CLINICAL VIGNETTE

Acromegaly Presenting in an Elderly Man with Type 2 Diabetes Mellitus and Hypogonadism

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Case Presentation

A 68-year-old male presents for a second opinion for the treatment of his mild Type 2 diabetes mellitus and hypogonadism, presenting with worsening glycemic control and increasing fatigue despite adequate testosterone repletion. He reports difficulty sleeping, requiring the use of temazepam to fall asleep but waking up a few hours later. He also reports new diagnosis of obstructive sleep apnea after undergoing a formal sleep study even though he is not obese. His wife reports he has been snoring louder in the last few months. He had been able to control his Type 2 diabetes mellitus with just a carbohydrate-controlled diet and exercise, keeping his HbA1c under 6.0%. However, he had noted sugars that have been higher than normal, fasting in the morning between 100-140 mg/dl. He had been on testosterone therapy for 5-years on testosterone gel and kept his levels generally between 300-600 ng/dl. He also reported early fatigue while exercising despite testosterone. He felt it was not working for him. Other problems included nasal congestion with recent removal of a nasal polyp. He also had a recent negative colonoscopy.

After initiation of Cpap for his sleep apnea, his dose of testosterone gel decreased. However, despite consistent dosing at 50% of his prior dose, the levels of testosterone fluctuated between 200-1000 ng/dl. He underwent further testing including IGF-1 and other pituitary hormones due to the difficulty in controlling his androgen levels.

Initial labs included an elevated IgF-1 at 589 with a Z-score of 4.0; normal IgF-1 for his age and sex is 41-279 ng/dl. He was off testosterone for 4 weeks with a level of 481 ng/dl. A repeat IgF-1 showed a level of 407 ng/ml with growth hormone of 4.7 ng/ml, prolactin 10.0, LH 3.2, and FSH 6.1.

An oral glucose tolerance test was done with 75g glucose load, which normally decreases serum growth hormone to 1 ng/ml within 2 hours of ingestion. The patient's growth hormone level at 1 hour was 7.1 ng/ml and at 2 hours was 7.5 ng/ml.

Upon additional questioning, he reported a growth on his pituitary that he did not need to be concerned about it. The pituitary MRI showed a 5 mm pituitary adenoma 3 years earlier. Records were not obtainable, so it was unclear if he had any biochemical testing done to rule out functioning adenoma. Repeat MRI of the pituitary now showed a 7 mm left lateral anterior pituitary adenoma.

He also reported increasing ring size with swelling and pain at his wrists. His BMI is 24, and his height is 5 feet 11 inches tall. On exam, he has a wide forehead and prominent jaw, especially compared to his 10-year-old driver's license picture showing less prominent forehead and jaw. His fingers have also enlarged, and he has not been able to wear rings. His dentist told him his teeth were shifting more as he got older, and he has a gap between his upper incisors. Despite using the Cpap for his sleep apnea, he continues to snore and have difficulty sleeping at night. He also is reporting worsening depression but refuses to take an antidepressant.

Patient underwent transnasal endoscopic removal of his pituitary adenoma and had a bilateral nasal polypectomy with free mucosal graft reconstruction of the sella. The surgical pathology revealed a pituitary adenoma, which was strongly immunoreactive for human growth hormone.

Post-surgery, patient did not require further testosterone therapy. His sleep apnea improved as did his depression. His blood sugars improved with HbA1c of 5.6% with the same level of exercise and carbohydrate control he had done in the past. He notes less joint pain and fatigue. His postoperative IGF-1 was 178 ng/dl, growth hormone 1.1 ng/ml, and total testosterone 524 ng/dl. A repeat MRI of the pituitary 6-months post operatively showed no evidence of residual tumor or recurrence.

Discussion

Acromegaly is defined as the persistent hypersecretion of growth hormone (GH). Diagnosis is based on elevated IGF-1, which is secreted by the liver as a result of GH stimulation.

GH itself is pulsatile and diurnal, as well as easily affected by stress levels, hence not a reliable measurement for the diagnosis of acromegaly. Acromegaly should be suspected in patients who have typical physical signs of acromegaly including macrognathia (enlarged jaw) and enlargement of hands, feet, and fingers; arthralgias and carpal tunnel can occur in the absence of joint overuse, spreading of upper teeth, and causing protrusion and enlargement of frontal bones. New onset snoring, type 2 diabetes mellitus, nasal polyps, sleep apnea in a non-obese patient, colon cancer, cardiomyopathy, and cardiovascular disease are often associated with acromegaly. Hypogonadism from sleep apnea and/or tumor suppression of LH and FSH may be the first presenting complaint for males and can often be misdiagnosed as low testosterone. These patients may also present with new-onset prediabetes or overt type 2 diabetes mellitus due to IGF-1 elevations that lead to elevated glucose levels from hyperinsulinemia and increased insulin resistance.

Diagnosis is established by a high IGF-1 with confirming oral glucose tolerance test as described in the case presentation when GH is inadequately suppressed by the 75 g load in 2 hours. Primary therapy is transsphenoidal surgery in most patients[1] to debulk and hopefully lead to total resection. However, persistent disease can occur following surgery, and medical therapy with dopamine agonist like cabergoline for mild IGF-1 elevations should be initiated. Patients with moderate to severe signs of GH excess and IGF-1 elevations following surgery may be treated with somatostatin receptor ligands (SRLs) or pegvisomant. Patients who have extensive cavernous sinus invasion may not benefit from surgery and would be initiated by SRLs as first-line therapy. SRLs, including octreotide and lanreotide, commonly cause side effects of abdominal cramping, diarrhea, and flatulence but usually improve over time; however, it is recommended that practitioners monitor for signs and symptoms of gallbladder disease as this can occur in approximately 25% of patients on SRLs.[1]

Pegvisomant is a human GH antagonist that competes with endogenous GH for binding its receptor and blocks peripheral production of IGF-1. Pegvisomant is used alone or in combination with SRLs. Pegvisomant does not stop GH oversecretion and can be associated with tumor growth in 3-5% and transaminitis, but it does help with glycemic control in those acromegalics who have diabetes mellitus. The current recommendation is combining therapies to minimize side effects and maximize benefit.[2]

Patients who have residual tumor post-surgery, who have tried and failed medical therapy and/or unable to tolerate the side effects, are recommended for radiation therapy (RT) or stereotactic radiotherapy (SRT). Conventional RT can be used as an adjuvant therapy to surgery and medical therapy. However, SRT is generally recommended over conventional RT because higher follow-up remission rates have been reported. Nearly two-thirds of patients achieved remission after 5 years of follow-up at one large academic center.[3] However, SRT is not recommended if the tumor is too close to the optic chiasm or if there is significant tumor burden.[2] Hypopituitarism occurs more than 50% of the time within 5-10 years, thus pituitary function should include regular testing for hypothyroidism, hypogonadism, and adrenal insufficiency.

Our elderly male patient presented with typical diagnoses of diabetes and hypogonadism frequently seen by endocrinologists and/or internists but was found to have the rare diagnosis of acromegaly upon further investigation. The importance of a good history and physical exam and review of an older driver's license ID helped point to acromegaly. The patient had many of the signs and symptoms of acromegaly, but because many can be attributed to normal aging and common to elderly men, the diagnosis was not immediately considered. It is also important to understand that surgery, while considered first-line, may not be curative and that monitoring post-surgery IGF-1 levels and symptoms must continue with medical therapy and/or radiation therapy for recurrence.

REFERENCES

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Submitted January 19, 2015