Case 3: Cushing's Syndrome

Leaders:

Mamdouh Al-Enezi

Tarfah Al-Obaidan

Members:

Abdullah Altowim

Khaled Almohaimede

Samiha Aljetaily

Summary of the case:

* Amani omar (female) a 27 year-old

Presenting problems	Clinical examination	Investigation
• Excessive facial hair • Gaining a lot of weight • Rounded (moon) face • Difficulties in climbing stairs • Severe back pain	• Vital signs (elevated blood pressure) • Severe acne and abnormal hair on upper lip & chin • Few bruises on arms & legs • Abdominal examination: truncal obesity, striae. • Lower limbs examination: thin thighs, proximal muscles weakness • Back: tenderness over L4 & L5	• Full blood count • Blood chemistry • Dipstick urinalysis: Glucose ++ • Hormonal assay • X-ray , CT scan , Ultrasound

*** Final diagnosis: Cushing Syndrome**

* Treated by: surgery, and she recovered well ☺

Definition of Cushing Syndrome:

A disorder that occurs when the body is exposed to high levels of the hormone cortisol.

Causes of Cushing Syndrome:

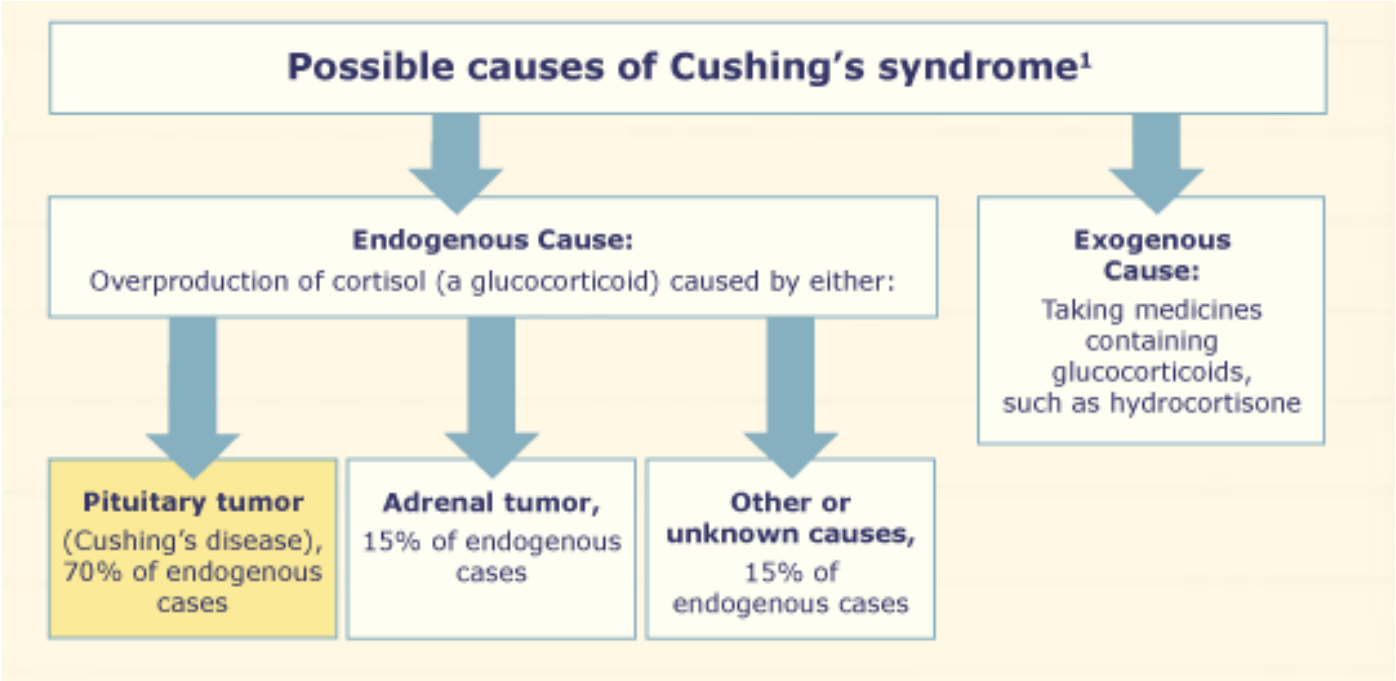
Exogenous (steroid therapy):

- For diseases such as SLE, asthma, rheumatoid arthritis...etc
- For immunosuppression after transplantation

Endogenous:

- ACTH- independent:
  Primary adrenal defect (adenoma).

- ACTH-dependent:
  - Overproduction of ACTH by pituitary.
  - Overproduction of ACTH by ectopic ACTH- producing tumor

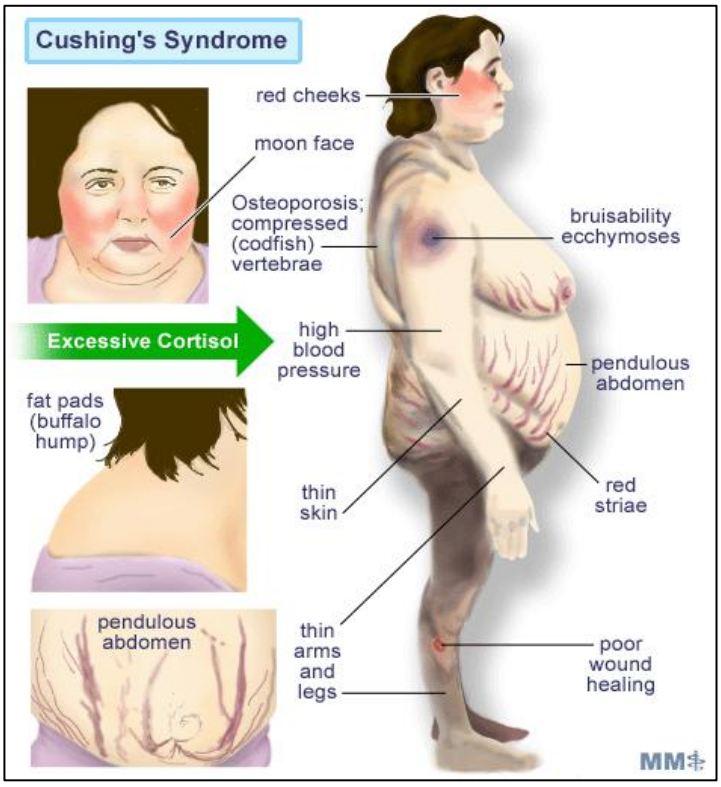


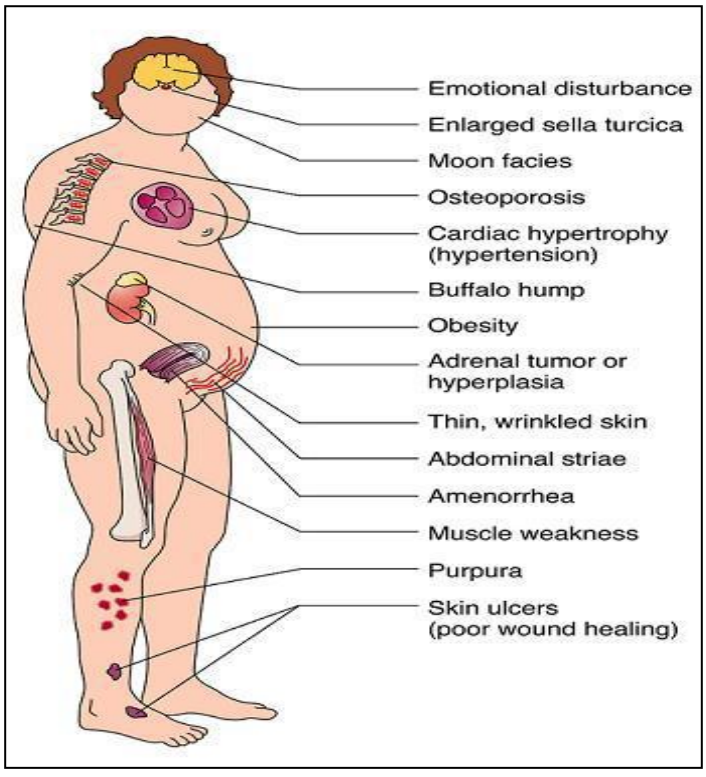
Signs & Symptoms:

- Upper body obesity (truncal obesity) [because of fat redistribution]
- Rounded face (moon face)
- Increased fat around the neck (buffalo hump)
- Thinning arms and legs

Signs & Symptoms (cont.):

- Fragile and thin skin
- Bruises (because of fragile skin)
- Striae in the abdomen which are purplish stretch marks (because of fragile skin and fragile capillaries). They might also appear on the thighs, buttocks, arms and breasts.
- Weakened bones
- Fatigue
- Weak muscles (proximal muscles)
- Hypertension
- Hyperglycemia
- Psychological changes: irritability, anxiety, depression
- Women usually have excessive growth of hair on the face, neck, chest, abdomen and thighs.
- For women: Irregular menstrual cycles
- For men: decreased fertility and loss of libido (sex drive)





Further questions to ask:

- When did the symptoms begin?
- What are the areas that are affected by increased hair growth?
- Past medical history
- Dietary history
- Body weight in childhood
- Physical activities
- History of medications
- Psycho-social history /any history of depression
- Family history of depression or obesity
- Alcohol intake or smoking

Differential Diagnosis:

1) Excessive facial hair:

- Increased sensitivity of hair follicles to circulating androgens Feverish
- Increased secretion of corticosteroids and androgens from adrenal glands(Cushing's syndrome)
- Drug-induced (Phenytoin)
- Familial
- Racial background (ethnic background)

2) Put on a lot of weight:

- Cushing's syndrome
- Psychological factors
- Excessive caloric intake
- Metabolic disorder
- Genetic and familial causes

Differential Diagnosis (cont.):

3) Rounded face:

- Excessive secretion of cortisol
- Mobilization of fat to the face
- Simple obesity
- Generalized anaphylaxis
- Generalized edema

4) Difficulties in climbing stairs:

- Problems with the proximal muscles of lower limbs
- Bone problems
- Joint problems
- Body weight problems
- Motor nerve problems

5) Severe back pain:

- Problem with inter-vertebral discs
- Problems with muscles of the back
- Osteoporosis
- Nerve compression
- Referred pain to the back

Clinical Examination:

- BMI (usually overweight or obese)
- Vital signs (elevated blood pressure)
- Severe acne and abnormal hair on upper lip & chin (because of androgens)
- Few bruises on arms & legs (because of fragile skin)

Clinical Examination (cont.):

- Abdominal examination: truncal obesity, striae.
- Lower limbs examination: thin thighs, proximal muscles weakness (cortisol causes protein catabolism)
- Back: tenderness over L4 & L5 (because of weakened bone since cortisol has anti vit-D effect)

Investigation:

- Full blood count
- Blood chemistry (elevated glucose, elevated cholesterol, elevated triglycerides)
- Hormonal assay:
  - elevated cortisol
  - elevated dehydroepiandrosterone {DHEA}
  - ACTH levels vary depending on the cause {ectopic ACTH tumor, adrenal tumor, pituitary problem}
- Radiology:
  - X-ray of spine
  - CT of upper abdomen
  - Pelvic ultrasound
- 24-Hour Urinary Free Cortisol Level
- Dexamethasone Suppression Test
- CRH Stimulation Test

Treatment:

Treatment depends on the specific reason for cortisol excess. Includes: surgery (resection of tumor), radiation, chemotherapy or drugs that inhibit cortisol (such as mitotane).

- **If the cause is exogenous cortisol:**
  If the cause is long-term use of glucocorticoid hormones to treat another disorder, the doctor will **gradually reduce the dosage** to the lowest dose adequate for control of that disorder. Then, the daily dose of glucocorticoid hormones may be doubled but given on alternate days to lessen side effects.

- **If the cause is a pituitary adenoma:**
  The most widely used treatment is **surgical** removal of the tumor, known as **transsphenoidal adenomectomy**

- **If the cause is an ectopic ACTH syndrome:**
  Cancer treatment: **surgery**, **radiotherapy**, **chemotherapy**, **immunotherapy**, or a **combination** of these treatments. The choice depends on the type of cancer and how far it has spread. Since ACTH-secreting tumors (for example, small cell lung cancer) may be very small or widespread at the time of diagnosis, cortisol-inhibiting drugs, like **mitotane**, are an important part of treatment. In some cases, if pituitary surgery is not successful, surgical removal of the adrenal glands (bilateral adrenalectomy) may take the place of drug therapy.

- **If the cause is an adrenal tumor:**
  Surgery is the mainstay of treatment for benign as well as cancerous tumors of the adrenal glands.

Prevention:

Early detection and treatment are the best options in order to prevent complications.

Revision Questions:

1- Discuss the anatomy and the function of the adrenal gland:

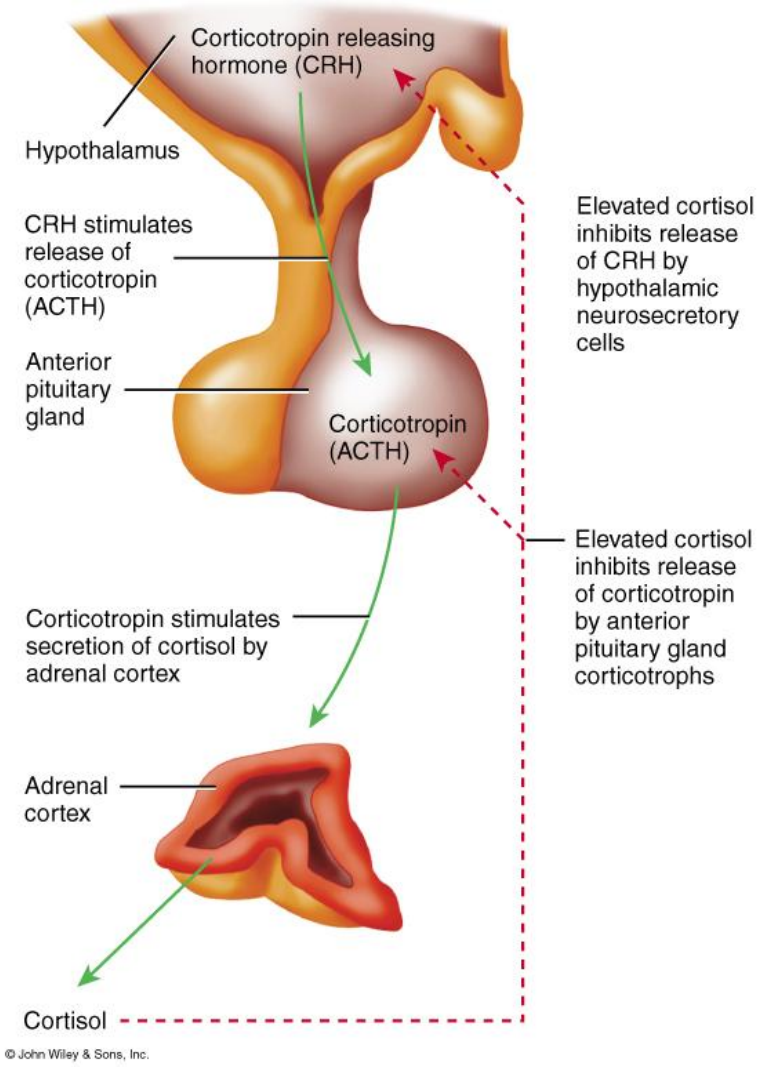
- Anatomy:

  The adrenal glands are paired endocrine organs that are composed of cortex and medulla.
  Three layers in the **cortex**: **Glomerulosa**, **fasiculata**, **reticularis**.
  The adrenal **medulla** has chromaffin cells

- Function: Produce adrenal hormones.
  From **cortex**: Three types of **steroids**:
  (1) Mineralocorticoids (aldosterone) zona glomerulosa
  (2) Glucocorticoids (principally cortisol) zona fasciculata
  (3) Sex steroids (estrogens and androgens) zona reticularis.
  From **medulla**: epinephrine & norepinephrine

	Structure	Hormone released	Function
Adrenal Cortex	Zona Glomerulosa	Mineralocorticoids (mainly Aldosterone)	↑ urine excretion of K+ ↑ reabsorption of Na+ ↑ retention of H_2O
	Zona Fasciulata	Glucocorticoids (mainly Cortisol)	↑ gluconeogenesis ↑ blood glucose ↑ retention of H_2O Anti-inflammatory effects
	Zona Reticularis	Androgens (mainly DHEA)	Sex hormone precursor

2- Explain the role of feedback mechanisms in the regulation of glucocorticoids secretion:



3- Explain Amani's signs, symptoms and results:

(explanation was provided next to some of the symptoms earlier)

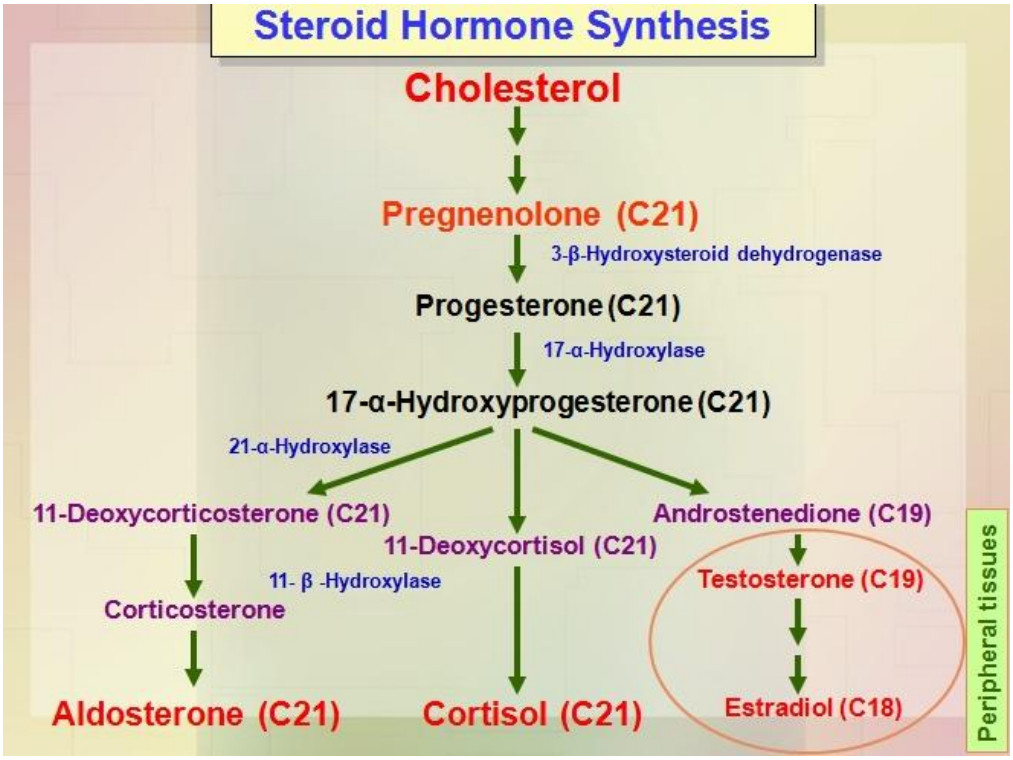
4- Discuss the impact of such disease on Amani's psychological health:

Cortisol over secretion might cause psychological disturbances since cortisol can affect neurotransmitters. Disturbances might be

depression, anxiety or others. The changes that happened to Amani's body might also affect her self-esteem, and thus will affect her psychological health.

Learning Objectives:

- Anatomy, histology and physiology of adrenal gland
- Understand hypothalamo-pituitary-adrenal axis and physiology of negative feedback mechanism
- Discuss **formation and physiological actions** of **glucocorticoids** and **androgens**



- Use basic sciences to interpret symptoms, signs and investigations of a patient with Cushing's syndrome
- Discuss pathology and pathogenesis of Cushing's syndrome
- Psychological impacts of Cushing on patients
- Management goals and options for Cushing's syndrome