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Original Research Paper

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SHORT STATURE: A CASE REPORT AND REVIEW OF LITERATURE OF CONGENITAL GROWTH HORMONE DEFICIENCY

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KEYWORDS :

Case Report

A 6-year 10month old female, third born child of a non-consanguineous union presented to our institute with history of not gaining height. The parents complained that the child did not outgrow clothes and shoes. She was not enrolled in school due to severe stunting though all the development milestones were normal. There was no history of constipation, head trauma, recurrent illnesses, or history suggestive of any systemic causes of short stature. She had three other siblings and appeared shorter than her younger 4-year-old brother.

She was born small for gestational age, 2.2kg, at full term conception, normally delivered with vertex presentation and uneventful perinatal events. Dentition was however delayed, with no deciduation of primary teeth by now.

The anthropometric measurements showed weight 6.5 kgs and height 68.5cm. Her height for age was below -2SD (WHO) and weight for age was also below -2SD (WHO). The mid parental height was 151 cm. Head circumference was 50 cm. The ratio of upper and lower segment was 1.1:1, being proportionate short stature (figure). She was Tanner stage 1 on sexual maturity rating. On examination, dysmorphic features noticed in form of frontal bossing, midfacial hypoplasia, crowding of facial features, bluish sclera, depressed nasal bridge and membranous anterior fontanelle. Truncal pad of fat was preserved along with small hands and feet.

Investigations showed no abnormalities in routine blood, stool and urine examinations. The blood glucose, renal function test, liver function test and thyroid function tests were all normal. No abnormalities were present in the chest Xray. However, her bone age was delayed (Bone age: 16 months). Clonidine stimulation test was done which was consistent with Growth hormone deficiency. The levels of GH at 30,60,90 and 120 minutes after taking clonidine were 0.1,0.2,3.2,2.8,1.1 ng/ml, suggestive of severe growth hormone deficiency. Cortisol and prolactin levels where within normal limits. MRI Brain showed a normal sized anterior and posterior pituitary.

Growth hormone 0.07 Units/kg or 21microgram/kg/day was started subcutaneously, once daily at bedtime, 7 days in a week in the patient along with supplements. The child has shown an increase in height of 2 cm in first month of treatment. Plan is to continue the therapy till desired growth is achieved along with regular clinical and laboratory monitoring.

DISCUSSION:

Growth hormone deficiency can be congenital or acquired. The incidence of isolated growth hormone deficiency is estimated to be 1 in 4,000 to 10,000 individuals worldwide.[1]

A mutation in a transcription factor (POUF-1, also known as PIT-1) is known to result in familial growth hormone deficiency. As many as 14 different mutations have been described.[2] In addition to growth hormone deficiency, affected individuals have had prolactin deficiencies and variable thyroid-stimulating hormone (TSH) deficiencies. Imaging of the pituitary gland usually reveals a hypoplastic or ectopic posterior pituitary. Growth hormone deficiency with other hypopituitarism associated with inactivating mutations of the *PROP1* (Prophet of PIT-1) transcription factor gene have been documented in reports. Congenital growth hormone deficiency may be associated with an abnormal pituitary gland or may be part of a syndrome such as septo-optic dysplasia (SOD) (de-Morsier syndrome), which may include other pituitary deficiencies, optic nerve hypoplasia, and absence of the septum pellucidum.

Acquired growth hormone deficiency may result from trauma, infections (e.g., encephalitis, meningitis), cranial irradiation, and other systemic diseases (particularly histiocytosis). A reported 12-86% of children with apparent isolated growth hormone deficiency have sellar developmental defects.[3] Isolated growth hormone deficiency is caused by mutations in one of at least three genes. Isolated growth hormone deficiency types IA and II are caused by mutations in the GH1 gene. Type IB is caused by mutations in either the GH1 or GHRHR gene. Type III is caused by mutations in the BTK gene.

Diagnosis of GHD is based on a combination of auxology, biochemical analyses such as growth hormone (GH) stimulation tests and insulin-like growth factor 1 (IGF-1), skeletal age, magnetic resonance imaging (MRI), and exclusion of other systemic diseases which can have a similar presentation.

Diagnosis of GHD is more challenging in resource constrained countries like India for various reasons. Recombinant human GH therapy was first approved for children with GHD in 1985 and later for the treatment of various conditions like idiopathic short stature (ISS), Turner

syndrome (TS), Noonan syndrome (NS), Prader-Willi syndrome (PWS), chronic renal failure (CRF), and small for gestational age (SGA).[4]

Learning points:

Early initiation of therapy could better the chances of achieving final adult height. Education and awareness about growth disorders among parents would help improve the diagnosis and treatment of children with GHD. The first point of contact in a patient's journey is that physician/pediatrician needs to be well equipped to identify cases of GHD.

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