

## **The OHSU Pituitary Unit**

### **Acromegaly**

Approximately 10% of pituitary adenomas secrete excess growth hormone (GH) which in adults causes a disease called acromegaly. The word "acromegaly" is of Greek derivation and literally means, "enlarged extremities". The vast majority of cases of acromegaly are caused by pituitary adenomas but other causes include tumors of the pancreas, lungs or adrenal glands. This section will focus on acromegaly caused by pituitary tumors.

### **Signs and Symptoms**

Due to the slow growth of GH secreting pituitary tumors, the physical characteristics of acromegaly typically develop very slowly over several decades. Acromegaly is particularly characterized by skeletal changes including enlarging hands and feet. For example, patients often recall having to resize their rings several times over a 15 to 20 year period and/or having to increase shoe size several times over the same time frame. Other skeletal changes include enlarging jaw and brow (frontal bossing). Despite the characteristic features of acromegaly, the gradual onset of physical changes often result in the disease being clinically missed for years. In fact, these tumors are often detected because of a mass effect (e.g., headaches, visual changes, other pituitary hormone deficiencies) rather than the physical changes caused by GH excess. Common features of acromegaly are listed in Table 1.

**Table 1 - Features of Acromegaly**

- Problems Due to GH Excess
  - Enlarged hands and feet
  - Enlarged jaw (with increased spacing between teeth)
  - Coarse facial features
  - Enlarged lips and tongue
  - Protruding brow
  - Arthritic joints and back pain
  - Thickened skin and skin tags
  - Oily skin and excessive sweating
  - Deep and "throaty" voice
  - Carpal tunnel syndrome
  - High blood pressure and vascular disease
  - Heart disease
  - Diabetes mellitus>
  
- Problems Due to Tumor Mass Effect
  - Pituitary hormone deficiencies
  - Headaches
  - Visual disturbances

## Diagnosis

Because of the slow onset of many of the signs and symptoms of acromegaly, its diagnosis is often delayed for years. The history and physical are typically characteristic since the disease has often progressed for years prior to diagnosis. Diagnostic laboratory tests include an elevated IGF-1 and/or an inability to sufficiently suppress serum GH levels after an oral glucose tolerance test (OGTT). Pituitary MRI (or CT) typically reveals a large pituitary mass but the tumor may be smaller if discovered early. In addition to diagnosing GH excess, patients should be evaluated and treated for pituitary hormone deficiency as discussed in the section: [How Do I Work With My Doctor To Find Out if I have a Pituitary Disorder?](#) Pituitary hormone replacement therapy is discussed in the section: [Pituitary Hormone Deficiency and Replacement](#) Several other associated disorders (e.g., diabetes mellitus, hypertension, heart disease, sleep apnea, colon polyps, and carpal tunnel syndrome) should be screened for and treated as appropriate.

**Clinical Pearl** - Although serum GH is elevated in most patients with acromegaly, measuring a random serum GH level is not a reliable way to diagnose the disease since GH release is pulsatile and levels fluctuate even in normal individuals. By contrast, IGF-1 is produced in the liver in response to GH stimulation and its value correlates with the average level of GH in the serum. Elevations in serum IGF-1 is therefore a much more reliable indicator of GH excess.

## Treatment

The principal treatment for acromegaly is surgical resection of the GH secreting pituitary adenoma. There are two main reasons to resect these tumors. First, GH secreting adenomas are often large (greater than 1 cm in diameter) at time of discovery and cause significant damage due to its size (e.g., optic chiasm compression, pituitary gland damage). Removing the tumor will in many cases improve vision and prevent the progression of pituitary damage. The second reason to resect GH secreting lesions is to prevent (and in some cases reverse) the negative physical manifestations and long term complications (discussed below) of acromegaly.

Since GH secreting pituitary adenomas are frequently large at time of discovery, it is often difficult for even expert surgeons to completely resect the whole tumor. If the resection is incomplete, although the complications of mass effect of the tumor may be mitigated by surgery, GH excess from the residual tumor may persist. Several options are available as additional (or adjuvant) therapy in this case. Somatostatin analogs will in many cases decrease GH levels to normal. There is a correlation between normalization of serum GH and IGF-1 levels and improvement of many of the signs and symptoms of the disease. Some newer medical treatments will be discussed below. Alternatively, conventional irradiation or stereotactic radiosurgery are also options as adjunct

therapy but the potentially large size of residual tumor tissue may make this approach problematic in some cases. Furthermore, radiation therapy typically leads to further pituitary damage and it can take years for radiotherapy to have its full therapeutic effect.

### **New Treatment Options**

Although transsphenoidal resection of GH secreting pituitary adenomas is the primary treatment option in most cases, additional treatment is often needed. Several newer options have become available in recent years. For example, a long acting release (LAR) formulation of octreotide (a somatostatin analog) is available which allows for once a month depot injection as opposed to the traditional three times a day injections of shorter acting preparations. Dopamine agonists are also effective in reducing serum GH and IGF-1 levels in some cases; longer acting preparations such as cabergoline often minimize side effects of treatment such as stomach upset.

Growth hormone antagonist (GHA) therapy is a new treatment option and may soon become the most widely used medical adjunct treatment for acromegaly. The GHA, Pegvisomant, has recently become available (2003) for general clinical use and appears to be both well tolerated and very effective at quickly normalizing GH and IGF-1 levels.

### **Assessment of Cure or Adequacy of Treatment**

Determining whether a patient with acromegaly has been cured or adequately treated can sometimes be a challenge. The goals of treatment are to 1) protect vision and minimize pituitary damage caused by the tumor, 2) to normalize serum GH and IGF-1 levels thus mitigating many of the signs and symptoms of GH excess, and 3) to adequately replace pituitary hormone deficiencies caused by the tumor or its treatment. It is also very important to follow and treat any long-term complications of the disease as described below.

### **Long-term Course and Potential Complications**

In addition to causing many of the physical changes described in Table 1, GH excess can result in increased risk of developing several long-term complications. Heart attacks, congestive heart failure, and stroke are the most common acromegaly associated causes of death. Patients with acromegaly also have an increased risk of developing colonic polyps (with a presumed increased risk of colon cancer) so those individuals typically receive a screening colonoscopy and are closely followed thereafter. There is also an increased risk of sleep apnea (poor oxygenation during sleep) which is often associated with heavy snoring. Prolonged periods of poor oxygenation during sleep is damaging to the lungs (this can lead to scarring of oxygen permeable tissues in the lung) which in turn can cause heart failure. This insidious process is referred to as "cor pulmonale". Patients with

acromegaly should be tested for sleep apnea and, if present, can be treated with an oxygenation apparatus at night (CPAP). Finally, patients with acromegaly are at increased risk of developing carpal tunnel syndrome that is characterized by wrist pain and finger numbness. If present, this can be treated surgically. As discussed above, it is also important to follow the overall function of the pituitary to assure that the remaining hormones are treated adequately.

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