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IGF-1 DEFICIENCY (SHORT STATURE)

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ABSTRACT

Growth represents a sentinel for the general health of a child. One of the uncommon yet treatable causes of short for age child is insulin like growth factor 1 deficiency. We report one such cases. The case is an 18 months old girl of Rawalpindi brought in Military Hospital Rawalpindi on 17th March 2012 with history of Short stature since birth. The patient was diagnosed as having insulin like growth factor 1 deficiency. Recombinant human insulin like growth factor-l (IGF-1) is the recommended treatment.

KEYWORDS

Growth hormone insensitivity (GHI); Recombinant human insulin like growth factor- 1 (IGF-1); IGF-1 deficiency.

INTRODUCTION

The term growth hormone insensitivity describes a group of disorders,both inherited and acquired, in which there are clinical and endocrine features of insulin-like growth factor 1 (IGF-1) deficiency and resistance to exogenous human growth hormone, associated with growth hormone secretion that would not be considered abnormally low. When the child's pituitary is producing GH in adequate amounts, but IGF-1 is decreased the child is diagnosed as "IGF-1 deficient". Furthermore, the degree to which I GF -1 secretion is impaired varies markedly across individuals[15]. Severe Short stature is defined as a height more than 2 standard deviations (SD) below the population mean[17].

CASE REPORT

An 18-month old girl, presented in Military Hospital Rawalpindi on 17th March 2012 with history of short stature since birth. Parents noticed that she was not gaining appropriate height as she was failing to match in her linear growth to her peers. Her parents visited many doctors where parents were strongly reassured and vitamin supplements were given but she did not show catch up growth. There was no history of headache, visual complaints, chronic diarrhea or any other relevant complaints. There was no past history of recurrent infections or hospitalization. She was born at term and was of normal birth weight. She was not breast fed; weaning was started at 06 months of age. She was immunized according to EPI schedule. Other siblings of the family were normal and healthy.

On general physical examination, an initial appearance was that of a grossly short for age child. The anthropometric data at the age of 18 months was equivalent to those of a 10 month old child. Upper and lower segment ratio was normal. Mid parental height for this child was calculated to be 164.5 cm.

Provisional diagnosis of severe short stature most likely of endocrine origin was made. X ray left wrist revealed bone age of 01 year. X-ray skull was normal. Ultrasonography of abdomen and KUB showed normal study. Apart from routine investigations antigliadin and anti reticulin antibodies were negative. Thyroid hormone profile was normal. Her serum cortisol levels did not reveal any loss of circadian rhythm. Basal growth hormone level was increased. IGF-1 was decreased. Thus a final diagnosis of IGF-1 deficiency was made.

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DISCUSSION

Compared to a well-nourished, genetically relevant population, short stature is defined as standing height below the 0.4th percentile for that gender and age". Short stature is further divided into proportionate and disproportionate types. Endocrine causes of short stature include, isolated growth hormone deficiency, hypothyroidism, multiple pituitary deficiencies and GH resistant syndromes", The non-endocrine causes like malnutrition, intrauterine growth retardation with no "catch up" growth, constitutional growth delay, cystic fibrosis, blood disorders should always be ruled out before making a diagnosis of growth hormone insensitivity or Laron type dwarfism". Mostly growth hormone resistance is congenital.

A "typical" clinical picture of the GH1 in a child includes severe proportional short stature, decreased height velocity, delayed bone age, delayed puberty, a high-pitched voice and overcrowded teeth. Intelligence is usually normal". Detailed history and examination are cornerstones to diagnosis. Growth charts are used to compare child's height and weight to a standard range[7]. Bone age is done to demonstrate the difference between chronological age and bone maturity"[8].

Laboratory workup of short stature should firstly focus on common causes and baseline. Investigations such as full blood counts, liver and renal function tests and assessment for - malnutrition and thyroid function should be undeliaken[5]. For confirming GHI, estimation of GH is indicated. Basal growth hormone levels are inadequate to diagnose the GH insensitivity, because it is secreted in a pulsatile manner and is rapidly cleared from plasma", Moreover, it is important to evaluate for GH pituitary reserve. This problem can be overcome by either post sleep GH levels or exercise stimulation test or Levo dopa stimulation test. Post sleep GH levels are based on the principal that highest concentration of GH is seen in plasma one hour after deep sleep. Specimen for GH assay is therefore drawn after one hour of induction of sleep. Similarly exercise is another important stimulus for GH secretion. The exercise stimulation test is often used as an initial screen for GH insensitivity. A normal or exaggerated response is observed[10].

The evaluation of a child with short stature and possible GHI should comply with the classical paradigm of clinical assessment followed by general (i.e. nonendocrine) investigations, hormonal assessment, and possible genetic analyses. Clinical assessment should include inquiries about family history of growth disturbance, consanguinity, birth weight and length, and recurrent infections. Examination should specifically assess the presence of possible facial dysmorphic features and microcephaly in addition to anthropometric evaluation. Investigations of the GH-IGF-I axis consist of determination of GH secretion and exploration of the IGF system. A GH provocation test is recommended unless the child has normal auxology or a basal IGF-I level above the mean for age. In the initial assessment, IGFBP-3 adds little, except in children under 3 yr of age, where low IGFBP-3 is helpful in the diagnosis of GH deficiency. Cranial imaging such as X-ray skull, CT scan and MRl should be done to look for any pituitary tumor[12,13].

Mecasermin is the recommended treatment. Given as subcutaneous injection 0.04-0.08 mg/kg bid initially with meal or snack. If tolerated, dose may be increased by 0.04 mg/kg/dose. IGF-1 therapy should be continued at least until growth ceases, but may need to be continued thereafter. Response is better if treatment started early.

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