

Child With Suspected Excessive Cortisol Production

Suggestive history and physical findings	Initial laboratory and/or radiologic work-up can include:	When to refer	Items useful for consultation	Additional information
<p><u>Symptoms/Signs:</u></p> <ul style="list-style-type: none"> • Progressive weight gain (mostly truncal) with slowing of linear growth • “Moon face”, buffalo hump • Fatigue, weakness, irritability and/ or personality changes • Hypertension • Hirsutism, violaceous striae (skin thinning), hyperpigmentation (ACTH excess) and ecchymosis (capillary friability) • Proximal muscle weakness <p><u>Medical history:</u> Exclude history of exogenous steroid intake</p> <p><u>Differential Diagnosis</u></p>	<p><u>The first step is to demonstrate excessive cortisol production</u></p> <p><u>Tests to consider after consultation with a Pediatric Endocrinologist:</u></p> <ul style="list-style-type: none"> • 24 hour urine collection for urinary free cortisol • Midnight salivary cortisol • Overnight dexamethasone suppression test 	<p><u>Urgent:</u> Any child with excessive weight gain <u>in combination with</u> slowing of growth velocity should be referred to a Pediatric endocrinologist</p> <p><u>Find a Pediatric Endocrinologist</u></p>	<p>Previous growth data/growth charts</p> <p>Pertinent medical records</p> <p>Recent laboratory and radiologic studies</p>	<p><u>Additional Information</u></p> <p>https://www.nadf.us/</p> <p>https://www.niddk.nih.gov/health-information/endocrine-diseases/cushings-syndrome</p> <p><u>References</u></p>

Differential diagnosis for Cushing disease/syndrome

- Exogenous obesity (typically no associated growth impairment)
- Depression/ physical stress
- Polycystic ovary syndrome
- Uncontrolled diabetes/ alcoholism (in adults)

Additional Information

- Additional Laboratory Testing:
 - Overnight dexamethasone suppression test: Single dose of 1 mg of dexamethasone given close to 11 pm should suppress the AM cortisol to <1.8 ug/dl (50 nmol/L).
 - Midnight salivary cortisol: Measuring a midnight salivary cortisol measures the free cortisol and is good screening test to rule out Cushings.
 - Low and high dose dexamethasone suppression test.
 - Corticotrophin releasing hormone test.
 - Complete metabolic panel, complete blood count and ESR. Vitamin D levels, calcium and PTH levels. Blood glucose can be elevated and there may be glycosuria as cortisol promotes gluconeogenesis. Frank diabetes and impaired glucose tolerance can develop in children with hypercortilism. Hematological and immune dysfunction, with cortisol stimulating erythropoiesis leading to polycythemia. Lymphopenia and eosinopenia are common. As cortisol affects vitamin D absorption in the intestines and increased loss of calcium from the kidneys there is often osteopenia/osteoporosis.
- Radiological studies:
 - MRI brain with pituitary cuts to image for adenoma if Cushing disease suspected.
 - This condition is rare (1/100,000) and some children will need to be referred to a center which specializes in doing advanced imaging such as Petrosal sinus sampling to localize the pituitary adenoma
 - CT scan or MRI (preferred) if adrenal adenoma or carcinoma is suspected (most common cause of Cushing syndrome in children <7 years)
 - DEXA scan as osteopenia is common in longstanding Cushing syndrome.

- Treatment options:
 - Surgical consultation to a Pediatric neurosurgeon/ surgeon if the cause is a pituitary adenoma or an adrenal tumor/ carcinoma. The first-line treatment for almost all children with Cushing's disease remains transsphenoidal surgery.
 - Options for Rx include medical management with ketoconazole and mitotane. Radiation therapy usually results in pituitary dysfunction.
 - After surgery the child will need long term monitoring for tumor recurrence as well as replacement with glucocorticoids.

Suggested References and Additional Reading:

- Stratakis CA. Cushing syndrome in pediatrics. *Endocrinol Metab Clin North Am.* 2012;41(4):793-803.
- Lodish M. Cushing's syndrome in childhood: update on genetics, treatment, and outcomes. *Curr Opin Endocrinol Diabetes Obes.* 2015;22(1):48-54.
- Lodish MB, Keil MF, Stratakis CA. Cushing's syndrome in pediatrics: An update. *Endocrinol Metab Clin North Am.* 2018;47:451-462.

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