Case Report

Acromegaly without acral changes: A rare presentation

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ABSTRACT

Acromegaly is diagnosed clinically by the universal presence of acral enlargement and typical coarse facies. We report a short, elderly female developing acromegalic facies for last 10 years without acral overgrowth. She is a patient of primary hypothyroidism, well controlled for last 20 years. Acromegaly was proven by high level of serum insulin like growth factor-1 (IGF-1) and elevated and nonsuppressed level of growth hormone (GH), with other hormonal profile being undisturbed. She had mild insulin resistance and systemic hypertension in absence of any visual field defect. Magnetic resonance imaging (MRI) of brain revealed pituitary hyperplasia without any detectable adenoma. No source of ectopic secretion of GH or growth hormone releasing hormone (GHRH) could be localized. Therefore, atypical presentation of acromegaly needs high degree of suspicion even if some of the common features are lacking. Here, we have biochemically proved acromegaly with typical facies, short stature but no acral overgrowth and pituitary adenoma despite longstanding disease activity, and thus eluding diagnosis for years.

Key words: Acral enlargement, acromegaly, pituitary hyperplasia

Introduction

Acromegaly is the syndrome caused by growth hormone (GH) hypersecretion as a result of somatotroph adenoma in majority and is rarely due to extrapituitary ectopic lesions. Its very slow but progressive disease activity usually leads to delay in diagnosis for decades. The clinical manifestations ranging from soft tissue swelling, acral overgrowth, jaw prognathism, hyperhydrosis, frontal bossing, arthralgia to florid arthropathy, diabetes, hypertension and cardiorespiratory failure are present in patients in variable combinations. We report a lady with acromegaly without typical acral overgrowth even after 10 years of disease activity, which is a rarity in literature.

Case Report

A 50-year-old postmenopausal lady presented to us with headache, increased sweating and exertional breathlessness since last 10 years. The suspicion of acromegaly was based on her phenotypic profile with coarse facial features including prominent supraorbital ridges, enlarged fleshy nose, thick lips and oily skin. These facial changes gradually developed over last 10 years as discerned by serial photography in the lady's archives [Figure 1]. She was obese with short stature. She was on 50 µg daily replacement dose of thyroxin since last 20 years when she was detected to be suffering from primary hypothyroidism. She also had positive history for arterial hypertension since last 5 years. She had blood pressure of 160/90 mm Hg and was taking 5 mg daily dose of amlodipine on admission.

Despite typical facial features, there were points that did not support the diagnosis of acromegaly. She did not have acral enlargement, frontal bossing, jaw prognathism and macroglossia. Patient also denied the enlargement of distal extremities with progress of time [Figure 2].

Biochemical diagnosis of acromegaly was made by measuring insulin like growth factor-1 (IGF-1) level and glucose-suppressed GH estimation. IGF-1 level was 913 ng/ml (normal range: 94–252 ng/ml). The basal GH was 11.2 µg/l, and 60 minutes and 120 minutes GH

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levels after 75 g oral glucose load were 9.6 and 5.4 µg/l, respectively. Skull X-ray showed slight enlargement of pituitary fossa and thick calvarium but no prognathism and frontal bossing. Magnetic resonance imaging (MRI) of brain revealed diffuse enlargement of pituitary suggestive of pituitary hyperplasia, but no adenoma was detected [Figure 3]. Radiological findings as evidenced by the X-ray imaging of extremities of the patient were also not suggestive of acromegalic soft tissue changes. The findings were: heel pad thickness: 20 mm (>21.5 mm in acromegalic women), sesamoid index: 30 (>32 in acromegalic women), width of second metacarpophalangeal (MCP) joint: 2.1 mm (>2.5 mm in acromegalic women), soft tissue thickness (width) at proximal mid phalanges: 24 mm (>26 mm in acromegalic women), tuftal width of 3rd finger: 9 mm (>10 mm in acromegalic women) [Figure 4].

Detailed physical and skeletal examination revealed the following: short stature with a height of 142 cm (less than 2.5 percentile for Indian women), large head (head circumference 55 cm), arm span equal to height, ratio of upper segment and lower segment 0.97, ratio of forearm to arm length 0.77, forearm:hand length 1.4, acral length 15.5 cm and weight 62 kg. Measurement of body proportions did not match with common forms of skeletal dysplasia; neither had she any deformity related to such dysplasia. No cranial, spinal, epiphyseal and bony changes seen in skeletal dysplasia were present in this case as evident by skeletal roentgenograms. She did not have any visual field defect on automated perimetry.

She was found to be euthyroid [free T4 1.1µg/dl with thyroid stimulating hormone (TSH) 0.78 µIU/ml on 50 µg levothyroxin]. Her fasting plasma glucose was 88 mg/dl and 2-hour post 75 g glucose load plasma glucose was 159 mg/dl, signifying impaired glucose tolerance. Levels of follicle stimulating hormone (FSH), luteinizing hormone (LH), prolactin and 9AM cortisol were 54.64 mIU/ml, 20.39

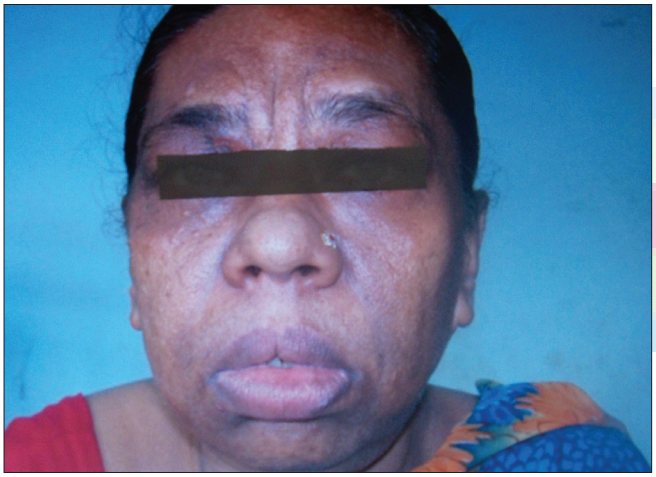

Figure 1: Acromegalic facies

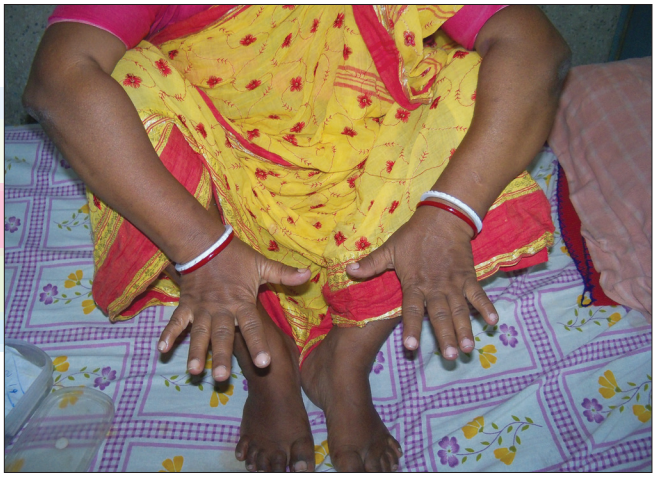

Figure 2: Short hands and feet without typical acral enlargement

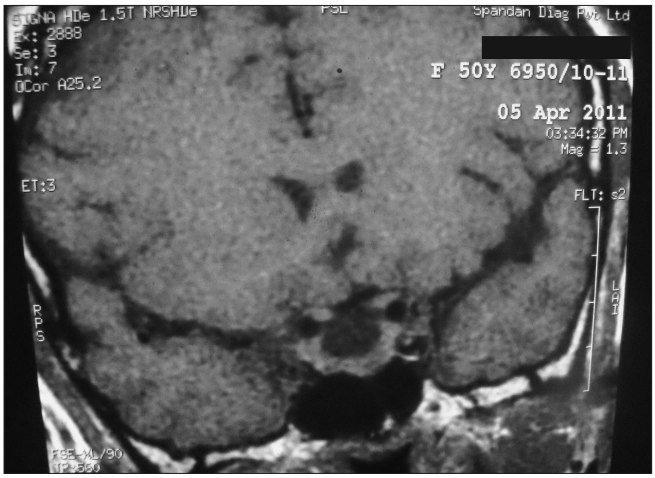

Figure 3: T1-weighted image of MRI brain (coronal view) shows large sella with pituitary enlargement

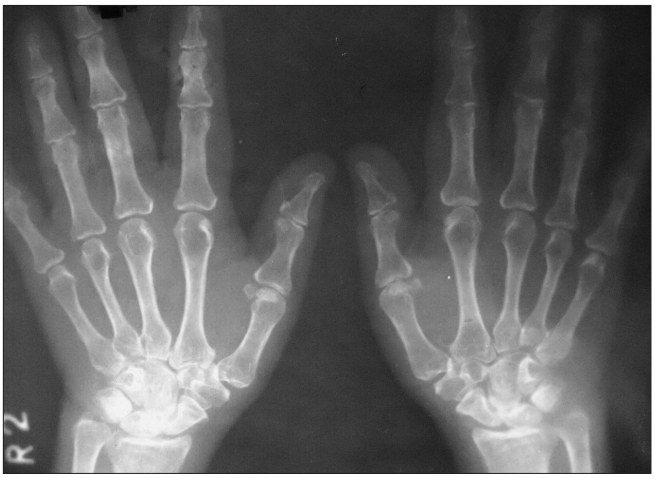

Figure 4: X-ray of both hands: Radiological measurements do not fulfil the diagnostic features of acromegaly

mIU/ml, 6.10 ng/ml and 14 µg/dl, respectively, all being within normal limits. Fasting serum insulin level was normal (4.17 µIU/ml), but 2-hour post 75 g glucose insulin level was mildly elevated (89.6 µIU/ml) indicating mild insulin resistance. C-peptide was within normal range (3.45 ng/ml). Search for extrapituitary ectopic hypersecretion of GH or growth hormone releasing hormone (GHRH) done by high-resolution computed tomography of chest (HRCT thorax) and abdominal scans was, however, unrewarding. Endoscopic and colonoscopic search also failed to detect any possible lesion. The patient was asked to undergo somatostatin scintigraphy nuclear scan which she could not afford. She had mild concentric left ventricular hypertrophy with diastolic dysfunction. Her lipid profile was within normal range.

Discussion

The case reported here is exceptional due to the absence of few extremely common clinical associates of acromegaly in the patient. The frequency of clinical features varies. As reported by previous studies, relative frequency of acral enlargement is 100%, hyperhydrosis 65%, headache 55%, hypertension 32%, diabetes 27% and visual field defect 6% only.[1] Acromegaly without acral enlargement in spite of its longstanding disease activity has never been reported earlier, to the best of our knowledge.

Clinical features similar to acromegaly are rarely seen in few other medical conditions like pseudoacromegaly and congenital hypothyroidism. Cases of pseudoacromegaly have been reported due to hyperinsulinemic state, primary pachydermoperiostosis and long-term minoxidil use without elevation in GH and IGF-1 level.[2] Similarly patient with congenital hypothyroidism simulating acromegaly has also been reported as a rare clinical picture.[3] She did not have any of the clinical pointers suggesting such abnormalities.

The most common cause for acromegaly is a somatotroph (GH secreting) adenoma of the anterior pituitary gland. Acromegaly resulting from ectopic GH or GHRH hypersecretion is exceedingly rare (<1%).[4] So, ours could theoretically be a case of GHRH secreting acromegaly. History, clinical examination and limited radiological examination like HRCT thorax and computed tomography (CT) pancreas did not point to any GHRH producing tumor. GHRH assay could not be performed due to the assay not being available commercially in India.

In the absence of documented pituitary adenoma, the patient has been offered medical therapy in the form of somatostatin analogue about which she is yet to decide.

Theoretically, one can argue a longstanding undetected and untreated primary hypothyroidism in this patient, causing pseudoacromegaly involving face sparing extremity, more so as she is having short stature. However, hypothyroidism in this patient causing pseudoacromegaly is highly unlikely because of the following facts. First, she had normal reproductive life being a mother of three fully normal children, with her last child birth at 27 years of age. Then, repeated GH assays done in other hospitals revealed persistent elevation and nonsuppressibility for last few years which, however, was not addressed. Lastly, her primary hypothyroidism was detected at the age of 30 and was adequately controlled thereafter, pointing to the fact that she had had primary hypothyroidism from her late twenties which is thereby very unlikely to produce acromegalic facies for last 10 years only. The patient had been attending endocrine outpatient departments of other state hospitals since the year 2000, but a definite diagnosis eluded her.

The instructive point regarding the case is that absence of typical acral overgrowth and pituitary adenoma on neuroimaging eluded her definitive diagnosis of acromegaly despite having typical facial changes and biological GH hypersecretion and despite attending superspeciality referral hospital outpatient departments for years, more so, with some known metabolic complications of GH excess like hypertension and mild insulin resistance. Generally, diagnosis of acromegaly and its cause is easy. But in odd cases, high index of suspicion is crucial so that atypical presentations do not miss diagnosis and are not left untreated.

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