CLINICAL VIGNETTE

Temporary Amenorrhea in a Patient

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Case Presentation

A 37-year-old Caucasian female saw her gynecologist after she missed her menstrual cycle for two months. As part of her evaluation, an elevated prolactin level of 93 ng/ml (normal <23 ng/ml) was found, and she was referred to endocrinology. By the time she presented to endocrine, her menstrual cycle had returned. She denied prior issues with her menstrual cycle with menarche at age 13 and normal pubertal development. She had two full-term pregnancies, which were complicated by gestational diabetes but managed with diet. She denied any galactorrhea or any visual disturbances. She had no significant headaches. On review of systems, she reported pain at her wrists that radiated to her hands. This pain was exacerbated by prolonged typing. She also noted mild pain in both shoulders occasionally.

On examination, her blood pressure was 100/64 with a resting pulse of 67. Her height was 5'2" with a weight of 154 pounds and BMI of 29.1. She had mild prominence of her forehead and broadened bridge of her nose. Her jaw was particular pronounced, and she was not hirsute. The oral exam was normal with no spreading of teeth or prominent tongue. There were no obvious neurologic deficits, and her visual fields were grossly intact. The rest of her exam was unremarkable with the exception of some thickening of the skin of her palms and soles of her feet as well as mild swelling of all her fingers. Repeat prolactin was 47.7 ng/ml. Given the persistent elevation in her prolactin and physical findings suggestive of growth hormone excess, labs to test pituitary axis were ordered as well as a pituitary MRI. Pituitary function appeared intact with the exception of an elevated non-fasting IGF-1 of 480 ng/ml (normal 331 ng/ml), which was higher, 540 ng/ml, on repeat. MRI showed a 19 mm cystic pituitary tumor that was abutting, but not displacing, the optic chiasm. A tentative diagnosis of acromegaly was given. Of note, her thyroid exam was normal with no evidence of masses. Formal visual field test showed no deficits in her vision. Fasting and post-prandial GH levels were 23 ng/ml (normal <7 ng/ml) and 24.1 (normal <2 ng/ml), respectively, confirming acromegaly. She was referred to the UCLA Pituitary Program.

Discussion

Acromegaly is a disorder of excessive levels of GH as well as IGF-1 and was considered rare in the past with an estimated prevalence rate of about 40 people out of one million,[1] based on a 1980 UK study. With improvement in awareness and testing capabilities that estimate is being reconsidered. A German study proposes a higher prevalence rate of about 1000 people out of one million.[2]

Physical signs of acromegaly in adults include overgrowth of facial bones – resulting in a prominent forehead and lower jaw. The jaw growth can lead to widening spaces between the teeth. Overgrowth of soft tissues can lead to thickening of palmar tissue as well as the soles of the feet – with increase in shoe size. Fingers can thicken and patients may note ring tightness. Given the insidious and gradual nature of acromegaly, patients may not notice the changes until the condition is in its later stages. Patients may also suffer from carpal tunnel syndrome and various arthropathies. Other associated conditions include sleep apnea (from soft palate overgrowth), type 2 diabetes mellitus, and cardiovascular disease.

Initial evaluation should measure IGF-1 levels rather than random GH levels.[3] IGF-1 is more stable given its much longer half-life than GH. An oral glucose tolerance test with 75 grams of glucose can be used to confirm the diagnosis, measuring GH levels pre- and post-glucose load. A post-prandial GH level of over 1 ng/ml is abnormal with 85% of acromegalic patients testing with levels over 2 ng/ml.[4]

Pituitary adenomas are the most common cause of acromegaly; imaging with MRI (preferred over CT) should be done once a biochemical diagnosis has been made. Although uncommon, ectopic sources should be considered if imaging of pituitary is negative.

It is estimated that 80% of acromegaly-related pituitary tumors are macroadenomas and trans-sphenoidal surgery is considered the best initial treatment. The goal of surgery is removal of tumor mass to normalize IGF-1 and GH levels. Surgical results are known quickly as GH levels normalize within an hour of a successful surgery. About 50% of patients with macroadenomas will have post-operative normalization of their GH levels. Outcomes are better for patients with microadenomas, where 80% of patients will have a drop in GH.[5]

Retesting of IGF-1 and GH should be done about 3 months after surgery. Repeat imaging should also be done around that time. Patients with persistent disease will require medical therapy. Somatostatin receptor ligands (SRLs) are the preferred initial choice. Patients intolerant of SRLs or not responding to treatment can be treated with pegvisomant, a

GH receptor blocker. Cabergoline or bromocriptine can be considered as adjuvant treatment.

For patients with residual tumor who are not responding to or are intolerant of medical treatment, radiotherapy or stereotactic radiotherapy can be considered. Radiation is usually successful in gradually lowering GH levels. However, there are risks of losing pituitary function with radiation.

Patients with acromegaly have higher mortality rates mostly due to cardiovascular and cerebrovascular disease. Acromegaly increases the risk atherosclerotic disease as well as biventricular hypertrophy. Because GH has anti-insulin properties, patients have higher risks of insulin resistance and type 2 diabetes mellitus. Sleep apnea also increases cardiovascular and respiratory risks. Risks for osteoporotic fracture are higher with acromegaly. Thyroid cancer is thought to be the most common cancer associated with acromegaly. There is still controversy as to whether acromegaly increases risks of colon cancer.

In summary, acromegaly is a disease of GH excess. Surgical excision of the pituitary tumor is initial treatment with medical therapies reserved for those with residual disease. Careful monitoring for the various co-morbidities is essential.

Our patient is underwent successful surgery with post-op IGF levels dropping to 155 ng/ml.

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