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# A Comprehensive Review on Acromegaly: A Complicated Endocrine Disorder

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**ABSTRACT**

Acromegaly is a disease or disorder that is caused by the hyper secretion of growth hormone from the anterior pituitary, that results in the excessive growth of tissues of body and dysfunctioning of other metabolic processes. Acromegaly is usually caused by the non-cancerous (benign) tumour and middle-aged people are mostly affected by it. Patients with acromegaly have pain in the joints, physical deformities, deepening of voice, bulging chest, protruding lower jaw, large feet and hands, oily skin, vision disorder or erectile dysfunction (impotence). Acromegaly occurs after the fusion of growth plates while gigantism occurs before the fusion of growth plates. This article reviews the pathophysiology and management of acromegaly as well as it highlights the etiology and epidemiology of acromegaly.

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## Introduction

Acromegaly is an inimitable disorder that is caused by overproduction of growth hormone usually from an adenoma of anterior pituitary gland [1]. The people that are diagnosed by this disease are mostly of 40 years, with equal number of men and women. The disease is exceptional and the prevalence is not clear; a recent review noted estimates of between 40 and 130 cases per million adults [2]. An authenticate diagnosis of acromegaly generally takes several years, that may lead to serious consequences for patients' health. The delay in the diagnosis may be due to the similar symptoms of acromegaly with that of hypertension and diabetes [3].

The purpose of this article is to make people familiar with signs and symptoms as well as treatment of acromegaly. Acromegaly is associated with multiple comorbidities, such as diabetes mellitus, sleep apnea, arthropathy, cardiovascular system disorder (e.g., hypertension) and menstrual irregularities. It is expected that the familiarity with the signs and symptoms of acromegaly will facilitate early evaluation and management of the disease [4-5]. Acromegaly cannot be prevented but early treatment may prevent the disease from getting worse and help avoid complications.

## Etiology

There are so many causes of acromegaly which can be divided into three parts: primary growth hormone (GH) excess, ectopic GH excess as well as excess growth hormone-releasing hormone (GHRH). Most acromegaly cases are caused by non-cancerous (benign) tumour (adenoma) of the pituitary gland. The adenoma produces too much growth hormone. The most commonly associated mutation involves activation of the alpha subunit of the guanine nucleotide stimulatory protein gene [6].

There are other causes of acromegaly that involves over production of GHRH. These can be divided into two parts i.e, peripheral cause and central cause. Peripheral cause involves the secretion of GHRH from small cell lung cancer, bronchial carcinoid tumours, adrenal adenoma etc, while central cause consists of hypothalamic hamartomas, choristoma and ganglioneuroma [7].

## Epidemiology

Acromegaly is an uncommon disease with an ubiquity of 4,600 per million population and approximately 116.9 new cases per million per year. The average diagnostic age of acromegaly is about 40 for men while 45 for women [8-9].

Acromegaly generally appears in the 3rd decade of life. According to a current research in Belgium, pituitary tumour may be more frequent and the generality of acromegaly would be approx. 100-130 cases per million inhabitants [10]. A lot of recent epidemiological studies have been carried out in Germany [11] on the detection method for acromegaly. Application of systemic measurement of insulin-like growth factor-I (IGF-I) in primary care patients in the general population one day discovers the epidemic of biochemistry. It has been observed that acromegaly is even greater (1,043 parts per million).

## Pathophysiology

The largest gland of body (pituitary gland) is located at the bottom of the brain and is responsible for secreting many hormones, including GH, which is regulated through complex feedback

mechanisms. Acromegaly is usually due to the presence of (benign) pituitary tumours. Depending on its size and location, the tumour mass may cause problems, such as loss of vision due to compression of the optic chiasm. However, tumours also secrete excessive amount of insulin-like growth factor-I (IGF-I). Long term excess of GH and IGF-I can cause a variety of important comorbidities, including cardiovascular complications, cerebrovascular events, gonadal dysfunction, glucose intolerance, diabetes, sleep apnea, impaired respiratory function, colon tumours and bone and joint disease [4, 12-14].

GH overproduction is also associated with increased mortality. If there are complication, especially cardiovascular disease, mortality will increase further [15]. Specially, the death rate of untreated acromegaly is two or three times than that of the general population. Hence, early evaluation and biochemical normalisation are essential to minimize the permanent life-limiting effects of excessive GH.

## Symptoms

Acromegaly can cause a number of symptoms, such as bad odour and sweating mainly at night); headache, altered size of pituitary adenoma, acral paraesthesia and pain in joints. It was also observed that the sound gradually deepened (Figure 1).

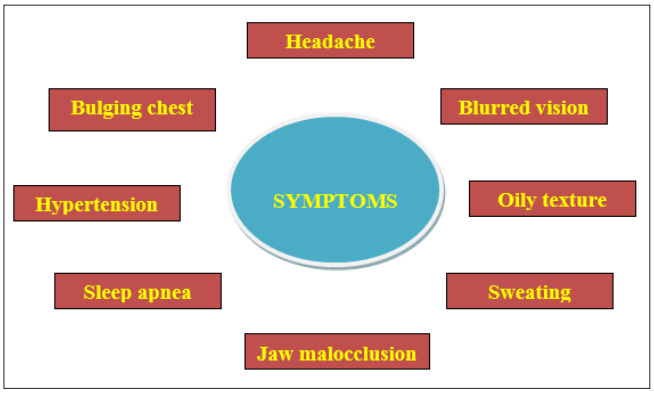


**Figure 1:** Different symptoms of acromegaly

## Diagnosis

Patients with long-term illnesses usually appear in the later stages with significant physiological features (e.g, enlarged hands, feet, lips and tongue; supraorbital bulge and protrusion of lower jaw) [16].

However, the appearance of the physical changes is insidious, yes, and patients are less likely to have complaints directly related to these characteristics of acromegaly; instead, they are more likely to show other diseases that are more common in primary care (e.g, cardiovascular disease, diabetes, hypertrophy, blood pressure and sleep apnea) (Figure 2).

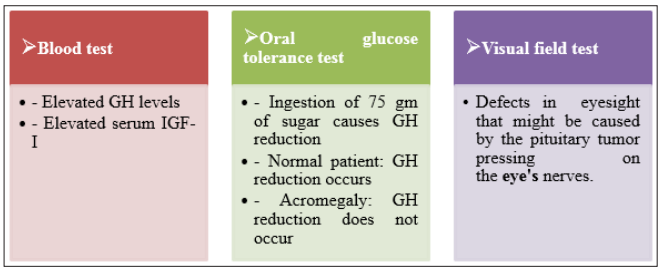


**Figure 1:** Diagnosis procedures for acromegaly

## Treatment and Management

The purpose of treatment of acromegaly includes the control of biochemical parameters (GH and IGF-I levels) and related signs and symptoms, the influence of local tumour masses, the treatment of comorbidities and the improvement of death rate [17].

**Surgical Therapy:** Surgery is optimal treatment for all large microversometers and adenomas, which can cause massive effects. Adenomas can also be performed as a method that can be performed and is likely to occur somatic cure. The best predictors for surgical healing include smaller tumours sizes, lower level of GH/IGF-I and surrounding structures (such as cavernous cavity). The study also showed that treatment with neoplastic medications with octreotide before surgery could increase the remission rate (Figure 3). However, more research is required to determine if this should be done daily or can benefit from this approach. In general, this type of surgery must be carried out in a central part with an experienced pituitary neurosurgeon which performs at least 50 operations [18].

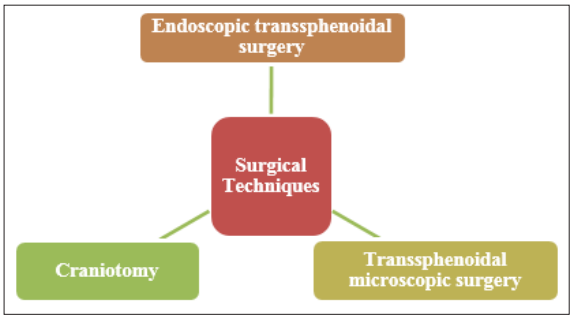


**Figure 3:** Available surgical treatment of acromegaly

**Medical Therapy:** The drug is suitable for patients who do not want surgery. The risk of surgery is too high and it is not suitable for surgery, because the tumour may not be removed after the initial surgery and the patient may reappear, but may not meet the conditions for repeat treatment. As mentioned above, preoperative drugs can also work. These are as follows (19-21).

1. Somatostatin analogues
I. Octreotide
II. Lanreotide
III. Pasireotide
2. Dopamine receptor agonists
I. Cabergoline
II. Bromocriptine
3. GH – Receptor antagonist
I. Pegvisomant

**Management of Acromegaly in Pregnancy:** GH secretion during normal pregnancy will vary. GH-secreting tumours have oestrogen receptors, especially those that secrete prolactin. The concern is whether the pregnancy status will increase the size of the tumour; however, in some studies, it has been found that most women do not experience significant changes in tumour size during pregnancy. However, since the risk still exists, women should be closely monitored through continuous visual monitoring [17, 21]. Radiotherapy: Treatment with radiation is preferred when patients are not able to cure with medication/drugs or via surgical method. The patients that are getting radiotherapy are monitored for hypopituitarism [22].

**Stereotactic Radiosurgery:** This is a precise radiotherapy that targets high doses of radiation at the tumour and minimises the risk

to nearby healthy brain tissue. It is a single high-dose radiation. The adenoma must be a few millimetres from the optic nerve abyss to avoid damage caused by this technique. in the absence of drug treatment, the remission rate of this method is 17% to 50%, and the time ranges from 2-5 years. This technology has more advantages than traditional fractional radiation therapy, which can provide better targeting and reduce radiation exposure to surrounding tissues, and shorten the time to control IGF-I and GH levels [22-24].

## Conclusion

Acromegaly is a serious disease associated with multiple comorbidities with and increased mortality. The delay in diagnosis is usually very long. This may be due to the lack of knowledge of the disease by health professionals, insidious episodes of different characteristics and possible typical complaints of patients with other more frequent disease in primary care. Health professionals who understand acromegaly can help alleviate this delay by identifying the signs and symptoms of the disease early. Treatment can begin immediately, which can reduce mortality.

For patients, the burden of disease and treatment is enormous. Often, more than one type of treatment is required, and long-term medication is often required. Comorbidities, especially those of a cardiovascular nature, may also require immediate attention. Even if the underlying hormonal abnormalities are successfully managed, several comorbidities will still exist, requiring additional long-term follow-up and treatment. It is clear that the care of these patients requires a highly coordinated multidisciplinary approach. It is also clear that any disease management strategy must focus on the needs of patients and do everything possible to improve patients' healthcare experience and minimize their treatment burden. The present study may be helpful for a systematic and targeted research for more convenient management of acromegaly.

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