing should be performed with lesions known to cause hypopituitarism or in the presence of symptoms of hypopituitarism.

Imaging

Pituitary adenomas are most commonly incidental findings, on brain imaging as in this case or on Brain MRI done for other clinical symptoms. Once a lesion is found, a dedicated pituitary MRI with gadolinium is the single best study to clarify the lesion.[14]

Pituitary Hormone Deficiencies

ACTH deficiency is tested with cortisol levels, typically with morning cortisol level either on serum or saliva. When central etiology is not already suspected due to imaging, testing for central etiology can be challenging. ACTH deficiency over time causes atrophy of the adrenal glands. In recent onset of ACTH deficiency, ACTH stimulation tests can be useful. However, are less helpful later in the course.[15]

Thyrotropin deficiency cannot be measured by TSH in hypopituitarism because by definition TSH cannot rise in a typical hormonal feedback loop. TSH may be low, inappropriately normal, or even slightly elevated if the etiology is secretion of biologically inactive TSH. Testing therefore depends on measuring total thyroxine (t4) and triiodothyronineIt3) or free T4.[16]

In men, testing for gonadotropic function starts with testing for low testosterone with a low morning testosterone level. This can be performed with testing for testosterone and sex hormone binding globulin in the morning or can be tested by morning free testosterone laboratory evaluation.[17] If serum testosterone is found to be low, inappropriately normal or low levels of luteinizing hormone can point to a central etiology.

REFERENCES

1. **Regal M, Páramo C, Sierra SM, Garcia-Mayor RV**. Prevalence and incidence of hypopituitarism in an adult Caucasian population in northwestern Spain. *Clin Endocrinol (Oxf).* 2001 Dec;55(6):735-40. doi: 10.1046/j.1365-2265.2001.01406.x. PMID: 11895214.
2. **Tanriverdi F, Dokmetas HS, Kebapcı N, Kilicli F, Atmaca H, Yarman S, Ertorer ME, Erturk E, Bayram F, Tugrul A, Culha C, Cakir M, Mert M, Aydin H, Taskale M, Ersoz N, Canturk Z, Anaforoglu I, Ozkaya M, Oruk G, Hekimsoy Z, Kelestimur F, Erbas T**. Etiology of hypopituitarism in tertiary care institutions in Turkish population: analysis of 773 patients from Pituitary Study Group database. *Endocrine*. 2014 Sep;47(1):198-205. doi: 10.1007/s12020-013-0127-4. Epub 2013 Dec 24. PMID: 24366641.
3. **Cuesta M, Garrahy A, Slattery D, Gupta S, Hannon AM, Forde H, McGurren K, Sherlock M, Tormey W, Thompson CJ**. The contribution of undiagnosed adrenal insufficiency to euvolaemic hyponatraemia: results of a large prospective single-centre study. *Clin Endocrinol (Oxf).* 2016 Dec;85(6):836-844. doi: 10.1111/cen.13128. Epub 2016 Jul 12. PMID: 27271953.
4. **Bleicken B, Hahner S, Ventz M, Quinkler M**. Delayed diagnosis of adrenal insufficiency is common: a cross-sectional study in 216 patients. *Am J Med Sci*. 2010 Jun; 339(6):525-31. doi: 10.1097/MAJ.0b013e3181db6b7a. PMID: 20400889.
5. **Burke CW**. Adrenocortical insufficiency. *Clin Endocrinol Metab*. 1985 Nov;14(4):947-76. doi: 10.1016/s0300-595x(85)80084-0. PMID: 3002680.
6. **Shafer RB, Prentiss RA, Bond JH**. Gastrointestinal transit in thyroid disease. *Gastroenterology*. 1984 May;86(5 Pt 1):852-5. PMID: 6706068.
7. **Woeber KA**. Thyrotoxicosis and the heart. *N Engl J Med.* 1992 Jul 9;327(2):94-8. doi: 10.1056/NEJM199207093270206. PMID: 1603141.
8. **Klein I, Ojamaa K**. Thyroid hormone and the cardiovascular system: from theory to practice. *J Clin Endocrinol Metab*. 1994 May;78(5):1026-7. doi: 10.1210/jcem.78.5.8175954. PMID: 8175954.
9. **Squizzato A, Romualdi E, Büller HR, Gerdes VE.** Clinical review: Thyroid dysfunction and effects on coagulation and fibrinolysis: a systematic review. *J Clin Endocrinol Metab*. 2007 Jul;92(7):2415-20. doi: 10.1210/jc.2007-0199. Epub 2007 Apr 17. PMID: 17440013.
10. **Manfredi E, van Zaane B, Gerdes VE, Brandjes DP, Squizzato A**. Hypothyroidism and acquired von Willebrand's syndrome: a systematic review. *Haemophilia*. 2008 May;14(3):423-33. doi: 10.1111/j.1365-2516.2007.01642.x. Epub 2008 Jan 21. PMID: 18218015.
11. **Heymann WR**. Cutaneous manifestations of thyroid disease. *J Am Acad Dermatol*. 1992 Jun;26(6):885-902. doi: 10.1016/0190-9622(92)70130-8. PMID: 1607406.
12. **Stěpán JJ, Lachman M, Zvěrina J, Pacovský V, Baylink DJ**. Castrated men exhibit bone loss: effect of calcitonin treatment on biochemical indices of bone remodeling. *J Clin Endocrinol Metab*. 1989 Sep;69(3):523-7. doi: 10.1210/jcem-69-3-523. PMID: 2788171.
13. **Snyder PJ**. Gonadotroph adenomas. In: *The Pituitary*, 2nd ed., Melmed S (Ed), Blackwell Science Inc., Malden, MA 2002. p. 575.
14. **Pressman BD**. Pituitary imaging. In: *The Pituitary*, 2nd ed., Melmed S (Ed), Blackwell Science Inc., Malden, MA 2002. p. 663.
15. **Dickstein G, Shechner C, Nicholson WE, Rosner I, Shen-Orr Z, Adawi F, Lahav M**. Adrenocorticotropin

stimulation test: effects of basal cortisol level, time of day, and suggested new sensitive low dose test. *J Clin Endocrinol Metab*. 1991 Apr;72(4):773-8. doi: 10.1210/jcem-72-4-773. PMID: 2005201.

16. **Beck-Peccoz P, Amr S, Menezes-Ferreira MM, Faglia G, Weintraub BD**. Decreased receptor binding of biologically inactive thyrotropin in central hypothyroidism. Effect of treatment with thyrotropin-releasing hormone. *N Engl J Med*. 1985 Apr 25;312(17): 1085-90. doi: 10.1056/NEJM198504253121703. PMID: 2984564.
17. **Bremner WJ, Vitiello MV, Prinz PN**. Loss of circadian rhythmicity in blood testosterone levels with aging in normal men. *J Clin Endocrinol Metab*. 1983 Jun;56(6): 1278-81. doi: 10.1210/jcem-56-6-1278. PMID: 6841562.