INTRODUCTION

Acromegaly is a disorder characterized by growth hormone (GH) hypersecretion and manifestations of GH excess. It is usually caused by pituitary tumors secreting GH or very rarely by extra pituitary source. GH and insulin like growth factor-1 (IGF-1) both act independently and dependently in inducing features of hypersomatotropism. Apart from soft internal organs and exocrine and endocrine glands including salivary gland, prostate and thyroid. Eye involvement in patients with acromegaly is described, albeit rarely. Proptosis and extraocular muscle involvement may occur with long standing GH excess. We describe here two cases of female with acromegaly, who presented with bilateral epiphora as the presenting symptom.

CASE REPORTS

Case 1

A 37-year-old female was referred by Ophthalmologist to our endocrine unit with a presumptive diagnosis of acromegaly. She had primary complaints of increased watering from both eyes for the past 4 years, which increased on lying down and on exposure to sunlight. There had also been gradual protrusion of both the eyes (left > right) for the past 2-3 years. She had shown to multiple ophthalmologists earlier without much respite with the therapy. She had also received ayurvedic medications with no relief. The Ophthalmologist took note of her change in physical features and referred to the endocrine unit with a presumptive diagnosis of acromegaly.

She had noticed changes in physical appearance with gradual changes in face, feet and hands for the past 4 years. There had also been mild generalized headache for the past 3 years. She had been amenorrheic for 7 months. She had developed hypertension 2 years back. Examination revealed an average built female with body mass index - 25.6 kg/m². There was frontal bossing, bulbous lips, prognathism, macroglossia, thickened skin of palms and feet and skin tags on the neck. Systemic examination was normal.
Eye examination revealed axial proptosis in the left eye with normal ocular motility and visual acuity in both eyes. Lacrimal gland was enlarged in both eyes (left > right) [Figure 1]. Schirmer’s test was normal.

Lab evaluation revealed normal hemogram, liver function and kidney function tests. Fasting and postprandial blood glucose levels were in the diabetic range (201 mg/dl and 220 mg/dl respectively) and lipid profile was deranged (T. cholesterol - 208 mg/dl, high density lipoprotein - 46 mg/dl, low density lipoprotein - 122 mg/dl, very low density lipoprotein - 40 mg/dl and triglycerides - 207 mg/dl). Hormone profile showed normal thyroid function test (TFT) and cortisol. Prolactin levels were 52.4 ng/ml and S. testosterone was low with normal luteinizing hormone (LH) and follicle stimulating hormone (FSH) levels (S. testosterone - 1.75 nmol/l, LH - 2.8 mIU/ml and FSH - 3.7 mIU/ml). Basal and post-glucose GH levels were elevated (0 h - 69.5 ng/ml, 1 h post-glucose GH - 358 ng/ml).

Magnetic resonance imaging (MRI) brain showed a moderately enhancing sellar mass (1.6 cm × 2.2 cm × 2.3 cm) with extension into suprasellar cistern and left cavernous sinus causing left internal carotid artery encasement suggestive of pituitary macroadenoma.

MRI orbit revealed proptosis left eye with bilateral lacrimal gland enlargement [Figure 2a and b].

Case 2
A 28-year-old female patient presented with the complaints of watery discharge from both the eyes for the past 6 years. Watering from the eyes increased when she was exposed to sunlight and wind. This was associated with upper eyelid pain and a gradual increase in eye enlargement (right > left). She consulted an Ophthalmologist who gave her frequent courses of antibiotics and acetazolamide, but the complaint persisted. For the past 1½ years, she also experienced diminution of vision and a constant headache throughout the day, which was not even relieved by analgesics. She underwent an MRI brain and was diagnosed with pituitary macroadenoma. She was referred to neurosurgery, where a diagnosis of GH secreting tumor was made and surgery performed. She developed transient diabetes perioperatively while on steroids. After the surgery, she was referred to our endocrine unit. Interrogation revealed that she had noticed a gradual weight gain, enlargement of feet (left > right) and coarsening of facial features over past few years. She had been amenorrheic for the past 8 years, after the last child birth. She had been taking thyroxine and steroid supplements post-surgery.

Examination revealed a 156.5 cm tall, 52.4 kg female with a muscular built and blood pressure-150/80 mm Hg. There was frontal bossing, prominent jaw and bulbous lips. Bilateral hand and feet enlargement along with increased heel pad thickness was noted. Galactorrhea was present. There was swelling of both the upper eyelids and right lower eyelid and proptosis of the right eye [Figure 3]. Investigations revealed normal hemogram, liver and kidney function tests. Her TFTs were normal on thyroxine 75 μg. Morning cortisol after stopping steroids for 1 day was 3.6 μg/dl. LH/FSH and estradiol levels (0.07 mIU/ml, 0.50 mIU/ml and 4.1 pmol/l respectively) were suggestive of hypogonadism. Prolactin levels were 21.7 ng/ml. Post-operative GH levels were high (301 ng/ml). Post-operative MRI brain revealed a sellar mass sized 3 cm × 3 cm × 40 cm with suprasellar extension and B/L cavernous sinus involvement.

**DISCUSSION**

The primary action of GH is mediation of growth and metabolic functions. GH elicits intracellular signaling through...
a peripheral receptor and initiates a phosphorylation cascade involving the Janus kinase-signal transducing activators of transcription (JAK-STAT) pathway. GH complexes with two diimerized GH receptor (GHR) components critical for subsequent GH signaling, followed by rapid JAK2 tyrosine kinase activation, leading to phosphorylation of intracellular signaling molecules, including the STATs 1, 3 and 5 critical signaling components of GH action. Phosphorylated STAT proteins are directly translocated to the cell nucleus, where they elicit GH specific target gene expression by binding to nuclear deoxyribonucleic acid. IGF-1, a critical growth factor induced by GH, is responsible for most growth promoting activities of GH and also directly regulates GHR function.

There are only few case reports of eye involvement in patients with acromegaly. Schwarz et al, postulated that there was possibly an exophthalmos producing activity in serum and in pituitary of patients with Cushing’s syndrome and acromegaly. Zafar and Jordan reported a case of 32-year-old woman who presented with bilateral lower eyelid swelling and extraocular muscle enlargement as the initial manifestation of acromegaly. The acromegaly, however, was not diagnosed until 6 years after her symptoms began. Burgos Peláez et al described three patients with acromegaly who developed hyperthyroidism due to Graves’ Basedow disease in the course of their disease. Patrinely conducted a retrospective analysis of 60 patients with non-thyroid enlarged extraocular muscles and found 3% of them had acromegaly. Heireman et al. described a 45-year-old man who presented with binocular diplopia in primary gaze for 1 year. Orthoptic evaluation showed 10-prism dioptr right eye hypotropia and 6-prism dioptr right eye esotropia. The elevation and abduction of the right eye were mechanically restricted. This was associated with systemic features and hormonal profile suggestive of acromegaly. Computed tomography (CT) of the orbit demonstrated bilateral symmetrical enlargement of the medial rectus and inferior rectus muscle bellies.

Epiphora is overflow of tears due to faulty apposition of the lacrimal puncta in the lacrimal lake, scarring of the puncta, paresis of the orbicularis muscles, obstruction of lacrimal passage or ectropion. Epiphora as a symptom of acromegaly has been described only on one occasion earlier. Tristante described a 60-year-old woman with acromegaly who presented with bilateral proptosis and watering from the eyes predominant on the right and existing since many years. Upper tarsus was much enlarged on the right; lacrimal glands were palpable under the upper lid and seemed enlarged as well. CT scan and confirmed the hypertrophy of subcutaneous lid tissues, lacrimal glands and ocular muscles.

**CONCLUSION**

These were 2 rare cases of acromegaly who presented with epiphora as the first symptom.

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