

Acromegaly: Oral Diagnostician's Role in Diagnosis: A Case Report

B S Mahesh¹, S Padmashree², Hima John³, J Rema⁴

¹Senior Lecturer, Department of Oral Medicine and Radiology, Vydehi Institute of Dental Sciences, Bengaluru, Karnataka, India, ²Professor and Head, Department of Oral Medicine and Radiology, Vydehi Institute of Dental Sciences, Bengaluru, Karnataka, India, ³Senior Lecturer, Department of Oral Medicine and Radiology, Anoor Dental College, Ernaulam, Kerala, India, ⁴Professor, Department of Oral Medicine and Radiology, Vydehi Institute of Dental Sciences, Bengaluru, Karnataka, India

Acromegaly is an acquired disorder related to overproduction of growth hormone (GH). The condition, though described more than 120 years ago, was only later found to be due to pituitary over secretion and adenomas. It is a rare condition with a tendency toward overgrowth of the mandible, maxillary widening, tooth separation, and skeletal malocclusion which makes its diagnosis important for us dentists. The majority of the cases in the past have been diagnosed by physicians and endocrinologists. Here, we present a case of a 38-year-old male patient who presented with the complaint of increase in the size of lips and forward movement of the jaws since 1 year. Clinical features, radiographic features, and arrival at the diagnosis of Acromegaly with the subsequent referral and treatment are discussed.

Keywords: Acromegaly, Growth hormone, Hypercementosis, Mandibular prognathism, Pituitary adenoma

INTRODUCTION

The term "Acromegaly" (acrogigantism) has its origin from the Greek words "akros" which means extremities and "mega" which means big.¹ The disorder has been cited in literature since ancient ages, but the pathology of pituitary gland that leads to this condition was the first described by an Italian anatomist, Andrea Verga, in 1864.²

Acromegaly being a rare disease has an annual incidence of 3-4 patients in a million.³ The chronic exposure to increased levels of growth hormone (GH) and insulin-like growth factor-1 (IGF-1) in Acromegaly leads to multisystem disorder that is associated with significant morbidity and increased mortality. In more than 95% of patients, pituitary somatotrophinoma is the causative factor.⁴

The resultant clinical presentations are characterized by increased skeletal growth, enlargement of soft tissues, and decreased life expectancy. The clinical manifestations may range from minimal physical changes to severe

disfiguring features. The early changes may go unnoticed by patients due to the inconspicuous nature of the disease. The more noticeable changes are those related to soft tissue enlargement and increased skeletal growth, especially in the head and neck region.⁵ Therefore, the patients, might report to us first with altered facial features. Hence, adequate knowledge about the signs and symptoms form the key to arrive at the diagnosis.

CASE REPORT

A 38-year-old male patient reported to the Department of Oral Medicine and Radiology with a chief complaint of increase in the size of lips and tongue since 1 year. He has also noticed increased spacing between the lower front teeth and also forward movement of the lower jaw since the past year. On evaluation of medical history, he gives a history of gradual decrease in eyesight and frequent episodes of headaches since past 1 year. No other relevant history elicited.

On general examination, it was noted that the patient had enlarged extremities and thickened soft tissues all over the body. The blood pressure was 136/90 mmHg and pulse rate: 76/min. The extremities (hands and feet) were bulbous, thickened and stubby (Figure 1). Enlarged nose and thickened lips were evident in the examination of head and neck (Figure 2). Mild prognathism of the mandible was also evident. Intraoral examination revealed moderately

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Corresponding Author:

Dr. B S Mahesh, Department of Oral Medicine and Radiology, Vydehi Institute of Dental Sciences, No. 82, EPIP Area, Whitefield, Bengaluru - 560 066, Karnataka, India. E-mail: drmaheshreddy1727@yahoo.com

enlarged tongue (Figure 3) and generalized gingival recession. Increased spacing was noted between the teeth. Based on the above features, a provisional diagnosis of Acromegaly was given. Paget's disease of the mandible and Gigantism was given as a differential diagnosis.



Figure 1: Fingers appear thickened and stubby



Figure 2: Enlarged lips, nose

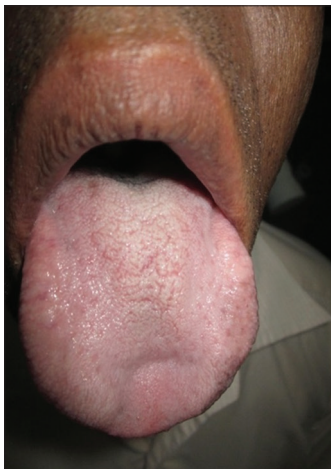


Figure 3: Enlarged tongue

Normal density of enamel, dentin, and pulp was noted in the intraoral periapical radiograph of the left lower molar. Hypercementosis noted in relation to 36. Root fragment was noted with respect to 37, horizontal bone loss of about 5 mm was noted suggestive of moderate periodontitis (Figure 4). Panoramic imaging revealed generalized moderate bone loss and root fragments with respect to 37 and 46.

True lateral skull view (Figure 5) showed enlarged sellaturcica, prognathic mandible with increased gonial angle and enlarged frontal sinus. Skull vault is thickened. Hand wrist radiograph shows the presence of osteophytes and mineralization of ligaments (Figure 6). Magnetic resonance imaging (MRI) showed a well-defined isointense lesion in sella with an extension measuring about 2.5 cm × 2 cm with a minimal parenchymal extension displacing pituitary stalk toward the right side and compression of optic chiasma is also noted (Figure 7a and b). MRI findings were suggestive of a pituitary macroadenoma.

The GH level was increased - 64 ng/ml (normal range in adults <2.5 ng/ml). Complete blood picture, random blood

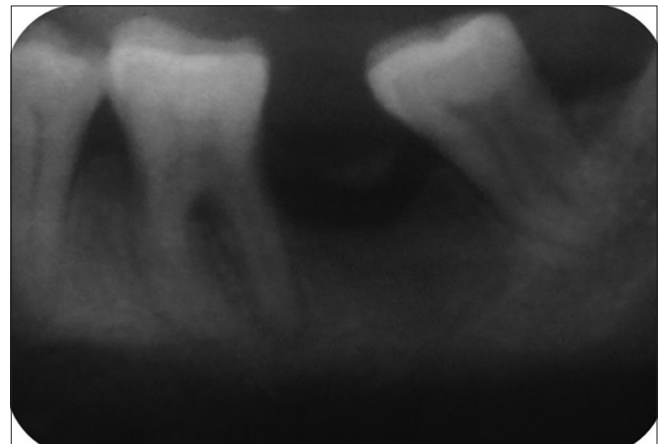


Figure 4: Hypercementosis irt 36



Figure 5: Enlarged sellaturcica, frontal sinus and prognathic mandible

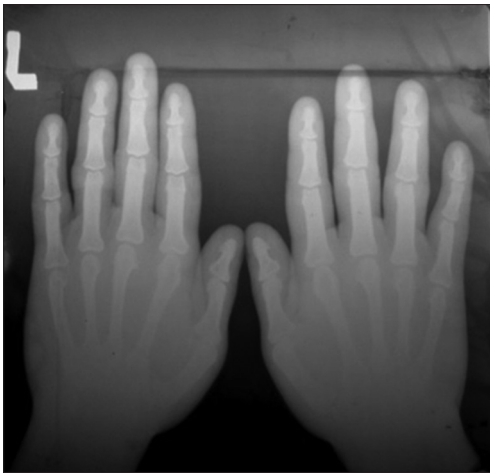


Figure 6: Hand wrist radiograph showing osteophytes and mineralization of ligamentous insertion

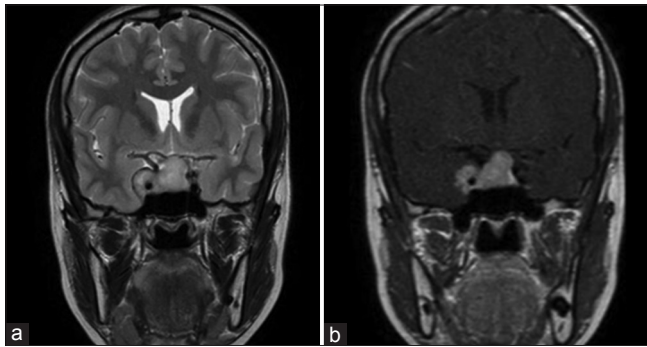


Figure 7: (a) Isointense lesion in the sella in the T1 weighted image, (b) focal mild hyperintensity on T2-weighted images

sugar, urine examination, blood urea, glucose tolerance test, lipid profile, liver function test, and thyroid profile were normal. Hence, a final diagnosis of pituitary macroadenoma leading to acromegaly was reached.

The patient was treated by transnasal transsphenoidal surgery. Excised tissue was sent for histopathological examination that revealed tumor tissue consisting of round or polygonal cells in a sinusoidal pattern, oval nuclei, eosinophilic granular cytoplasm with prominent nucleoli in some cells. No mitosis or necrosis was noted, thereby suggestive of pituitary adenoma. Post-operative computed tomography of brain was suggestive of a residual tumor. Medical management by octreotide acetate: 50 µg/day 3 times a day to 1500 µg/day was given. The radiation therapy was advised to treat the residual lesion and he received 90 grays of divided doses over a span of 28 cycles. After completion of radiotherapy, the GH level was evaluated again and was found to be 42 ng/ml and patient is still under follow-up.

DISCUSSION

Acromegaly is an acquired progressive disorder, characterized by disfigurement, mainly involving the face

and extremities, but also multi-organ involvement, that leads to systemic manifestations. The disease is manifested due to the excessive production of GH post epiphyseal closure. This excessive GH release is attributable to benign pituitary tumor (adenoma) in more than 90% of cases.¹

The cells within these tumors usually secrete GH alone or with prolactin. Adenomas capable of producing different types of hormones and metastatic pituitary carcinomas are rare.⁶ Symptoms associated with Acromegaly are of varied types like, such as sweating especially at night that is malodorous, acroparesthesia, headache, and joint pain. Gradual deepening of the voice is also observed as seen in this case. Glycosaminoglycan deposition and increased collagen production by connective tissue lead to skin thickening. The extremities (hands and feet) are bulbous, the fingers are spade-like and the soft tissue is thickened. These changes in the extremities are not only due to soft tissue deposition or increased growth of bone and cartilage but also due to deformation of bone.^{2,4,5}

Periosteal new bone formation leads to an increase in skeletal growth, especially at the level of the mandible in response to both GH and IGF-I. The facial features of Acromegaly patients are characteristic, and generally look alike in this respect: The nose is broadened and thickened, the malar bone becomes prominent, the lips are thick, and the facial lines are marked. Frontal bossing may be noted as the forehead and overlying skin become thickened. Jaw malocclusion is a common phenomenon in these patients as there is a tendency towards mandibular overgrowth with prognathism, maxillary widening, and teeth separation. Cortical bone thickens, and its porosity is decreased. The deep voice in acromegaly patients is due to hypertrophy of the sinuses, along with laryngeal hypertrophy. The spine is affected with bony deformation, with upper dorsal kyphosis and compensatory lumbar hyperlordosis.⁴ The differential diagnosis considered is Paget's disease in which the clinical picture may be alike, but the radiographic cotton wool appearance is typical in Paget's disease and laboratory investigation that would reveal elevated levels of serum alkaline phosphatase.

Skull radiographs typically show enlarged sellaturcica and enlargement of the paranasal sinuses (especially the frontal sinus). The angle between the ramus and body of the mandible may increase. The anterior flaring of the teeth and the development of an anterior open bite could be due to the combination of the above features, along with the enlargement of tongue. In Acromegaly, excessive growth occurs in the condyle and ramus, that results in a Class III skeletal relationship between the jaws. The alveolar processes may also increase in height and thickness. Hypercementosis may be seen the posterior teeth as a

result of functional and structural demands on teeth. In an attempt to compensate for the growth of the mandible, supraeruption of the posterior teeth may occur.

In patients with acromegaly, cardiovascular complications are the most common cause of morbidity and early mortality. Hypertension is caused by increased sodium reabsorption in the kidney and endothelial dysfunction, and asymptomatic cardiac hypertrophy occurs in 60% of untreated acromegalic patients. Patients can also present with valve disorders, arrhythmias, hyperkinetic syndrome (increased cardiac index), and conduction disorders. Dyspnea may be observed during exercise, and systolic function is altered. If cardiovascular symptoms are not addressed, congestive heart failure may result. Elevated GH levels are also associated with insulin resistance, glucose intolerance, hyperinsulinemia, and Type 2 diabetes mellitus.⁷

The main aim of treatment in acromegaly is to lower the GH level to <2.5 µg/l. Treatment plan include surgery, radiotherapy, and medical therapy. Radiotherapy is effective in controlling tumor growth and GH secretion; however, achievement of biochemical targets may take a long time almost up to a decade, and some safety issues have been raised with this treatment modality.^{4,8}

More recently, medical management has been increasingly used as primary treatment in selected patients unsuitable for surgery. Dopaminergic agonists like cabergoline, somatostatin analogues like octreotide, and GH receptor antagonists like pegvisomant, are the clinically available medical therapies for management of acromegaly.^{8,9} Surgical therapy includes transsphenoidal approach and transnasal endoscopic approach frontotemporal craniotomy.⁴

Successful treatment of pituitary adenomas may result in reversal of soft tissue abnormalities. However, bony changes may require corrective orthognathic surgery. Orthodontic and maxillofacial surgeons who are the part of the surgical team, should be well aware of the complications of this disease. The dentist may be approached by these patients with the complaints of malocclusion, difficulty in speech due to enlarged tongue, mobility of teeth or missing teeth as a complication of diabetes mellitus.¹⁰ Dental

management may be complicated by blindness, diabetes mellitus, hypertension, cardiomyopathic dys arrhythmias, or hypopituitarism.

In our case, the patient came with the complaint of enlarged lips and forward movement of the lower jaws and the medical history he gave was that of episodes of headache and altered vision. Relevant investigations and adequate referral lead to the prompt intervention of the condition.

CONCLUSION

A dangerous sequel of acromegaly, pituitary apoplexy, has life-threatening episodes caused by hemorrhagic infarction or necrosis of a pituitary tumor. Therefore, early detection sometimes prevent a potentially life-threatening event. Hence, this case shows that an oral diagnostician also has a substantial role in the early detection, prompt intervention, and management of such cases.

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