Hypothyroidism in a patient with Down syndrome – Not what you might expect!

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INTRODUCTION

The differential diagnosis for functional decline in an individual with Down syndrome is broad and includes thyroid disease and other autoimmune conditions, metabolic abnormalities, obstructive sleep apnea and mental health diagnoses.

OBJECTIVE

We will review the differential diagnosis for hypothyroidism and approach to diagnosis and treatment.

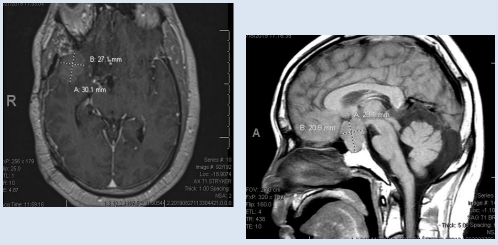
CASE PRESENTATION

28-year-old male with Down syndrome presented to his new PCP's office with a 45 lb. weight loss over a year, fatigue, and withdrawal from preferred activities. Prior labs were interpreted as normal but significant for a normal TSH with a low Free T4. Repeat labs demonstrated a low FT4 and a mildly elevated TSH. The patient was started on levothyroxine and developed worsening symptoms including hypotension.

He was referred to endocrinology for evaluation of central hypothyroidism after being started emergently on oral steroids for suspected adrenal insufficiency. Further investigation revealed pan-hypopituitarism, MRI confirmed a ~ 2.8 cm pituitary adenoma as shown in the image. A trans-sphenoidal resection was attempted, however, due to the fibrous nature of the tumor the procedure was aborted. Biopsy showed a grade 1 meningioma with a ki67 proliferation index of 5.5%. Subsequently, the patient underwent craniotomy for the debulking of the tumor with a slight improvement in vision. Post-operatively, labs show persistent pan-hypopituitarism.

LABS AND IMAGING

TSH	5.16	0.45– 4.5 uIu/ml
FT4	0.43	0.82 – 1.77 ng/dl
TPO Ab	10	0-34 IU/ml
Cortisol	0.7	6.2 – 19.4 mcg/ml
Total testosterone	<3	264 -916 ng/ml
Prolactin	19.6	4-15.2 ng/ml
ACTH	16.1	7.2 – 63 pg/ml
IGF-1	212	98-282 ng/ml



MRI of pituitary showed a 2.1 x 2.6 x 2.8 cm sellar and supra-sellar mass with extension into the right cavernous sinus concerning for pituitary macroadenoma with mass effect on the optic chiasm.

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DISCUSSION

While autoimmune hypothyroidism is common, brain tumors and central hypothyroidism are rare in individuals with Down syndrome. To the best of our knowledge, this is the first reported case of an intra-sellar meningioma in a patient with Down syndrome.

Teaching points from the endocrinologist:

- Hypothyroidism can be
  - Primary – failure of thyroid gland
  - Central – failure of the pituitary or hypothalamic pituitary axis

Central hypothyroidism is rare and is caused by disorders of the pituitary or hypothalamus such as mass lesions, infiltrative disorders, infections etc. In patients with central hypothyroidism, serum free T4 is low or low-normal, but serum TSH may be low, normal, or even slightly elevated unlike primary hypothyroidism wherein TSH is elevated generally above 10.

In this case, deterioration in the patient's clinical status after starting thyroid replacement therapy prompted consideration of underlying adrenal insufficiency and a recognition that the cause of the patient's hypothyroidism was likely central. In retrospect, patient's significant weight loss prior to presentation was an important clue.

Common presenting features of central adrenal insufficiency (AI) are fatigue, weakness, and hyponatremia. Hypotension is less prominent when compared to primary AI. Hyperkalemia is absent as the Renin–aldosterone system is intact in these patients.

Teaching points from the PCP:

The patient's BP was low normal on presentation which is not uncommon in individuals with DS. Due to the patient's cognitive status on presentation, it was hard to gather if he had visual changes and he denied headache. As he improved with treatment of AI and hypothyroidism, he was able to complete visual field testing which did demonstrate visual loss.

He has done remarkably well and completed a course of radiation therapy despite the COVID-19 pandemic. A completely different patient has emerged post treatment, who at a recent telehealth follow up actively participated in the patient encounter with minimal assistance from his older brother. He continues on thyroid and steroid replacement and recently started testosterone.

The case illustrates the importance of comparing the patient with Down syndrome to their own baseline and thinking beyond common differentials in patients with Down syndrome.

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