CLINICAL VIGNETTE

Hirsutism – A Manifestation of Acromegaly

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Case Presentation

A 45-year-old woman presented with worsening hirsutism and weight gain for one year. Her past medical history includes Polycystic Ovarian Syndrome (PCOS), and obesity s/p Roux-en-Y gastric bypass more than 15 years prior to presentation.

She was diagnosed with PCOS at age 17 with irregular menstrual period, acne, hirsutism, and weight gain. Oral contraceptive pills were prescribed but stopped after a few months due to mood swings. At age 30, she underwent Roux-en-Y gastric bypass surgery with improvement in menstrual regularity and hirsutism. She gave birth to a healthy boy at age 35 and maintained her weight with low calorie diet and daily exercise until age 44 when she gained 20lb and noticed worsening hirsutism. She attributed her symptoms to increased work stress. Her symptoms worsened despite Metformin 500mg twice a day.

Physical examination included normal blood pressure, heart rate, temperature, and oxygenation. Her height was 5'1, weight 180lb with BMI of 34. She had no goiter, but her exam was notable for coarse facial features with enlargement of nose and frontal bone, widened teeth space, protruding of her jaw and hirsutism. Her Ferriman Gallway score for hirsutism was 12. (A score of 1 to 4 is given for nine areas of the body. A total score less than 8 is considered normal, a score of 8 to 15 indicates mild hirsutism, and a score greater than 15 indicates moderate or severe hirsutism. A score of 0 indicates absence of terminal hair).[1] There was no hand swelling.

Her laboratory results were significant for an elevated Insulin like Growth factor -1 (IGF-1) level of 214 ng/ml (62-204 ng/ml), elevated DHEAS level of 245.3 µg/dl (41.2-243.7 µg/dl), and a Testosterone level of 40 ng/dl (7-55 ng/dl). Acromegaly was suspected and she underwent growth hormone (GH) tolerance test which was positive: GH 0.2 ng/ml (0.0 to 1 ng/ml), 0.5 ng/ml, 4.7 ng/ml, 1.5 ng/ml, 0.4 ng/ml. The MRI showed a 6 mm anterior pituitary adenoma. She was referred for surgery. She will follow up with Endocrine clinic after the surgery.

Discussion

Hirsutism is the presence of excessive terminal hair growth (dark, coarse hair) in androgen dependent areas. These include upper lip, chin, chest, upper and lower abdomen in which women typically have little or no hair.[1,2] It can be caused by many etiologies. The most common cause of hirsutism is Polycystic Ovarian Syndrome and one of the rarest etiologies is Acromegaly. This patient was diagnosed with PCOS at age 17. However, her physical exams showed acromegalic features, which lead to the clinical suspicion for Acromegaly.

The most common cause of Acromegaly is somatotroph (GH-secreting) adenoma of the anterior pituitary.[3] The Onset of Acromegaly is insidious, and its progression is usually very slow. The average interval from the onset of the symptoms until diagnosis is about 12 years.[4] This patient was diagnosed with Acromegaly twenty-eight years after the diagnosis of PCOS. Most patients have a macroadenoma, tumor greater than 10mm at diagnosis, related to diagnostic delay and posing challenging in surgical managements.[5]

Acromegaly causes many clinical symptoms. Some symptoms are from direct compressive effects of pituitary mass such as headache, visual field defect (bitemporal hemianopsia), cranial nerve palsies.[6] A somatotroph macroadenoma may cause decreased secretion of other pituitary hormones, most commonly gonadotropins. Hyperprolactinemia may occur in about 30% of patients.[3] Many women present with menstrual irregularity, with and without galactorrhea and some have hot flushes and vaginal atrophy.[7] Men may have erectile dysfunction and loss of libido. Thyroid stimulating hormone (TSH) and corticotropin (ACTH) deficiency occur less commonly than other pituitary hormone deficiencies.[3] Long term GH and IGF-1 excess result in overgrowth of many tissues including connective tissue, cartilage, bone, skin, and visceral organs. The Characteristic finding are macrognathia, enlarged swollen hands and feet, coarse facial features with enlargement of nose and frontal bones and widen space between teeth.[3] Patients may have macroglossia, deepening of the voice, paranesthesia of the hands.[3] Hirsutism may present in women.[3] Joint symptoms are a common presenting feature of the disease with back pain and kyphosis common.[3] Thyroid gland enlargement may be diffuse or multinodular.[3] Patient may have cardiovascular abnormalities including hypertension, left ventricular hypertrophy and cardiomyopathy.[8] Sleep apnea presents in about 40% to 50% of patients.[9] Uncontrolled Acromegaly is also associated with Insulin resistance, overt Diabetes Mellitus, and Impaired glucose tolerance.[10] Patient also have increased risks of colonic neoplasia and colonic diverticula.[3] Acromegaly causes increased mortality. Therefore, it is very important to make the correct diagnosis and control the biochemical disease.

Acromegaly is diagnosed by biochemical testing and does not require the presence of typical phenotypic features or the presence of a pituitary tumor on MRI. The best single test for diagnosis is measurement of serum IGF-1.[11] If a patient has elevated IGF-1 level, he/she should undergo testing for GH hypersecretion.[11]

The most specific dynamic test for establishing the diagnosis is an oral glucose tolerance test (OGTT). When performing the test, it is important to measure serum GH at baseline and every 30 minutes for two hours after glucose administration. The criterion for the diagnosis of Acromegaly is a GH concentration greater than 1 ng/ml.[12] In normal subjects, serum GH concentrations fall to 1 ng/mL or less within two hours after ingestion of 75 g glucose. In contrast, the post-glucose values are greater than 2 ng/mL in over 85 percent of patients with Acromegaly.[12]

The goals of therapy in patients with Acromegaly are to lower the serum IGF-1 concentration to within the normal range for the patient's age and gender, control adenoma size and reduce mass effects, improve symptoms, and reverse metabolic abnormalities such as diabetes mellitus.[11] Transsphenoidal surgery is initial therapy.[11] For patients with an abnormal serum IGF-1 and moderate symptoms of GH excess after transsphenoidal surgery, medical therapy with long-acting somatostatin analog or Pegvisomant is recommended.[11] If medical therapy is ineffective, stereotactic radiation therapy is indicated.[11]

Following the initial treatment, patients should be evaluated every 3 to 4 months with both clinical examination and measurement of serum IGF-1 levels.[13] MRI should be repeated 12 weeks after surgery and then yearly for the first several years.[13] Colonoscopy should be performed at baseline and every 5 years in patients found to have a polyp or those with persistently elevated IGF-1 levels and every 10 years in those without polyps and with normal IGF-1 level.[13]

Conclusion

It is very important to get detailed history and perform physical exams when assessing a patient with hirsutism because it may be a manifestation of Acromegaly. Mortality is increased in patient with Acromegaly and making the correct diagnosis can reduce morbidities and mortality and improve quality of life.

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