Review Article

International Journal of Pharmacy and Industrial Research

Available Online at: www.ijpir.com

ISSN Print 2231 – 3648
Online 2231 – 3656

A review article on acromegaly

Dr.R.Manivannan, Dr.S.Kameshwaran*, P.Gnanasekar, S.Mohanraj

Excel College of Pharmacy, Komarapalayam, Namakkal (DT) – 637303, India

Corresponding Author: Dr.S.Kameshwaran
E.Mail: kamesh.pharm@gmail.com

ABSTRACT

Acromegaly is a rare, chronic, progressive condition characterized by excess growth hormone (GH) secretion and elevated concentrations of circulating insulin-like growth factor 1 (IGF-1). In the vast majority of cases, it is caused by pituitary adenoma. Owing to the insidious nature of the condition, clinical diagnosis, based on signs linked to GH excess, is often postponed. Consequently, when diagnosed with elevated morbidity and premature death, patients often have systemic complications. As an experimental screen for patients with suspected acromegaly, serum IGF-1 assessment is recommended. The oral glucose tolerance exam with concomitant GH assessment remains the gold standard diagnostic examination. Acromegaly treatment is aimed at reducing the levels of GH and IGF-1, increasing the symptoms of patients and reducing any local compressive effects of pituitary adenoma. Surgery, prescription therapies (such as dopamine agonists, somatostatin receptor agonists, and the GH receptor pegvisomant antagonist) and radiotherapy are the medication choices for acromegaly. It is recommended to use a multidisciplinary approach, often involving combined care modalities. Related morbidity and death can be minimized with disease prevention. The Endocrine Society's newly released evidence-based recommendations discussed critical health concerns related to acromegaly assessment and treatment. This analysis addresses developments in our understanding of acromegaly pathophysiology, the identification of multiple types of the condition, and reflects on current modalities of care and possible pharmacological treatments for acromegaly patients.

Keywords: Acromegaly, growth hormone, pituitary adenoma, somatostatin receptor ligand

INTRODUCTION

In 1864, Verga identified and added to the collection of the Anatomical Museum of Modena, Italy, the skull of a woman afflicted by prosopectasia (derived from the Greek terms prosopon, face, and ektasis, stretching). This patient suffered from common somatic disfigurement, arrhythmias, and osteoartropathy over her lifespan, while a postmortem test indicated a giant pituitary pituitary (1). Brigidi recorded a summary from the autopsy of the Italian actor Ghirlenzoni in 1881 that was scientifically consistent with acromegaly (2). This individual had visceromegaly and swollen hypertrophic pituitary. Both Verga and Brigidi, however, confused the pathogenesis of the condition, which was traced (3). It was only in 1909, however, that Harvey Cushing (4) announced the remission after partial hypophysectomy of clinical symptoms of acromegaly, thereby suggesting the etiology of the condition and its possible cure as well. Progressive somatic disfigurement and a large spectrum of systemic symptoms are considered to characterize acromegaly (5). However, it was only in 1909 that Harvey Cushing (4) announced the remission of clinical effects of acromegaly after partial hypophysectomy, indicating the etiology of the disease and its potential

Dr. S.Kameshwaran
Excel College of Pharmacy, Komarapalayam, Namakkal (DT) - 637303,
Tamilnadu, India

remedy as well. Progressive somatic disfigurement and a broad variety of systemic effects are known to describe acromegaly (6).

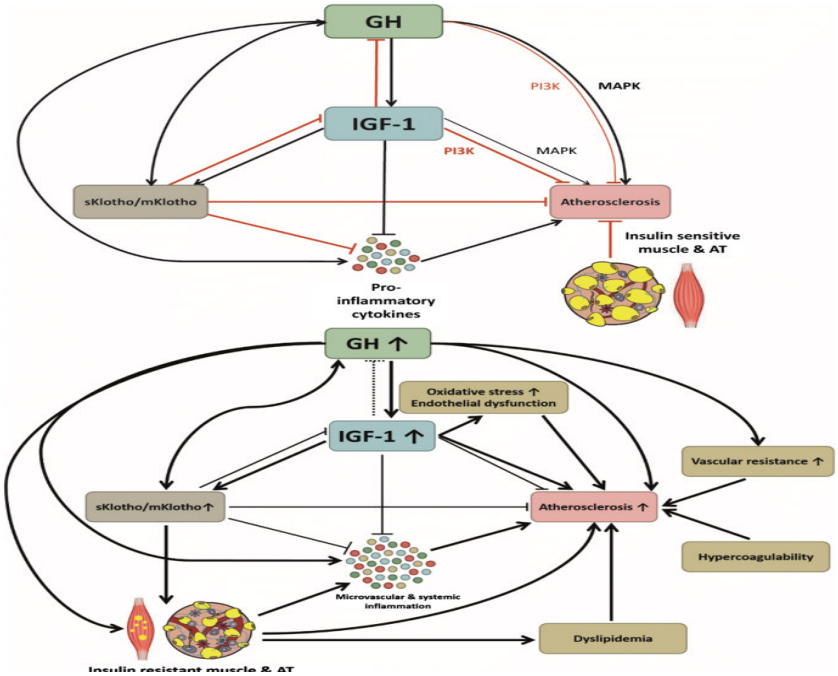

Figure1 : Pathophysiology of GH

The improvement of surgical procedures, radiotherapy instruments and the availability of pharmacological compounds acting on somatotrophic pituitary cells have greatly altered the approach to this condition, which is an exemplary paradigm for studying the pathophysiology of GH and IGF-I behavior on nearly all body organs and systems.(Figure 1)

ETIOLOGY

Pituitary Tumor: In more than 95% of cases, an overgrowth hormone is caused by a pituitary tumor, usually a benign pituitary gland microadenoma.

Non-Pituitary Tumor: In a few examples, cancers of the adrenals, lungs, and pancreas are involved. Growth hormone or growth hormone-releasing hormone (GH-RH) is secreted by these tumors. Higher levels of growth hormone enable the liver to develop insulin-like growth factor-11 (IGF-1). The excessive growth of body tissues is induced by elevated IGF-1 levels. (7)

Epidemiology

With about 116.9 new cases per million per year, Acromegaly has a worldwide prevalence of around 4,600 per million people. Mean age for men at 40 and 45 for women at diagnosis. Acromegaly typically occurs in the third decade of life.(8)

PATHOPHYSIOLOGY

Acromegaly is diagnosed with pituitary microadenoma in about 95 percent of instances, whereas the remaining 5 percent are from non-pituitary ectopic growth hormone or GH-RH causes. The release of IGF-1 from the liver is a typical result of an excessive increase in growth hormones. In the multisystemic manifestation of acromegaly, the effects of IGF-1 on body tissues results. Often referred to as somatomedin C, IGF-1 is encoded by the IGF-1 gene onSince the fusion of the growth plates, the pathological influence of IGF-1 culminated in the acral growth spurts manifesting as large hands and feet and a pronounced jaw and forehead. The consequence of elevated IGF-1 appears before the termination of chromosome 12q23.2. It is clearly distinct from the linear rise in size that occurs in gigantism. [9] Acromegaly leads to elevated IGF-1 that affects the following pathways of metabolism:

Insulin competencies for the insulin receptor, resulting in relative insulin tolerance that could be responsible for the co-existing diabetes mellitus in 10 to 20% of acromegaly patients.Products of general somatic hypertrophy, such as macroglossia, acromegalic heart, large kidneys and bulky skeletal muscles, are seen as swollen body organs.Somatic development through the nearly ubiquitous insulin-like growth factor-1 receptor (IGF-1R) binding. IGF-1R is a tyrosine kinase receptor that results in phosphorylation and activation of many intracellular signaling pathways, one of which is the activation of the AKT pathway that results in the growth and proliferation of somatic cells.

SYMPTOMS

Doughy-feeling skin over the face and extremities ,Thick and hard nails**(Figure 2)**, Deepening of creases on the forehead and nasolabial folds, Noticeably large poresThick and edematous eyelids, Enlargement of the lower lip and nose (the nose takes on a triangular configuration), Wide spacing of the teeth and prognathism , Cutis verticisgyrata (ie, furrows resembling gyri of the scalp) , Small sessile and pedunculated fibromas (ie, skin tags), Hypertrichosis, Oily skin (acne is not common), Hyperpigmentation (40% of patients), Acanthosis nigricans (a small percentage of patients) , Excessive eccrine and apocrine sweating, Breast tissue becoming atrophic; galactorrhea, High blood pressure,

Mitral valvular regurgitation, Mild hirsutism (in women) (10).

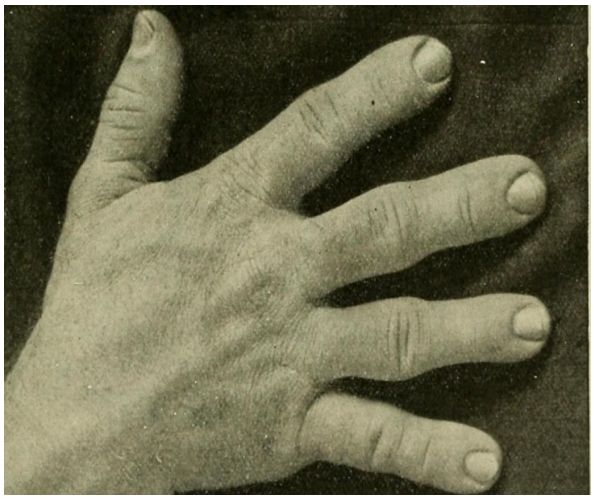

Figure2 :Hard nails

TREATMENT/MANAGEMENT

Treatment Guidelines

In most patients, pituitary gland reduction may be the primary therapy.
After 12-16 weeks after treatment, an ultrasound scan should be performed to assess if there is any residual tumor left.
Follow-up to ensure that there are no signs and symptoms of hypopituitarism in the patient
Health treatment is provided for residual illness patients. (11)

Surgical Treatment

Endonasal Transsphenoidal Surgery :A minimally invasive procedure using an endoscope to extract the pituitary adenoma through a minor incision in the nose or upper lip will promptly alleviate the effects of pressure as well as reduce levels of elevated growth hormone (GH). Compared to standard transsphenoid surgery, healing time is shorter.
Transnasal Transsphenoidal Microscopic Surgery: It is a conventional pituitary surgery that uses a microscope to image the tumor directly. For an endonasal procedure similar to transnasal transsphenoidal microscopic surgery, recent retrospective findings have demonstrated gross complete resection and IGF-1 resolution.

Radiotherapy

Conventional radiotherapy: Often offered as an adjunct to surgery, either to avoid relapse or when surgery is insufficient to bring about an adequate reduction in GH amounts. It is associated with the risk of neighboring brain tissues being irradiated.
Stereotactic radiosurgery: It is precision radiotherapy, aiming radiation to the tumor at elevated doses, and minimizing the damage of healthy brain tissues nearby.(12)
Medical Therapy: Either as an adjunct to surgery or when surgery is not desirable.
Somatostatin analogs (octreotide, Lanreotide): These function on the somatostatin receptor to allow growth hormone secretion to be inhibited. It is usually administered as an intramuscular injection once a month. It may also be used prior to surgery to shrink large pituitary adenomas.(Figure 3)
Dopamine receptor agonists (cabergoline, bromocriptine): These function on receptors of D2 and are not as effective as the analogues of Somatostatin. They are used as adjuncts sometimes. In minimizing GH levels, cabergoline is more potent than bromocriptine.
GH- Receptor antagonist (Pegvisomant): This novel drug inhibits the receptor growth hormone, reducing IGF-1 levels while being unchanged by GH levels.(13)

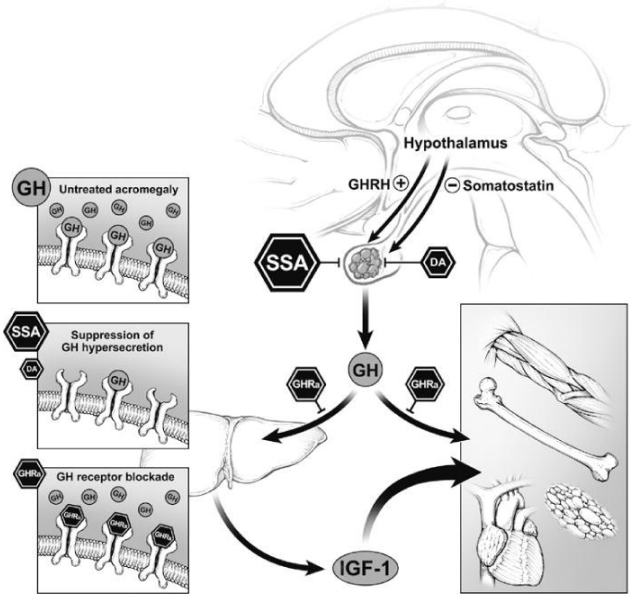

Figure3 :Somatostatinanalogs

CONCLUSION

A crucial component for encouraging medication completion and better treatment performance in acromegaly is the option of treatment that minimizes patient pressures and maximizes benefits. Identification of early diseases and timely care reduce comorbidities and promise the best effects and can cover the overall therapy bill.Developments in precision medicine and novel treatment modalities which require comprehensive histopathology in centers that conduct greater quantities of resections of the pituitary tumor; however, it becomes difficult to devise a treatment strategy to facilitate commitment when long-term or lifetime treatment is indicated. Setting concrete, realistic quality of life expectations for the patient will provide a framework for the implementation of an attainable recovery program.Promoting adherence allows the patient, in the light of their particular personal aspirations and life condition, to have a detailed knowledge of the illness, its effects and progression over the life cycle. When they should be self-administered, people are more likely to stick to a medication regimen, view treatment as a way of preventing negative outcomes, or perceive positive benefits with less therapy side effects. New therapies based on longer dosing intervals can enhance the quality of life, particularly if delivered orally, and can also help minimize patient and provider pressures associated with long-term therapies. Follow-up is important but invasive for patient supervision and therapy changes and can require versatility or a paradigm change from typical clinic visits.The development of a viable recovery service involves the coordination of the treating doctor, nurse and patient, and the early intervention of local and primary health care teams of the patient. To retain disease management, complex changes can be suggested over the life of a patient with acromegaly.(14)

REFERENCES

1. Verga A1864A singular case of *prosopectasia*. In: Bernasconi G, ed.*Rendiconti del RealeIstituto Lombardo di Scienze e Lettere*1:110–118.
2. Lane JM, LawsER2001 History of acromegaly. In: WassJ, ed. Handbook of acromegaly. Bristol, UK: Bioscientifica; 1–16
3. MarieP1886Sur deux casd'acromegalie.*Rev Med*6:297–299.
4. Cushing H 1909 Partial hypophysectomy for acromegaly.*AnnSurg* 50:1002–1017
5. Melmed S 1990 Acromegaly.*NEngl J Med* 322:966–977
6. Colao A, LombardiG 1998 Growth hormone and prolactin excess.*Lancet* 352:14551461
7. Matyjaszek-MatuszekB,ObelE,LewickiM,Kowalczyk-BołtućJ,Smoleń A, Prevalence of neoplasms in patients with acromegaly - the need for a national registry. Annals of agricultural and environmental medicine
8. Sharma AN,TanM,AmsterdamEA,Singh GD, Acromegalic cardiomyopathy: Epidemiology, diagnosis, and management. Clinical cardiology.
9. Buchman M, Bell S, Kopchick JJ, Growth Hormone Discovery and Structure. Pediatric endocrinology reviews
10. Al-Bedaia M, Al-Khenaizan AS. Acromegaly presenting as cutis verticisgyrata. *Int J Dermatol*.
11. Granada ML, Biochemical following-up of treated acromegaly. Limitations of the current determinations of IGF-1 and perspective. Minerva endocrinologica.
12. LeonartLP,BorbaHHL,FerreiraVL,RiverosBS,Pontarolo R, Cost-effectiveness of acromegaly treatments: a systematic review. Pituitary.

13. Ahmad MM,BuharyBM,AlMousawiF,AlshahraniF,BremaI,AlDahmaniKM,BeshyahSA,AlMalki MH, Management of acromegaly: an exploratory survey of physicians from the Middle East and North Africa. Hormones (Athens, Greece).
14. Chieffo C, Cook D, Xiang Q, Frohman LA. Efficacy and safety of an octreotide implant in the treatment of patients with acromegaly. *J. Clin. Endocrinol. Metab*.