CLINICAL VIGNETTE

An Interesting Case of Postpartum Depression

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Case

A 40-year-old female with history of postpartum depression, central hypothyroidism and pituitary microadenoma presented for evaluation of new onset hypertension, fatigue, anxiety, and irritability.

She was first noted to have suppressed TSH of 0.43 (reference range: 0.47-4.68 mIU/mL) and low free T4 of 0.67 (reference range: 0.78-2.19 ng/dL), total T3 1.15 (0.97-1.69 ng/dL) after delivering her first child. Delivery was uncomplicated and there was no prior personal or family history of thyroid disease. She had no steroid, dopaminergic or somatostatin analog use or prior trauma or cranial irradiation. Due to persistently low TSH and FT4 readings, she was started on levothyroxine, which was gradually increased to 100 mcg daily. Testing included elevated thyroglobulin (Tg) antibody of 14.6 (reference range <4), with normal thyroid peroxidase (TPO) antibody and thyroid stimulating immunoglobulin. Subsequent TSH readings while on levothyroxine remained low with normalized free T4 levels.

The patient presented to the Emergency Department for intermittent chest pain, shakiness, and elevated blood pressures following COVID-19 vaccine. Physical exam was notable for blood pressure measured at 175/118 mmHg and body mass index of 31. Inpatient evaluation was unremarkable with normal CT angiogram, serial troponins, 24-hour urine metanephrines, plasma metanephrines, 24 hour and urine free cortisol. Renal duplex ultrasound was also negative. TSH was 0.135 (0.35-4.94 ng/dL) and FT4 was 1.26 (0.7-1.48 ng/dL). Aldosterone-renin ratio was unremarkable at 6.25. Her blood pressure normalized on amlodipine, atenolol and hydrochlorothiazide.

Additional testing for central hypothyroidism included insulin like growth factor 1, adrenocorticotropic hormone, morning cortisol, late night salivary cortisol, and prolactin were all normal. The patient reported regular menses, indicating normal gonadal function. Pituitary MRI demonstrated a 5 mm pituitary adenoma. TSH with HAMA (heterophilic anti-mouse antibody) was unchanged after treatment to remove HAMA interference. Free T4 by equilibrium dialysis was consistent with prior free T4 measured by immunoassay.

Discussion

Prevalence of postpartum thyroiditis ranges from 1 to 17 percent.[1] Classically, postpartum thyroiditis is characterized by an initial stage of primary hyperthyroidism, with low TSH, occurring between 1-3 months postpartum lasting 2-8 weeks. Primary hypothyroidism, with elevated TSH, follows in approximately half of these women around 4-6 months postpartum. In approximately 1 in 5 women, subclinical or clinical hypothyroidism persists. Women with TPO antibody positivity were 5.7 times more likely to develop postpartum thyroiditis.[2] The prevalence in patients with positive Tg antibody is less well defined.

Secondary or central hypothyroidism is rare approximately 1,000-fold less common than primary hypothyroidism. Central hypothyroidism results from a functional or anatomic pituitary or hypothalamic disorder, impairing TSH secretion. Central hypothyroidism often coexists with additional pituitary deficiencies, as in combined pituitary hormone deficiencies (CPHD) due to mass effect related to compressive or infiltrative pituitary lesions. Given the rarity of isolated central hypothyroidism, lab assay interference should be ruled out before establishing the diagnosis of central hypothyroidism. If no assay interference is detected, pituitary MRI should be performed to assess for anatomic abnormality i.e. pituitary macroadenoma, craniopharyngioma, or other compressive mass impeding thyrotropin production. These cause more than half of central hypothyroidism cases.[3] Less common etiologies include pituitary apoplexy, pituitary surgery or radiation, hemochromatosis, tuberculosis, syphilis, sarcoidosis, fungal infections, toxoplasmosis, histiocytosis. Other causes include autoimmune lymphocytic hypophysitis or anti-CTLA4 (cytotoxic T lymphocyte protein 4) antibody associated hypophysitis or head trauma affecting the pituitary stalk. Multiple genes have been reported as causing congenital forms of central hypothyroidism, some of which are associated with panhypopituitarism. Congenital central hypothyroidism is generally more severe than acquired central hypothyroidism.[4] Systemic non-thyroidal illness (NTI) can mimic the biochemical pattern of central hypothyroidism.[5] However, in NTI, free T3 is low, versus elevated free T3 in mild to moderate central hypothyroidism.

If clinical picture with low TSH and low FT4 is concerning for hyperthyroidism, T3 should be checked to rule out T3 toxicosis. Abnormal free thyroxine (T4) has the highest predictive value in diagnosis of central hypothyroidism. Additional less often used tests include: >20% progressive decrease in FT4 levels from baseline, abnormal TSH response to TRH (not available in US), blunted nocturnal TSH rise (generally limited to

hospitalized patients).[4] Genetic forms of central hypothyroidism are related to mutations in thyrotropin releasing hormone and thyrotropin releasing hormone receptor, TSH may have impaired functionality. Levothyroxine should be started at 1.0-1.6 mcg/kg/d and adjusted to achieve mid normal free T4 levels, measured before the daily dose of levothyroxine.[3] Prior to initiation of levothyroxine evaluation for adrenal insufficiency should be performed.[4] A normal TSH raises concern for inadequate replacement. Labs should be rechecked 3-6 weeks following dosing adjustments.[5] Younger patients may require larger replacement doses than older patients, and patients on estrogen or growth hormone replacement require significantly higher doses of thyroid hormone replacement.[4] Our patient's TSH remained suppressed with a free T4 in the upper normal range on her levothyroxine supplementation, signifying adequate replacement. Her presentation of postpartum central hypothyroidism remains unusual.

REFERENCES

1. **Nicholson WK, Robinson KA, Smallridge RC, Ladenson PW, Powe NR**. Prevalence of postpartum thyroid dysfunction: a quantitative review. *Thyroid*. 2006 Jun;16(6):573-82. doi: 10.1089/thy.2006.16.573. PMID: 16839259.
2. **Burman KD**. Postpartum thyroiditis. In: *UpToDate*, Ross DS (Ed), UpToDate, Waltham, MA. (Accessed on September 1, 2022.)
3. **Persani** L. Clinical review: Central hypothyroidism: pathogenic, diagnostic, and therapeutic challenges. *J Clin Endocrinol Metab*. 2012 Sep;97(9):3068-78. doi: 10.1210/jc.2012-1616. Epub 2012 Jul 31. PMID: 22851492.
4. **Lania A, Persani L, Beck-Peccoz P**. Central hypothyroidism. *Pituitary*. 2008;11(2):181-6. doi: 10.1007/s11102-008-0122-6. PMID: 18415684.
5. **Beck-Peccoz P, Rodari G, Giavoli C, Lania A**. Central hypothyroidism – a neglected thyroid disorder. *Nat Rev Endocrinol*. 2017 Oct;13(10):588-598. doi: 10.1038/nrendo.2017.47. Epub 2017 May 26. PMID: 28549061.