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Case Report

Acromegaly - A case report

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Abstract

Acromegaly is a disorder characterized by Growth Hor-mone (GH) hypersecretion, multisystem-associated morbidities, and increased mortality. Growth hormone is secreted by anterior part of the pituitary gland and it influences the growth of bone and soft tissue. Hypersecretion or hyposecretion of this hormone has a marked influence on the normal development of an individual. It also has marked influence on the development of oro-facial features, including the alignment of teeth, and mandibular prognathism, which compromises the aesthetics of an individual. Hence dental professionals have a role in diagnosing this disorder. We present here, a case report of Acromegaly.

Key words: Growth hormone, Acromegaly, Pituitary gland, Prognathism.

Introduction

The word acromegaly comes from the Greek words acro for "e*xtremities*" and megaly for "*enlargement*". Acromegaly is a hormonal disorder that results from excessive secretion of growth hormone (GH) in the body[1]. Growth hormone is secreted by anterior part of the pituitary gland[2]. The prevalence is about 7 cases per 100,000, with an annual incidence of 0.3 cases per 100,000 [3].

In acromegaly, the pituitary gland produces excessive amounts of GH. In more than 95 percent of people with acromegaly, a benign tumour of the pituitary gland, called an adenoma, produces excess GH. These adenomas are diagnosed in middle age and show an equal predilection for both the genders. The most serious health consequences of acromegaly are type 2 diabetes, high blood pressure, increased risk of cardiovascular disease, and arthritis. Gradually, bone changes alter the patient's orofacial features which are manifested as thickening of the eye brow, elongation of lower jaw, enlargement of nasal bone, and spacing between teeth[3].

Case History

A 54 yrs. male patient visited the outpatient department with the complaint of difficulty in chewing, and protruding lower jaw, since 1 year. The changes were insidious in onset, progressed slowly and were associated with gradual change in voice, growth of extremities, general tiredness and excessive sweating. These were associated with coarsening of facial features which compromised his aesthetics. There was no associated pain in the jaw or joints.

Medical/surgical history revealed that he had undergone transnasal transphenoidal surgery for pituitary tumour 1 ½ years back which was then diagnosed as macroadenoma. He had been under medication following surgery for five to ten days. (Tab..Eltroxin-0.1mg (Levothyroxine sodium) once daily, Tab. Wysolone -5mg (Prednisolone) once daily, Tab oflox-200mg once daily(Ofloxacin), Inj. Humalong R 20units(Insulin), Inj. Lantus 8 units (Insulin). Tab. Piozone -15mg (Pioglitazone), Cap. Becosules (B-complex) once daily.) He was also diagnosed with hypertension, hyperglycemia, and hyperthyroidism. Extra oral clinical examination revealed facial asymmetry, lip incompetence, mandibular

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prognathism, and retrusion of maxilla, proptosis, prominent nose and supraorbital ridges. Skin over the forehead appeared thickened. Fingers and toes appeared large and broad. Intraoral examination revealed, macroglossia, Angle's class-III malocclusion with anterior open bite, interdental spacing in lower anterior teeth(41, 42, 43,31,32,33,) multiple missing teeth,(16,18,35,36,37,46,48) carious teeth(45,) and poor oral hygiene. A diagnosis of Angle's class-III malocclusion with anterior open bite associated with acromegaly was considered 9 as shown in Fig 1. The patient was subjected to radiographic examination which included lateral Cephalograph, orthopantomograph, skull view, and hand and wrist view. Lateral Ceph revealed mandibular prognathism, marked sella turcica enlargement with steepening of angle of mandible. OPG showed hypercemoentosis (36, 37, and 46, 47) and multiple missing teeth. PA showed thickening of the border of skull, and hand wrist showed tufting of fingers as shown in Fig 2.

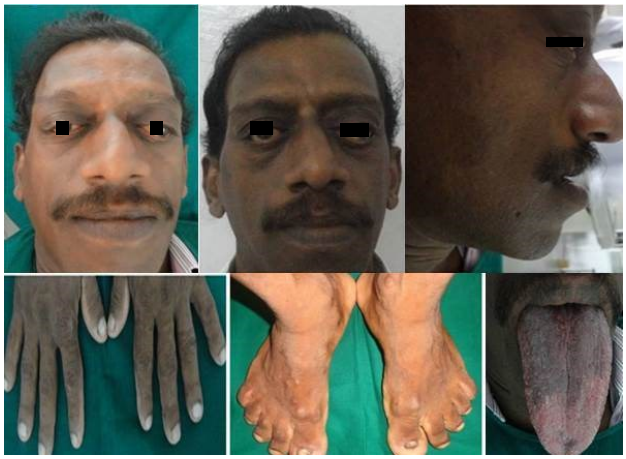

Fig:1 – Showing signs and symptoms of Acromegaly.

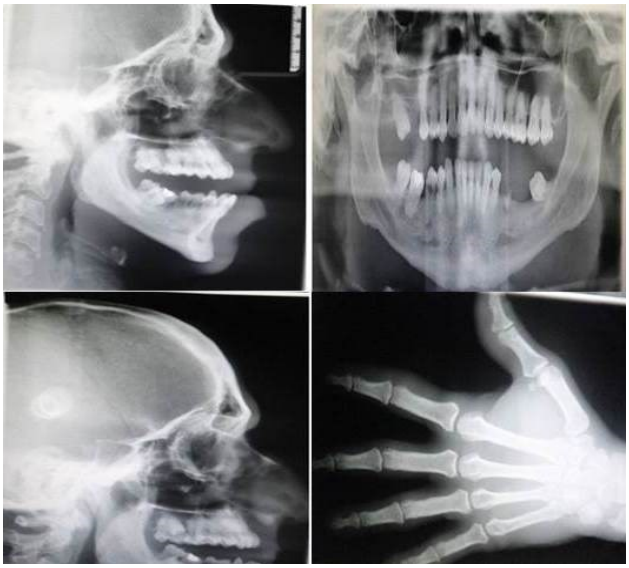

Fig:2 – Orthopantomograph, skull view in Acromegaly

The haematological examination revealed that random blood glucose was 136 mg % and the high blood pressure. Considering the patient's uncontrolled diabetes and hypertension, dental treatment was deferred and he was referred to an endocrinologist for further evaluation[3].

Discussion

Acromegaly is an acidophilic tumor that occurs after adolescence that is, after the epiphyses of the long bones have fused with the shafts, in which the person cannot grow taller, but the bones can become thicker and the soft tissues continue to grow[4]. This is a multisystem disorder due to excessive secretion of growth hormone by the somatotropic cell in the anterior part of pituitary gland [5]. The pituitary gland is a small, bean-shaped structure that lies at the base of the brain within the confines of the sella turcica and has a central role in the regulation of most of the other endocrine glands.

Pituitary adenomas are the most common cause of pituitary hormone hyper secretion in adults. They account for approximately 15% of all intracranial neoplasms[6]. It is most often diagnosed in middle-aged adults as acromegaly and due to insidious onset and slow progression; it is often diagnosed four to more than ten years after its onset [7]. The incidence of acromegaly is approximately 5 cases per million per year and the prevalence is 60 cases per million. Over 90% of patients with acromegaly have a benign monoclonal pituitary adenoma, which are not surrounded by hyperplastic tissue. Densely granulated adenomas grow slowly and occur in patients over the age of 50. Sparsely granulated adenomas grow faster and occur in younger patients. In more than 95% of patients, the aetiology is pituitary somatotrophinoma. Somatotroph adenomas are monoclonal in origin and develop from genetic changes[8].

All the major anterior pituitary hormones, except for growth hormone, exert their principal effects by stimulating target glands. Growth hormone exerts its effects directly on all or almost all tissues of the body [4]. When their physiological level is altered due to pathological conditions, it can lead to a clinical syndrome. Pituitary adenoma is a benign neoplasm that arises from one of the five anterior pituitary cell types. The tumors arising from somatotropic cells results in hypersecretion of the growth hormone which can lead to acromegaly in adults. G-protein is a stimulatory protein that has a pivotal role in signal transduction in several endocrine organs, including the pituitary. The α-subunit of G_s ($G_s\alpha$) is encoded by the GNAS1 gene, located on chromosome 20q13. A mutation in the α-subunit of the stimulatory proteins ($G_s\alpha$) that interferes with its intrinsic GTPases activity therefore

results in constitutive activation of $G_s\alpha$, persistent generation of cAMP, and unchecked cellular proliferation state[9]. The clinical manifestation of this pathophysiology results in its effect mainly on structures like bone and soft tissue. There are two principal mechanisms of bone growth. First, in response to growth hormone stimulation, the long bones grow in length at the epiphyseal cartilages, where the epiphyses at the ends of the bone are separated from the shaft. Second, osteoblasts in the bone periosteum and in some bone cavities deposit new bone on the surfaces of older bone. Simultaneously, osteoclasts in the bone remove old bone. When the rate of deposition is greater than that of resorption, the thickness of the bone increases. These changes are manifested as mandibular prognathism, nasal bone prominence, frontal bossing and increase in vertical height [7]. Bone mineral density is also altered in acromegaly. Cortical bone thickness (as measured by the metacarpal index and histomorphometric parameters) and its porosity is decreased. The normal trabeculaer pattern could be decreased or increased. The upper part of the body shows dorsal kyphosis and compensatory lumbar hyperlordosis. Acromegalic patients have progressive osteophytosis. The excess of GH has a deleterious effect on the joints in these patients[10].

In our patient significant progressive mandibular prognathism was observed. It has been postulated that post pubertal overproduction of GH leads to highly disproportionate growth of the jaws and facial bones, which is mainly as a result of periosteal bone apposition due to reactivation of the subcondylar zones. This result in enlargement of the ascending ramus and prominence of the mandible compared to maxilla, which is the most noticeable profile characteristic of an acromegalic patients[11].

As a sequlae to this mandibular growth, macroglossia occurs which can cause flaring and spacing of teeth. A study conducted showed that**,** 50% of the subjects had increase in tongue size, the histology of which showed enlargement of muscle fibers especially anteriorly in acromegaly. Along with this, the soft palate also shows enlargement which can lead to sleep apnea. Sleep apnea is manifested as snoring and daytime sleepiness in acromegaly. The impact of respiratory complication is high in acromegaly. The impaired respiratory functions in these patients occur due to factors involving upper airway and bone musculature of chest and lung elasticity. Using Polysomnography, a study conducted by Attal and Chanson found an average rate of 69% for obstructive sleep apnoea in patients with active disease in prospective and retrospective studies[12]. Types of apnoea in acromegaly were either central or obstructive[13, 14] .

In our study, the patient also reported with sleep apnea which may be attributed to the excessive soft tissue enlargement of posterior palate. Growth is most conspicuous in soft tissues, skin, and viscera and in the bones of the face, hands, and feet. Skin thickening is due to glycosaminoglycan deposition and increased collagen production by connective tissue. A Study done by Gloria Lugo, Lara Pena, et al showed, that excess GH in humans is associated with increased activity of the epithelial sodium channel, which contributes to the volume expansion and soft tissue manifestations[15]. Pigmented skin tags are frequent and could be due to GH/IGF-I excess or arise as a consequence of insulin resistance and dyslipidaemia and are used as a marker for colonic polyps [7, 15].

The hands and feet were also enlarged with broad sausage-like fingers. Acromegaly also affects the different organs in the system like the liver which secretes several small proteins called somatomedins. Growth hormone excess is also associated with a number of other disturbances, including abnormal glucose tolerance and diabetes mellitus, generalized muscle weakness, hypertension, arthritis, osteoporosis, and congestive heart failure [9, 7].

Radiographic features are striking, with the enlargement of sella turcica being the important feature in acromegaly patient. The other features are, prominent supraorbital ridges, hypercemoentosis, large pulp chambers, and increase in size of mandible, interdental spacing, hand and wrist, shows tufting of fingers. Patients with acromegaly usually exhibit enlargement of all parts of the neuro cranium and orofacial bones except the maxilla[5].

Significant progress have made in the management of acromegaly although there are several of limitations. Treatment modalities include medical, surgery and radiotherapy. Medical therapies for management of acromegaly include dopaminergic agonists, somatisation analogues, and growth hormone receptor antagonists and surgical therapy includes transsphenoidal approach and transnasal endoscopic approach frontotemporalcraniotomy [3]. Radiotherapy includes gamma knife. Remission of the tumour after a period of time is to be evaluated which can be an important factor in giving a prognosis to the treatment. Soft tissue management is less complicated because after normalizing the GH, soft tissue reverses back to normal, whereas the osseous changes are not reversible and may need surgical intervention[5].

The recurrence rate following surgical correction can result due to continued release of GH and

varies between 20% and 38% in different studies. This view is also supported by Josef Marek and Martin Gosau1etal[16,17,11] who states that 1-2 % adenoma can recur. Our patient had an uncontrolled glucose level, a progressive mandibular lengthening, and persisting coarse facial features, all of which indicate a persisting hypersecretion of pituitary gland which needs to be further evaluated by an endocrinologist.

The prognosis is varying in different literature. An article by Kinnman J shows a 6% recurrence [18], even though, new advances in stereotactic radiotherapy, gamma-knife radiotherapy, and novel therapeutic agents have improved pituitary tumor management[6] and despite of all the measures taken to prevent the hyper secretion of GH , a minute amount can be traced in blood after a prolong period of time, can lead to further systemic manifestation of the disease . A few reports suggest that patient with acromegaly have an increased mortality rate compared to that of general population due to uncontrolled diabetes mellitus , hypertension which can collectively lead to ventricular dysfunction and cardiac failure[19-22].

Conclusion

A case of acromegaly has been reported with its clinical and radiographic features. Acromegaly is an insidious disease with characteristic orofacial changes. Management of this disorder requires a multidisciplinary approach with a close cooperation between the various medical and dental specialities. It is important for the dental professional to familiarise with the clinical manifestations which can aid in early detection and adequate treatment and hence reduce the mortality and morbidity of the disease.

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