بسم الله الرحمن الرحيم
Cushing Syndrome

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Cushing's Syndrome
DEFINITION

Cushing syndrome is the result of abnormally high blood levels of cortisol or other glucocorticoids.
Normally, the production of cortisol follows a precise chain of events.
Cortisol performs vital tasks in the body including:

- Helping maintain blood pressure and cardiovascular function.
- Reducing the immune system's inflammatory response.
- Balancing the effects of insulin, which breaks down glucose for energy.
- Regulating the metabolism of proteins, carbohydrates, and fats.
- Help the body respond to stress.
Source of excess cortisol

Exogenous

A.C.T.H. dependent

Endogenous

A.C.T.H. independent
CLINICAL MANIFESTATIONS

- Moon facies
Generalized obesity

Older children most often have more severe obesity of the face and trunk compared with the extremities.

Growth is impaired, with length falling below the 3rd percentile, except when significant virilization produces normal or even accelerated growth.

Gradual onset of obesity and deceleration or cessation of growth may be the only early manifestations.
CLINICAL MANIFESTATIONS

★ Hypertension is common and may occasionally lead to heart failure.
★ Hypertension and hyperglycemia usually occur; hyperglycemia may progress to frank diabetes.
★ An increased susceptibility to infection may also lead to fatal sepsis.
CLINICAL MANIFESTATIONS

★ In children with adrenal tumors, signs of abnormal masculinization occur frequently; accordingly, there may be hirsutism on the face and trunk, pubic hair, acne, deepening of the voice, and enlargement of the clitoris in girls.

★ Pubertal development may be delayed amenorrhea may occur in girls past menarche.
CLINICAL MANIFESTATIONS

★ Purplish striae on the hips, abdomen, and thighs are common.
★ Weakness, headache, and emotional lability may be prominent.
★ Osteoporosis is common and may cause pathologic fractures.
Emotional instability
Moon face
Buffalo hump
Osteoporosis
Thinning of scalp hair
Acne
Increased facial hair
Cardiac hypertrophy and hypertension
Adrenal:
- hyperplasia
- tumor
Striae of skin
Easy bruising
Muscle wasting:
- Weakness
- Thin extremities
INVESTIGATIONS

1 - Measurement of cortisol level in - blood
   - saliva
   - urine
INVESTIGATIONS

2– A single-dose dexamethasone suppression test is often helpful; a dose of 25–30 μg/kg (maximum of 2 mg) given at 11 p.m. results in a plasma cortisol level of less than 5 μg/dL at 8 a.m. the next morning in normal individuals but not in patients with Cushing syndrome.

3– T.S.H. and free T4 level.
INVESTIGATIONS

4- A glucose tolerance test is often abnormal despite elevated levels of insulin.

5- Levels of serum electrolytes are usually normal, but potassium may be decreased, especially in patients with tumors that secrete A.C.T.H. ectopically.
After the diagnosis of Cushing syndrome has been established, it is necessary to determine whether it is caused by a pituitary adenoma, an ectopic ACTH-secreting tumor, or a cortisol-secreting adrenal tumor. A.C.T.H. concentrations are usually suppressed in patients with cortisol-secreting tumors, are very high in patients with ectopic ACTH-secreting tumors,
but may be normal in patients with A.C.T.H.-secreting pituitary adenomas.

After an intravenous bolus of corticotropin-releasing hormone (C.R.H.), patients with A.C.T.H.-dependent Cushing syndrome have an exaggerated A.C.T.H. and cortisol response, whereas those with adrenal tumors show no increase in A.C.T.H. and cortisol.
LABORATORY FINDINGS

7-The 2-step dexamethasone suppression test consists of administration of dexamethasone, 30 and 120 μg/kg/24 hr in 4 divided doses, on consecutive days. In children with pituitary Cushing syndrome, the larger dose, but not the smaller dose, suppresses serum levels of cortisol. Typically, patients with A.C.T.H.–independent Cushing syndrome do not show suppressed cortisol levels with dexamethasone.
INVESTIGATIONS

8- C.T. and M.R.I. detects virtually all adrenal tumors.
M.R.I. may detect A.C.T.H.-secreting pituitary adenomas, but many are too small to be seen; the addition of gadolinium contrast increases the sensitivity of detection.
10- Bilateral inferior petrosal blood sampling to measure concentrations of A.C.T.H. before and after C.R.H. administration may be required to localize the tumor when a pituitary adenoma is not visualized.
DIFFERENTIAL DIAGNOSIS

1- Obesity, particularly when striae and hypertension are present.
2- Generalized glucocorticoid resistance; Affected patients may be asymptomatic or exhibit hypertension, hypokalemia, and precocious pseudopuberty.
3- Pseudocushing disease.
4- Hypothyroidism.
TREATMENT

1-Medical:

Cyproheptadine: a centrally acting serotonin antagonist that blocks ACTH release, has been used to treat Cushing disease in adults; remissions are usually not sustained after discontinuation of therapy. This agent is rarely used in children.
TREATMENT

Inhibitors of adrenal steroidogenesis (metyrapone, ketoconazole, aminoglutethimide) have been used preoperatively to normalize circulating cortisol levels and reduce perioperative morbidity and mortality.
TREATMENT

• LYSODREN (MITOTANE®)
Lysodren is an adrenocortico-lytic drug; this means that it causes the adrenal cortex to lyse or dissolve. This drug has to be given carefully as the body needs cortisone to survive. If too much drug is given; it can dissolve the adrenal cortex entirely and your patient may die at worst, or have to stay on cortisone supplements for the rest of his/her life at best.
TREATMENT

2- surgical:

Transsphenoidal pituitary microsurgery is the treatment of choice in pituitary Cushing disease in children. The overall success rate with follow-up of less than 10 yr is 60–80%. Low postoperative serum or urinary cortisol concentrations predict long-term remission in the majority of cases. Relapses are treated with re-operation or pituitary irradiation.
# TREATMENT

## Radiotherapy

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<thead>
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<th>Pros</th>
<th>Cons</th>
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<tbody>
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<td>Non-invasive</td>
<td>1–Delayed effect.</td>
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<td>2–Lower cure rate.</td>
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<td>3–Potential risk of damage to optic nerve.</td>
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<td>4–Potential adverse neurocognitive effect.</td>
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<td>5–Potential for late secondary tumors.</td>
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If a pituitary adenoma does not respond to medical treatment or if ACTH is secreted by an ectopic metastatic tumor, the adrenal glands may need to be removed. This can often be accomplished laparoscopically.
TREATMENT

Adrenalectomy may lead to increased A.C.T.H. secretion by an unresected pituitary adenoma, evidenced mainly by marked hyperpigmentation; this condition is termed {Nelson syndrome}.
TREATMENT

Benign cortical adenomas are treated with unilateral adrenalectomy. Such adenomas are occasionally bilateral; then the treatment of choice is subtotal adrenalectomy. In either instance, an excellent therapeutic result is achieved by removing the tumor.
TREATMENT

Rarely, the tumors are bilateral and require total Adrenalectomy; since it is often impossible to differentiate benign from malignant tumors by histologic appearance alone.
# TREATMENT

## Bilateral Adrenalectomy

<table>
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<th>Pros</th>
<th>Cons</th>
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<td>1–Effective in achieving disease remission.</td>
<td>1–Risk of Nelson’s syndrome.</td>
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<td>2–rapid cure.</td>
<td>2–Potential growth of ectopic adrenal tissue.</td>
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<td>3–Need for life long glucocorticoid replacement.</td>
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<td>4–Mineralocorticoid deficiency.</td>
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TREATMENT

Management of patients undergoing adrenalectomy requires adequate preoperative and postoperative replacement therapy with a corticosteroid until there is recovery of the hypothalamic–pituitary–adrenal axis.
POST OPERATIVE COMPLICATIONS

😊 poor wound healing.
😊 sudden collapse, particularly in infants.
😊 Substantial catch-up growth, pubertal progress, and increased bone density occur, but bone density remains abnormal and adult height is often compromised.
😊 Sepsis, thrombosis, and pancreatitis.
PROGNOSIS

1 - Removal of tumor may lead to full recovery.
2 - Adrenocortical carcinomas frequently metastasize, especially to the liver and lungs, and may have an unfavorable prognosis despite removal of the primary lesion.
3 - Untreated cushing syndrome may cause severe illness or even death.
References

1. KLIEGMAN NELSON TEXT BOOK of pediatrics {18th edition}


6. Stewart PM , Kone NP, The adrenal cortex, In; Kronenberg H, Melmed S, Polosnisky k, Larsen PR, eds.
THANKS