Acromegaly: A Case Report
Giriraja Kanakapura, Pavitra ChandraShekar, Vishnudas Prabhu

Abstract
Acromegaly is a rare condition characterized by excess production of growth hormone after the closure of epiphyseal plates. We present a case of 50 year old female patient with a diabetic ulcer on the left foot and with features of bony over growth, soft tissue involvement, facial features and visceromegaly which suggest acromegaly.

Key Words: Acromegaly; Human Growth Hormone; Bone Diseases; Endocrine System Diseases; Pituitary Diseases; Hyperpluitarism; Macroglossia.

Introduction
Acromegaly is a chronic progressive disorder due to growth hormone (GH) hypersecretion and elevated levels of insulin-like growth factor-1 (IGF-1). The overall incidence of acromegaly is estimated to be 3 to 5 new cases per million.1,2 The disorder has been recognized since ancient times, the pathology of pituitary “prospectsasia” was first described by Andrea Verga in 1864 and the clinical features of acromegaly was discussed by Pierre Marie in 1886. The term Acromegaly is derived from Greek word ‘akras’ meaning extremities and ‘megas’ meaning big. With an estimated prevalence of 40-70 cases per million and an incidence of 3-5 new cases per million 2, it ranks as a rare disease. Excess GH secretion leads to disproportionate skeletal growth, coarse facial features, soft tissue swelling as well as metabolic disorders and a tendency for malignancies that inexorably result in increased mortality and morbidity rates if the disease is left untreated.3,4 This case report will describe acromegalic patient with diabetic ulcer and will discuss about clinical feature, diagnosis, and treatment aspect.

Case Report
A 50 year old female patient reported with a complaint of an ulcer over left 3rd toe since one week. The ulcer was oval in shape, with the edges inflamed and oedematous, with no discharge and not associated with pain. Five years before, the patient had been diagnosed diabetes mellitus type 2 and hypertension had been prescribed metformin and insulin for glucose control and nefidipine, but it was not regularly used. She also felt weakness, increased appetite and thirst.

She mentioned of frequent generalized headaches, blurring of vision, weight gain, menstrual irregularities and excessive hair growth on the body. On physical examination patient was well built stature, prominent frontal bossing thickened lips, large nose and mandibular enlargement with prognathism (Fig 1) horse voice features and of broadened hands (Fig 2) and feet, thick palms and thick heel pads and fingers widened. The symptoms was firstly noted at about seven years ago when the patient reported increasing of finger ring size. She also felt the changes of mild hair growth and oiliness on her face. On intra oral examination it was observed the patient had an overbite, moderately enlarged tongue (Fig 3), spacing between anterior teeth and gingival recession. Upper and lower anterior teeth exhibited grade 3 mobility. Caries upper right and left molars and root stumps of upper right second molar. On clinical examination the patient appeared weak. She was 174 cm tall and weighed 90 kgs. On initial examination, her blood pressure was 140/100 mmHg, heart rate was 88 bpm and respiratory rate was 24/minutes. Patient was afebrile.

Laboratory studies revealed a blood glucose level of 620 mg/dL with positive ketone bodies. Hormonal profile showed increment of growth hormone level 2 hour after a standard 78 grams oral glucose load and of IGF-1 level with low level of FSH and LH. CT Chest and CT of abdomen was done to rule out bronchial carcinoid, pancreatic islet cell
tumour, small cell lung carcinoma, adrenal adenoma, which are the possible causes increase GH secretion. Other marked abnormalities were high cholesterol and triglyceride level, 320 mg/dl and 690 mg/dl consecutively. Radiographic examination of foot exhibited mineralization of ligamentous insertion (Fig 4).

Intraoral periapical radiograph of the upper right second molar shows normal radiodensity of enamel, dentin and pulp. Bulkier roots of all molars suggested of hypercementosis with a continuous lamina dura. Interdental horizontal alveolar bone loss was seen extending 5 mm below the cemento-enamel junction involving the furcation area. Lateral cephalogram showed enlarged frontal sinus, steep mandibular angle and class III profile with prognathic mandible (Fig 5). Electrocardiography and chest x-ray examination revealed normal result. Based on medical history, clinical manifestation, and initial workup, patient was assessed as diabetic ketosis, acromegaly, obese and dyslipidemia.

For further evaluation we planned to consult department of ophthalmology, pulmonology, dentistry, dermatology, and cardiology consultation. The dermatological opinion was thickening and oiliness of face, acanthosis nigricans was seen along with mild hirsutism. The cardiological opinion on 2D echo showed asymmetrical septal hypertrophy and cardiomyopathy. The pulmonology opinion on pulmonary function showed obstructive lung disease. The ophthalmological examination revealed exophthalmos without any field defects.

The dental opinion was that the patient had to undergo prosthetic treatment for missing teeth, endodontic treatment for the caries teeth and orthodontic treatment for malocclusion with corrective orthognathic surgery for large mandible. The patient was treated with intravenous insulin to control blood glucose level, metformin 500 mg twice daily, gemfibrozil 300 mg twice daily. Surgical removal of the growth hormone secreting adenoma is the initial treatment of choice, but because our patient declined for surgery and she could not afford somatostatin analogy’s, dopamine agonist bromocriptine was started for twice daily with incremental dose.

Figure 1: Patient of acromegaly with wide nasal bridge, large lips, broad nose, frontal bossing, protruding jaw (a), enlargement of hand, compared with healthy subject (b) and macroglossia (c).

Figure 2: Radiograph showing mineralization of ligamentous insertion (a) and enlarged frontal sinus, steep mandibular angle and Class III prognathism (b).
Discussion
Acromegaly is a rare chronic endocrine disorder caused by an increase in secretion of growth hormone by pituitary tumors and rarely by extra pituitary disorders. The disease is characterized by increase in levels of GH and IGF-I. Benda 1900 established the relation of pituitary tumor which comprised of hyper functioning adenohypophyseal eosinophilic cells to acromegaly. The clinicopathological features of acromegaly were documented by Cushing, Davidoff, and Bailey. The etiology of acromegaly can be classified into three types. Primary excess growth hormone secretion, Extra pituitary tumor and excess Growth Hormone Releasing Hormone secretion.1,3,4 (Table 1) GH is synthesized and has pulsatile secretion from the somatotrophic cells of the anterior lobe of the pituitary gland, circulating GH stimulates synthesis and secretion of insulin-like growth factor 1 (IGF-1) from the liver. In more than 90% of the patients the etiology is pituitary tumors. These tumors mimic stimulation of adenylyl cyclase by GHRH receptor activation causing autonomous GH secretion.3,4

Patients with acromegaly usually present with symptoms relating to dental, orthopedic, cardiac or rheumatologic disorders. The diagnosis of acromegaly is based on clinical, radiological, and biochemical findings. Many of the classic clinical features present in acromegaly patient as stated in the literature are found in this case. The patient complained of weakness, increased appetite and thirst, oily skin, dental problems and menstrual irregularities. At physical examination the patient had facial changes including large lips and nose, wide nasal bridge, protruding jaw, and frontal skull bossing. Examination of the extremities found enlargement of hands and foot. The patient nutritional status is obese.

Characteristic features of acromegaly as stated in the literature are large fleshy lips and nose, spade-like hands, frontal skull bossing, and cranial ridges. Enlarged tongue, bones, salivary glands, thyroid, heart, liver, and spleen are the effects of generalized visceromegaly. Hepatosplenomegaly may be clinically apparent. Usually patients report of increase in size of the hat shoe or ring. The acral changes can lead to facial coarsening and skeletal disfigurement, especially if excess GH secretion begins prior to epiphyseal closure.5,6 These include mandibular overgrowth with prognathism, maxillary widening, teeth separation, jaw malocclusion, overbite, large nose, and coarse, oily skin with large pores. Prognathism, thick lips, macroglossia, and hypertrophied nasal structures can obstruct airways. Exophthalmos may be present, but it may be masked by frontal bossing. Sonorous voice deepening occurs in association with laryngeal hypertrophy and enlarged paranasal sinuses.6,7

Table 1: Etiology of Acromegaly (Adapted from Melmed S. Acromegaly. N Engl J Med 1990;322:966-977)1

<table>
<thead>
<tr>
<th>Primary excess growth hormone secretion</th>
<th>Extra pituitary tumor</th>
<th>GHRH secretion</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pituitary Adenoma</td>
<td>Pancreatic islet cell tumor</td>
<td>Central</td>
</tr>
<tr>
<td>• Densely granulated GH cell adenoma</td>
<td>Lymphoma</td>
<td>Hypothalamic tumor</td>
</tr>
<tr>
<td>• Sparsely granulated adenoma</td>
<td></td>
<td>Peripheral</td>
</tr>
<tr>
<td>• Mixed GH cell and PRL cell adenoma</td>
<td></td>
<td>Bronchial Carcinoid</td>
</tr>
<tr>
<td>• Mammosomatotroph cell</td>
<td></td>
<td>Pancreatic islet cell tumor</td>
</tr>
<tr>
<td>• Acidophil stem cell</td>
<td></td>
<td>Small cell lung cancer</td>
</tr>
<tr>
<td>• Plurihormonal silent somatotroph</td>
<td></td>
<td>Adrenal adenoma</td>
</tr>
</tbody>
</table>

Pituitary Carcinoma

Ectopic

Familial

• Multi-endocrine neoplasia type 1
• Mu-cune Albright syndrome
• Familial Acromegaly
• Carneys syndrome

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Arthropathy is frequently seen in patients, they exhibit features such as joint swelling, hypermobility and cartilaginous thickening, and these problems often persist after treatment. Local periartricular fibrous tissue thickening can cause joint stiffening,
deformities, and nerve entrapment. Knees, hips, shoulders, lumbosacral joints, elbows, and ankles are affected as mono or polyarticular arthritis. Spinal involvement includes osteophytosis, disc space widening, and increased antero-posterior vertebral length, which can result in dorsal kyphosis. Neural enlargement and wrist tissue swelling can lead to carpal tunnel syndrome in up to half of all patients.\(^5\)\(^6\)\(^7\) Chondrocyte proliferation with increased joint space occurs early, and ulcerations and fissures of weight-bearing cartilage areas are often accompanied by new bone formation. Debilitating osteoarthritis can result in bone remodeling, osteophyte formation, subchondral cysts, narrowed joint spaces, and lax periarticular ligaments. Osteophytes commonly occur at the phalangeal tufts and over the anterior aspects of spinal vertebrae. Ligaments can ossify, and periarticular calcium pyrophosphate deposition occurs.\(^8\)\(^-\)\(^11\)

Hyperhidrosis and malodorous oily skin are common early signs in patients. Facial wrinkles, nasolabial folds, and heel pads thicken, and body hair may become coarsened, attributed to glycosaminoglycan deposition and increased connective tissue collagen production. Skin tags are common and may be markers for the adenomatous colonic polyps. Raynaud's phenomenon is reported in up to one third of patients.\(^1\)\(^2\) (Table 2).

<table>
<thead>
<tr>
<th>Local Tumor Effects</th>
<th>Somatic Effects</th>
<th>Visceromegaly</th>
<th>Endocrine And Metabolic Effects</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cardiovascular, Asymmetric septal hypertrophy, Cardiomyopathy, Congestive heart failure, Hypertension, Left-ventricular hypertrophy.</td>
<td>Electrolytes, Increased aldosterone, Low renin.</td>
<td></td>
<td></td>
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<tr>
<td>Colon</td>
<td>Lipids, Hypertriglyceridemia</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Polyps</td>
<td>Minerals, Hypercalciuria, increased 1,25(OH)2D3 Urinary hydroxyproline.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Musculoskeletal, Acroparesthesia, Arthralgias, Arthritis, Carpal tunnel syndrome, Gigantism, Hypertrophy of frontal bones, Jaw malocclusion, Prognathism, Proximal myopathy.</td>
<td>Multiple endocrine neoplasia type 1, Hyperparathyroidism, Pancreatic islet cell tumors.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pulmonary, Narcolepsy, Sleep apnea—central and obstructive, Sleep disturbances.</td>
<td>Reproduction, Decreased libido, impotence, low sex hormone—binding globulin, Galactorrhea, Menstrual abnormalities</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Skin, Hyperhidrosis, Oiliness, Skin tags</td>
<td>Thyroid, Goiter, Low thyroxine-binding globulin.</td>
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</table>

Complications commonly manifested in acromegaly are symptomatic cardiac disease which is a major cause of morbidity and mortality. Hypertension is present in about 50% of patients with active acromegaly, and half of these have evidence of left ventricular dysfunction. Left ventricular hypertrophy is also observed in about half of normotensive patients with acromegaly. Cardiovascular disease accounts for about 60% of deaths in patients with acromegaly. Irregular laryngeal mucosa, cartilage hypertrophy, tracheal calcification, and cricoarytenoid joint arthropathy lead to unilateral or bilateral vocal cord fixation or laryngeal stenosis with voice changes. Obstructive sleep apnea, characterized by excessive daytime sleepiness with at least five episodes of apnea per hour of sleep causes daytime somnolence, especially in men with acromegaly, who also might have a ventilation-perfusion defect with hypoxemia. Sleep apnea may also be central in origin and associated with higher GH and IGF-I levels.\textsuperscript{5,7,13}

Cardiovascular disease, respiratory disorders, diabetes, and malignancy account for enhanced mortality in acromegaly. Diabetes mellitus, occurring in 20% of patients, was associated with 2.5 times the predicted mortality, and hypertension was present in about half of all patients. The most significant mortality determinants are GH levels and the presence of coexisting cardiac disease. Moreover, control of GH levels less than 2.5 μg/L after surgery or medical treatments, significantly reduces morbidity and mortality.\textsuperscript{13,15}

There are three goals of treatment of acromegaly, they are control hypersecretion of GH, decrease morbidity/mortality related to hypersecretion and reduce mass effects of tumor. Surgical removal of tumor is usually initial therapy. The other treatment options are radiotherapy, medical, Radiotherapy, Medical therapy, Dopamine agonists, Somatostatin analogues, GH receptor antagonists.\textsuperscript{16}

**Conclusion**

This report describes a rare case of acromegalic patient with diabetic foot ulcer. This patient had classical acromegalic appearance, that has been proven biochemically and radiologically. The patient also had uncontrolled diabetes mellitus. Blood glucose control in this patient requires high dose of insulin. In conclusion, careful evaluation, diagnosis and follow-up appears to be essential in the management of patients with acromegaly.

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**Acknowledgement**

We would like to thank all the staff members of the Oral & Maxillofacial Pathology department for their support & cooperation.

**References**


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Source of Support: Nil, Conflict of Interest: None Declared.

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