Short Stature
PPA clinical meeting 3.12.2008

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House Officer

Case prepared under supervision of

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Case History

- **Personal Profile**
  - **Name**: XX
  - **Age**: 13 yrs
  - **Resident of Islamabad**

- **She has been coming to us since 5 yrs**
Case History

- Presenting Complaints
  - Not gaining height 5 yrs
  - Not gaining weight 5 yrs
Case History

History of Presenting Complaints

- Parents brought their daughter to OPD with C/O not gaining Height & Weight as compared to rest of their children.

- There was H/O Anorexia, nausea, constipation and easy fatigue ability.
Case History

- There was no concurrent H/O
  Loose motions, persistent cough, palpitations etc.

Also no H/O
  joint pain, vertigo, dizziness
or
  Trauma, surgery, cranial irradiation
Case History

- **Birth History:**
  - SVD in CDA Hospital.
  - No prenatal exposure and illness or evidence of IUGR,
  - At birth average Height and weight
  - No perinatal problems i.e.
    - Prolonged jaundice,
    - Hypoglycemia,
    - Puffy extremities.
Case History

Nutritional History:
- Breast fed for 6 months.
- Family food is not taken satisfactorily.

Developmental History:
- Sitting at 6 months, Walking at 1 yr
- No developmental delay is recorded.

Immunization History:
- EPI schedule
- BCG scar present
**Family History:**

Parents are first cousins with average height & built.
3 brothers & 1 sister are of normal height & built
1 Brother died at the age of 9 months due to gastroenteritis.
Case History

○ **Family History:**
  - mother is carrier of thalasseamia trait
  - No family H/O
  - Tuberculosis, Fits, Diabetes mellitus, Mental retardation, Short stature.

○ **Socio economic History:**
  - Lower middle class.
  - Healthy environment including adequate sleep, exercise, psychosocial factors are also favorable for growth & development.
General Physical Examination

- A young thin built girl with pallor, no dymorphism or disproportions looking short for her age
- Anthropometric measurements $<$ 3rd centile
- Vital signs with in normal range.
- No sign of malnutrition or other remarkable physical findings.
Systemic Examination

- **GIT:**
  Abdomen soft, non tender, no visceromegaly /ascites

- **CVS:**
  Apex beat 4\textsuperscript{th} ICS medial to MCL
  S1+S2+0

- **Resp S:**
  No significant finding
Systemic Examination

- **CNS**:
  - Intact higher mental functions & speech
  - Motor & Sensory systems & Cranial nerves intact
  - Cerebellar signs absent.

- **SMR**:
  - No sign of puberty
Stature measurements 8 yrs

wt : 14 kg
Ht : 102 cm

< 3rd centile

Weight age : 3 yrs
Height age : 4 yrs

Ratio : U/ L 52/50 cm = 1.04 : 1
Arm span : 104 cm

Target Height: 150.5 cm
Mid parental Height : 153 cm
Initially for 6 months we managed her with Dietary advice and multivitamins & Iron but no significant improvement in height & weight.

- Detailed evaluation was done by doing certain tests.

- **Differentials for short stature were**
  * Constitutional delay,
  * Familial short stature &
  * Idiopathic short stature
  * Endocrinial causes

- Growth measurements were plotted.
Investigations

- **Blood CP:**
  - WBC: $9.8 \times 10^3 / \mu l$
  - Hb: 9.2 G/dl
  - Platelets: $358 \times 10^3 / \mu l$

- **Hb electrophoresis**: Beta thalassemia trait

- **RBS**: 98 mg %
Radiological Aid

- Bone Age at 9 yrs
  more than 7 & less than 9 yrs

- Chest X ray: Clear lung fields, normal cardiac shadow

- Abdominal USS: Normal profile
Investigations

- Stool RE
- Urine RE
- RFT, WNL
- LFT
- TFT

- Chromosomal Karyotyping:
  Report awaited

- Cealiac profile was negative.
Growth Hormone levels

2005

Basal level : 1.23 m IU /l  ( < 14 n IU /l)
GH after L dopa: 4.76 n IU/ l  ( NV: 0)

2007

Basal level : 0.26 m IU /l  ( < 14 n IU /l)
GH after L dopa: 9.7 n IU/ l  ( NV: 0)

Suboptimal response to GH stimulation test. Insulin Tolerance test was advised.
### Growth Hormone levels & Insulin Tolerance Test

<table>
<thead>
<tr>
<th></th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Plasma glucose basal</strong></td>
<td>4.4 (3.3—6.1 m mol/L)</td>
</tr>
<tr>
<td><strong>Plasma glucose (at induction)</strong></td>
<td>1.7</td>
</tr>
<tr>
<td>Glucose 30 min</td>
<td>4.9</td>
</tr>
<tr>
<td>Glucose 60 min</td>
<td>5.0</td>
</tr>
<tr>
<td><strong>GH basal level</strong></td>
<td>0.19 (&lt;14m IU/L)</td>
</tr>
<tr>
<td>GH (at induction)</td>
<td>3.8</td>
</tr>
<tr>
<td>GH 30 min</td>
<td>3.0</td>
</tr>
<tr>
<td>GH 60 min</td>
<td>0.52</td>
</tr>
</tbody>
</table>

**Inadequate response to insulin tolerance test**
Final Diagnosis

- Short stature due to isolated Growth Hormone Deficiency.
Replacement Therapy was started in April 2008 after consultation & evaluation by Dr Gulbeeen Shahid (endocrinologist PIMS)

- Eutropin 4iu SC injections 3 times /wk at night.
<table>
<thead>
<tr>
<th>Age yrs</th>
<th>Height</th>
<th>Weight</th>
</tr>
</thead>
<tbody>
<tr>
<td>8</td>
<td>102 cm</td>
<td>14 kg</td>
</tr>
<tr>
<td>8.5</td>
<td>103 cm</td>
<td>15 kg</td>
</tr>
<tr>
<td>9</td>
<td>106 cm</td>
<td>15 kg</td>
</tr>
<tr>
<td>9.5</td>
<td>107 cm</td>
<td>15 kg</td>
</tr>
<tr>
<td>10</td>
<td>111 cm</td>
<td>16 kg</td>
</tr>
<tr>
<td>10.5</td>
<td>115 cm</td>
<td>16 kg</td>
</tr>
<tr>
<td>11</td>
<td>120 cm</td>
<td>17 kg</td>
</tr>
<tr>
<td>11.5</td>
<td>120 cm</td>
<td>18 kg</td>
</tr>
<tr>
<td>12</td>
<td>121 cm</td>
<td>20 kg</td>
</tr>
<tr>
<td>12.5</td>
<td>122 cm</td>
<td>21 kg</td>
</tr>
<tr>
<td>13+</td>
<td>130 cm</td>
<td>23 kg</td>
</tr>
</tbody>
</table>
Effects of Therapy

- Gain in Height: 8 cm
- Gain in Weight: 2 Kg

Ratio U/ L:
62.5/64.5 cm = 0.96 : 1
Height Velocity

Clinical Longitudinal
British Standard:
Tanner–Whitehouse (1976)®

Surnane:
Forename:
Date of birth:

<table>
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<tr>
<th>Age</th>
<th>Height (cm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>8 yrs</td>
<td>131 cm</td>
</tr>
<tr>
<td>9 yrs</td>
<td>136 cm</td>
</tr>
<tr>
<td>10 yrs</td>
<td>141 cm</td>
</tr>
<tr>
<td>11 yrs</td>
<td>146 cm</td>
</tr>
<tr>
<td>12 yrs</td>
<td>151 cm</td>
</tr>
<tr>
<td>13 yrs</td>
<td>156 cm</td>
</tr>
</tbody>
</table>

Height Velocity

Longitudinal whole year centiles
when peak velocity occurs
all centile curves
67%
50%
16%
Girls

Height velocity

Anabolic steroids

Age, years (decimal)

©Novocare
Height & weight.

[Image of growth chart for girls aged 2 to 18 years, showing stature and weight by age with centiles marked.]
Current Age 13 yrs

- Weight 23 kg = weight age 8 yrs
- Height 130 cm = Height age 9 yrs

- Expected weight = 46 kg
- Expected Height = 157 cm

- Target Height = 150.5 cm
The parents of a healthy 8 yr old girl are concerned that she is the shortest among her siblings & class mates.

Her height & growth curves as shown already.

A thorough history reveals that she was a full term infant, has had no significant medical problems, she is developmentally appropriate.

Other than being small for her age, no abnormalities are noted on physical examination.

Careful measurements of her upper & lower body segments are normal for age.

Her parents of average height had normal pubertal ages. Father : 14yrs & Mother : 16yrs
How do you define short stature in a child?

**DEFINITION**

- Short stature is defined as height $< 2 \text{ to } 2.5 \text{ SD}$
  
  (less than 2 to 2.5 standard deviations)

  below the mean for age and gender
Calculate mid-parent height:

- **Boys**
  
  Mid parental height = mother's height + father's height /2 + 7cm
  Target centile range = mid parental height +/- 10cm

- **Girls**
  
  Mid parental height = mother's height + father's height /2 - 7cm
  Target centile range = mid parental height +/- 8.5cm
Evaluation of Short Stature

- Triad of
  - History
  - PE
  - Investigations
*Evaluation of Short Stature

*EXAMINATION

**Respiratory System**
- Chest deformities
- Signs of chronic lung disease e.g.
  - cystic fibrosis, asthma

**Cardiovascular System**
- Signs of congenital heart disease
- Hypertension
- Signs of cardiac failure
Evaluation of Short Stature

*EXAMINATION*

**Abdomen**
- Hepatomegaly
- Splenomegaly
- Masses
- Ascites

**Renal**
- Urine output
Evaluation of Short Stature

*EXAMINATION

CNS

Visual acuity and visual fields
Nystagmus
Signs of hydrocephalus
Focal signs
INVESTIGATIONS

- FBC
  - Aneamia
  - Leucocytosis
  - Leucopaenia
  - Thrombocytopaenia
- ESR, CRP
- Electrolytes and liver enzymes
- Carotene, folate, prothrombin time
- Celiac panel
INVESTIGATIONS

- Urinalysis and pH
- Karyotype
- Cranial imaging - MRI
- Bone age
- TFT
- Prolactin
- IGF 1, IGF BP3
- Growth hormone stimulation tests
OPTIMISE TREATMENT OF CHRONIC DISEASES

ENSURE GOOD NUTRITION AND NOT OVERNUTRITION

APPROPRIATE THERAPY FOR TUMOURS

REPLACEMENT THERAPY FOR DEFICIENCY SYNDROMES
Features of Congenital GHD

- Normal BW&BH.
- Unexplained hypoglycemia.
- Prolonged hyperbilirubinaemia.
- Clinical appearance.
Features Suggestive of GHD

- Short stature
- Poor growth velocity
- Delayed bone maturation
- Increased subcutaneous fat
- Dentition is delayed
- High pitched voice
- Age of pubertal onset
*Diagnosis*

- History.
- Physical exam.
- Auxologic criteria.
  - Height.
  - Mid parental ht.
  - Growth velocity.
  - Bone age.
  - Tanner staging.
*Investigations.*

- **GH profiles.**
  - Spontaneous GH secretion.
  - Urinary GH excretion.

- **Pharmacological tests.**
  - GH provocation test.

- **Serum markers of GH secretion.**
  - IGF-1 and IGFBP-2,3 levels.

- **Radiological investigations.**

- **Other profiles.**
Treatment

- **Preparations**
  - Humatrope  Eli Lilly  4iu/1.33mg
  - Eutropin  4 iU  LG Life sciences  Korea

- **Dose**
  (3iu=1.0mg)
  - 0.18 – 0.3mg/kg/wk
  - 0.025 – 0.035/kg/day

- **Response depends**
  - Age at the start of treatment
  - Severity of GHD
  - Duration of the disease
  - Genetic potential (parental height)
  - Dose and frequency of administration of rhGH
**Treatment...**

- Duration.
- When to stop Rx.
- Contraindication.
- Follow up.
  - Growth parameters.
  - Bone age.
  - Tanner staging.
  - Side effects of therapy.
**Side Effects of GH Treatment**

- Pseudotumor cerebri.
- Salt and water retention.
- Hypothyroidism.
- Slipped capital femoral epiphysis.
- Worsening of scoliosis.
- Acute pancreatitis.
- Possible glucose intolerance and hyperinsulinism.
- Leukemia.
Other Intervventional Therapy

- Anabolic steroids.
- IGF-1.
- GHRH.
- Delaying puberty.
- Surgery and limb lengthening.
*Other Indication For GH

- Turner syndrome.
- End stage renal failure.
- Idiopathic short stature.
- IUGR.
- Prader-willi syndrome.
Prognosis

Prognosis is determined by response to Growth hormone replacement therapy and is generally favorable.