Estrogen is an essential regulator of bone maturation, growth plate fusion, and cessation of longitudinal growth(1). Therefore, an increase in adult height may be achieved in short children by blocking estrogen biosynthesis. Aromatase is the key enzyme for estrogen biosynthesis and aromatase inhibitors (AI) have been used primarily in women with breast carcinoma. The use of aromatase inhibitors may provide a means to delay skeletal maturation and increase final height in children with short stature(2).

Use of aromatase inhibitors to improve the final height has been extensively reported in idiopathic short stature or constitutional delay in puberty(3). However, the addition of aromatase inhibitor therapy to growth hormone (GH) in patients of GH deficiency is not widely studied(4). This combination may augment the growth potential and final height achieved in cases of GH deficiency. We report the pattern of growth in a child after addition of letrozole to GH therapy in a case of idiopathic growth hormone deficiency.

CASE REPORT

A 13 year old boy presented to us with short stature. Evaluation revealed growth hormone (GH) deficiency. He was treated with GH replacement for 10 months and to further boost up the growth potential, an aromatase inhibitor Letrozole was added to GH therapy. After one year of combination therapy, patient had significant improvement in predicted adult height without a negative impact on pubertal progression.

Key Words: Aromatase inhibitors, Estrogen, Growth hormone, Letrozole.
hepatic tests were normal. He was observed for 6 months and due to poor growth velocity (2 cm increase in 6 months) he was tested for GH deficiency after adequate priming. The peak GH levels following stimulation with clonidine was 0.26 ng/mL and GH deficiency was confirmed by low IGF1 - 50.3 ng/mL (131-718) and IGFBP3 – 809.7 ng/mL (1700-6940). His LH – 0.4 IU/L, FSH – 0.8 IU/L and testosterone – 120 ng/dL were prepubertal. He was initiated on GH therapy at the age of 14 yrs with a dose of 0.3 mg/kg/week. After 10 months of GH therapy, in view of height centile below his target height centile, the use of additional therapy to augment growth was planned and Letrozole was started at a dose of 2.5 mg daily along with GH therapy. The height improvement is shown in growth chart (Fig. 1) and other clinical details are given in Table I. Due to significant improvement in stature without bone age advancement, we discontinued both GH and Letrozole after 1 year. The height velocity after therapy is about 13.5 cm per year over past 2 years with use of GH and Letrozole. The liver function tests and glycemic levels were normal throughout the period of observation. However, we did not evaluate any markers of bone turnover during the entire period of observation.

**DISCUSSION**

Our case demonstrates the beneficial effect of letrozole along with GH therapy in augmenting the final adult height in a case of GH deficiency. The predicted adult height improved significantly while pubertal maturation proceeded unimpeded. Growth charts account for spontaneous pubertal progression and our patient demonstrated growth velocity of 13.5 cm per year, higher than seen with onset of spontaneous puberty in GH deficient individuals(5,6).

Growth response to therapy with GH is dependent on various factors(6). The available options to augment the growth response and final

<table>
<thead>
<tr>
<th>TABLE I</th>
<th>CLINICAL DETAILS OF PATIENT BEFORE AND AFTER THERAPY WITH GH AND LETROZOLE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Parameter</td>
<td>Pre treatment</td>
</tr>
<tr>
<td>Duration of Observation</td>
<td>6 months</td>
</tr>
<tr>
<td>Height gain (cm)</td>
<td>2</td>
</tr>
<tr>
<td>Height centile</td>
<td>&lt; 5th centile</td>
</tr>
<tr>
<td>Growth velocity (cm/yr)</td>
<td>4</td>
</tr>
<tr>
<td>Bone age</td>
<td>11 yrs</td>
</tr>
<tr>
<td>Predicted adult height* (cm)</td>
<td>170</td>
</tr>
<tr>
<td>Pubertal status</td>
<td>Tanner stage 1</td>
</tr>
</tbody>
</table>

* As per Bailey & Pinneau charts.
adult height are simultaneous use of gonadotropin-releasing hormone analogs (GnRHa) or aromatase inhibitors. The GnRHa therapy is associated with significant detrimental effects on metabolism and bone mineral density(7). These effects make the use of these analogs unsuitable for long term use. Thus, the use of AI offers the advantage of continued virilization and maintenance of pubertal body composition in boys while potentially delaying skeletal maturation. Our patient had a height increment of 13 cm during 10 months of GH therapy and combination therapy of GH and letrozole resulted in height increment of 13 cm in 12 months. This suggests that letrozole improves the final height in GH deficiency and augments the response to GH therapy as demonstrated by earlier observations(4).

Letrozole was well tolerated by our patient. Potential adverse effects of aromatase inhibitors are decreased bone matrix accumulation and delayed pubertal progression. However, we did not estimate bone mineral density in the child because of letrozole use for one year only and lack of standardization of dual energy X-ray absorptiometry scan in pediatric age group(8).

**Contributors:** KVS, JM, AV worked up the patient clinically. KVS, JM reviewed the literature and drafted the manuscript initially. KVS, KDM co drafted and revised the manuscript. KDM will act as the guarantor and the final manuscript was approved by all authors.

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**REFERENCES**


