SAINT JOHN'S HEALTH CENTER
BRAIN TUMOR CENTER

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Cushing's Disease

Introduction

Cushing's disease is caused by an ACTH-secreting pituitary adenoma. This serious endocrinopathy is a subset of Cushing's syndrome which refers to elevated blood cortisol levels. Cushing's syndrome may arise from tumors of the pituitary or adrenal glands or from tumors elsewhere in the body (ectopic ACTH-producing tumors). Cushing's syndrome is caused by a pituitary adenoma in over 70% of patients. Most ACTH-secreting adenomas are microadenomas. Cushing's disease is relatively uncommon, affecting 10-15 of every million people/year, most commonly adults aged 20 - 60 years; women account for over 70% of cases. Given that Cushing's disease causes so many common problems affecting the general population such as obesity, hypertension and diabetes, many patients with Cushing's disease go undiagnosed for years or perhaps are never diagnosed.

Symptoms

Body changes including weight gain in the face (moon face), above the collar bone (supraclavicular) and back of neck (buffalo hump) are commonly seen in patients with Cushing's disease. Skin changes include easy bruising, with purplish stretch marks (stria) and red cheeks (plethora), and excess hair growth (hirsutism) on the face or body. High cortisol levels also cause weakness, fatigue and muscle wasting. Women may develop absence of menses (amenorrhea) and decreased libido. Additional serious consequences may include hypertension, diabetes mellitus, depression and osteoporosis.

Diagnosis

Patients are often diagnosed with Cushing's disease after several years of symptoms which might include progressive weight gain, new onset hypertension or diabetes and mood changes. Comparison of old and recent photographs will often demonstrate changes in appearance. Unfortunately, the diagnosis of Cushing's disease is often long delayed and can be difficult to make. An endocrinologist should always supervise the evaluation for Cushing's disease.

Hormonal diagnosis*:* The first step in diagnosing Cushing's disease is to confirm the presence of excessive cortisol secretion. This diagnosis is most easily made by performing a low-dose dexamethasone suppression test, a 24-hour urinary free cortisol collection, and/or a midnight serum cortisol level or a midnight salivary cortisol test. Once the diagnosis of Cushing's syndrome is established, the source of the excess cortisol is determined: either from an adrenal gland tumor, an ectopic ACTH-producing tumor, or a pituitary ACTH-producing adenoma. Serum ACTH levels and a high-dose dexamethasone suppression test are typically used for this determination. Petrosal Sinus Sampling is an angiographic test used to distinguish between ectopic ACTH production and pituitary ACTH production (Cushing's disease). Petrosal sinus sampling should never be performed before the diagnosis of ACTH-dependent Cushing's syndrome is established.

Imaging: Once the diagnosis of Cushing's syndrome is confirmed hormonally, a pituitary MRI can detect the presence of an adenoma in approximately 70% of cases. Dynamic post-gadolinium coronal MRI is a recent technique that helps diagnose small adenomas that may not be seen on a conventional pituitary MRI. CT scans of the adrenal glands are very useful for determining the presence or absence of an adrenal tumor causing Cushing's syndrome.

Treatment

Endonasal Endoscopic Surgery*:* Surgical removal is the primary means to achieve long term remission in Cushing's disease; at experienced pituitary tumor centers remission rates range from 80-90% for microadenomas and 30-70% for invasive adenomas or macroadenomas. Because of improved visualization, the endonasal endoscopic approach is rapidly becoming the preferred method for removal of most pituitary adenomas, including ACTH-secreting adenomas.

Medical Therapy: In patients who fail to have remission of their Cushing's disease or syndrome state after surgery, there are several medications that can lower cortisol levels. These include "adrenal-directed" medications ketoconazole and aminoglutethimide which inhibit steroid (cortisol) production in the adrenal glands. They are initially effective but have some side effects, and the overall long-term control of Cushing's disease with these drugs is rather poor.

Radiosurgery (SRT) or Stereotactic Radiotherapy (SRS): For patients whose Cushing's disease is not controlled with surgery, SRT (multiple doses) and SRS (one dose), which provide precise doses of radiation to the tumor, are effective in controlling cortisol levels and tumor growth in 50 – 70% of patients. However, lowering of cortisol levels generally takes significantly longer with SRT compared to SRS. Also, SRT and SRS may result in loss of normal pituitary function over 5 to 10 years. Neurologic complications such as visual loss and temporal lobe damage rarely occur with SRT and SRS.

For a visual tour of endonasal and keyhole surgery for brain, pituitary & skull base tumors, visit our BTC YouTube channel: *www.youtube.com/user/BrainTumorCenter*