Cushing's syndrome

Introduction:

Definition and Overview:

Cushing's syndrome is a condition in which there is too much cortisol (a hormone made by the outer layer of the adrenal gland) in the body. It is commonly diagnosed between the ages of 30 to 40.

Historical context:

It has been more than a century since Dr. Harvey Cushing (the syndrome is named after his name) saw his first patient with Cushing's disease (CD), a woman named Minnie G.

Epidemiology:

All causes considered ranging between 1 out of 12,658 to 17,544 individuals per year. If we are talking about the number of patients affected by Cushing syndrome then they are about 40 to 70 people out of every million.

Etiology:

Causes and Risk Factors:

Cushing syndrome happens when the body has too much of the hormone cortisol for a long time. This can result from the body making too much cortisol, or from taking medicines called glucocorticoids, which affect the body the same way as cortisol. (so we have two factors one internal and the other is external)

Genetic and Environmental Influences:

The genetic cause of Cushing disease is often unknown. In only a few instances, mutations in certain genes have been found to lead to Cushing disease.There are no environmental triggers known and it's not hereditary.

Clinical Features:

Signs and Symptoms:

There are common symptoms for Cushing syndrome such as weight gain in the trunk with thin arms and legs, weight gain in face which is called moon face. A fatty lump between the shoulders is shown up and this may be referred to as a buffalo hump. Pink or purple stretch marks take place on the stomach, hips, thighs, breasts and underarms. The skin gets thin and frail that bruises easily. Slow wound healing can be worse in case of diabetes.

But symptoms differ among men and women, women may experience thick, dark hair on the face and body. This condition is called hirsutism.
And their periods may get irregular or stop. While men may experience lower sex drive ,reduced fertility, and problems getting an erection.

Disease Stages and Progression:

Early stage: weight gain and more body fat.
Symptoms of Cushing's syndrome can start suddenly or gradually. They tend to get slowly worse if not treated.

Complications:

Cushing syndrome can occur from glucocorticoid medicines used to treat inflammatory diseases, pain, and prevent organ rejection. Long-term, excessive use can cause a condition known as **exogenous Cushing syndrome**. which causes health problems such as a low immune system, which may lead to frequent infections. Damage to the eyes, kidneys, and nerves is due to untreated high blood sugar and diabetes.

Furthermore, adrenocorticotropic hormone (ACTH), produced by the pituitary gland, can be affected by tumors or adrenal gland issues, leading to Cushing syndrome which is known as **endogenous Cushing syndrome.**

Without treatment, Cushing syndrome can cause complications, including bone loss, also called osteoporosis, which can lead to broken bones. high blood pressure, also called hypertension. Type 2 diabetes. Can cause serious or multiple infections and loss of muscle mass and strength.

Diagnosis:

Diagnostic Criteria:

Diagnostic criteria that suggest Cushing's syndrome are UFC greater than the normal range for the assay, serum cortisol greater than 1.8 µg/dl (50 nmol/liter) after 1 mg dexamethasone (1-mg DST), and late-night salivary cortisol greater than 145 ng/dl (4 nmol/liter).

Diagnostic Tests and Procedures:

Cushing syndrome, caused by excessive cortisol production, is often caused by glucocorticoid medicines. Diagnosis is complex and requires an endocrinologist's examination. But there are some tests that may help identify the cause if not glucocorticoid-related, such as:
Urine and blood tests: they measure hormone levels, including cortisol, ACTH, and other hormones. Healthcare providers may recommend other tests to monitor cortisol levels before and after hormone medicines.

Saliva test: it detects cortisol levels in individuals without Cushing syndrome, which typically rise and fall during the day. A small sample collected at night can indicate high cortisol levels.

CT or MRI scans : they are imaging tests that take pictures of the pituitary and adrenal glands to detect any abnormalities, such as tumors.

Inferior petrosal sinus sampling: it is a test that determines if Cushing syndrome is caused by an ACTH-producing pituitary adenoma or another organ tumor.
These tests help your health care provider diagnose Cushing syndrome. They also may help rule out other health conditions.

Differential Diagnosis:

Cushing's syndrome is diagnosed in major referral centers using plasma ACTH levels below 5 pg/ml, which indicate ACTH-independent Cushing's syndrome, depending on available biochemical tests and imaging.

Pathophysiology:

Mechanisms of Disease Development:

Simply when the body makes too much cortisol. But Cushing's disease is a specific type of Cushing's syndrome caused by a pituitary tumor leading to excessive production of ACTH (adrenocorticotropic hormone). Excessive ACTH stimulates the adrenal cortex to produce high levels of cortisol, producing the disease state.

Cellular and Molecular Changes:

the biochemical features of Cushing syndrome consist of excessive endogenous secretion of cortisol, loss of the normal feedback of the HPA axis, and disturbance of the normal circadian rhythm of cortisol secretion.

Impact on Body Systems:

fatty hump between the shoulders, a rounded face, and pink or purple stretch marks on the skin. Cushing syndrome also can cause high blood pressure or bone loss. Sometimes, it can cause type 2 diabetes.

Management and Treatment:

Medical and Surgical Treatments:

Surgically removing pituitary tumors, adrenal tumors and ectopic tumors is effective, but you'll have to adjust to new, lower cortisol levels.

Pharmacological Therapies:

Medicines to control cortisol production at the adrenal gland include ketoconazole, osilodrostat (Isturisa), mitotane (Lysodren), lev ketoconazole (Recorlev), and metyrapone (Metopirone).

Lifestyle and Dietary Modifications:

Excess cortisol from Cushing's syndrome can increase blood pressure, leading to hypertension. Avoid processed foods packed with sodium, which contributes to high blood pressure. Focus on fruits, vegetables, and reduced-sodium soups, dressing, and spreads.

Rehabilitation and Supportive Care:

Be familiar with their medications, learn to recognize any emergencies such as an adrenal crisis, and know what to do if one happens. Ask for help.

Prevention and Control:

Primary, Secondary, and Tertiary Prevention Strategies:

Primary prevention efforts are typically implemented before the onset of the health issue, secondary prevention focuses on early detection and intervention, and tertiary prevention addresses existing conditions.

Public Health Interventions:

the health care provider may recommend removing the adrenal glands. This is called a bilateral adrenalectomy. This procedure immediately stops the body from making too much cortisol.

Vaccination and Screening Programs:

Urinary free cortisol (UFC) determination has been widely used as an initial screening tool for Cushing syndrome because it provides measurement of cortisol over a 24-hour period .

Prognosis:

Disease Outcomes and Survival Rates:

Untreated Cushing's disease (CD) is associated with a very poor prognosis, estimated 5 years' survival of 50%.

Factors Influencing Prognosis:

Cushing syndrome can possibly be fatal if you don't get treatment. Without treatment, hypercortisolism can cause health problems, including: Infections. Blood clots, especially in the lungs and legs.

Quality of Life:

patients gets impaired significantly resulting from physical pain, emotional turmoil of unacceptable changes in their general external appearances, limitation of activities of daily living and also immense lassitude and fatigue.

Current Research and Future Directions:

Recent Advances and Discoveries:

The presence of a USP8 mutation (Any change in the DNA sequence of a cell) in all the body's cells is a newly discovered cause of Cushing syndrome. The finding will help researchers understand complex signaling processes between cells and develop potential treatments for resisting or halting replication of the mutation.

Ongoing Clinical Trials:

ISTURISA is a prescription medication proven to reduce the amount of cortisol your body makes to help you reach and maintain normal cortisol levels.

Future Research Needs:

It is going through observing genetic factors as it is newly discovered that mutation is one of the factors included in this syndrome. As the mutation is a change in the DNA sequences.

Case Studies:

Example Cases:

Amy Schumer is a known actress and comedian, she has publicly opened her health issues, including her unexpected weight gain, fatigue, and facial swelling.

She physically explained herself that she has been suffering from central obesity with increased fat around the abdomen, facial rounding and swelling, presence of a dorsocervical fat pad (buffalo hump), skin changes, including easy bruising and purple striae (stretch marks) on the abdomen.

After doing some tests and images it was found that she has elevated serum cortisol levels, lack of diurnal variation in cortisol secretion, elevated 24-hour urinary free cortisol, low-dose dexamethasone suppression test: No suppression of cortisol levels, ACTH levels (pending to determine the type of Cushing's syndrome). So, Amy was diagnosed with Cushing's syndrome.

About the treatment she was advised to manage any secondary conditions such as hypertension or diabetes if present and based on imaging results, if a pituitary adenoma was found, transsphenoidal surgery would be recommended. If an adrenal tumor was identified, an adrenalectomy would be planned.

Finally, in her follow-up she has to make regular follow-up appointments to monitor hormone levels and overall health, having support for lifestyle modifications, including diet and exercise and psychological support to manage emotional and mental health challenges associated with the syndrome and its treatment.
In conclusion, Amy would likely experience significant improvement. Weight reduction, normalization of physical appearance, and resolution of other symptoms would be expected over time in her long-term follow-up.