Growth and maturation in pseudo-hypoparathyroidism; a longitudinal study in 5 patients

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Abstract. In 4 girls and 1 boy with pseudo-hypoparathyroidism growth and physical maturation were followed longitudinally for 7–13 years until adult height had been reached. As a result of early puberty and cessation of growth all patients were relatively shorter as adults than in their childhood years. The difference between average height at the age of 8.0 years and average adult height was 2.25 SD. This observation offers an explanation for the finding in the literature that short stature is more common in adults with this disease than in children. Skeletal age was advanced in all cases and the development of the tubular bones of the hand was more advanced than the development of the round bones. It is possible that this difference resulted from inappropriately early closure of the epiphyseal discs of disproportionally short metacarpals and phalanges. On the other hand it may be an aspecific phenomenon of advanced skeletal maturation.

Stature of patients with pseudo-hypoparathyroidism (PHP) usually is reported to be short. In a large series of 87 adult cases the incidence of short stature, defined as height below 155 cm, was 80% (Nagant de Deuchchaisnes & Krane 1978). In children short stature seems to be less common however: Werder (1979) found a stature below the 3rd percentile in 8 children out of 14 (57%). Early onset of puberty and accelerated skeletal maturation have repeatedly been observed in PHP. Early puberty was first noted by Elrick et al. (1950) in 2 out of 4 patients studied. Several years later Steinhach & Young (1966) concluded from their own investigations and from a survey of the literature that accelerated maturation of the skeleton had occurred in 9 out of 60 patients. Recently Werder (1979) reported a comparable incidence of early puberty and advanced skeletal maturation in a smaller number of patients.

These data from the literature suggest that early puberty in children with PHP of normal or low-normal stature tends to result in subnormal adult height following early closure of the epiphyseal discs and cessation of growth. A longitudinal study of growth and maturation of such children should reveal this in the individual case. In the study by Werder (1979) a number of growth curves are shown, but puberty was not included in each case and the curves were not evaluated numerically. We could not find additional data and we therefore decided to investigate retrospectively growth and maturation in the small number of patients known to us.

Materials and Methods

Subjects

Five patients (4 girls and 1 boy) were studied. The diagnosis rested upon the finding of a decreased level of serum-Ca and an increased level of serum-P, which did not become normal upon repeated administration of parathyroid extract (MacGregor & Whitehead 1954). Since parathyroid extract also failed to increase the urinary excretion of cyclic adenosine monophosphate all patients had PHP type I (Nagant de Deuchchaisnes &
Krane 1978). Short metacarpals and phalanges were present in 4 patients. Throughout the period of observation the children were treated with vitamin D or dihydro- 
tachysterol in dosages sufficient to keep serum-Ca within normal limits. One of the patients in addition had pri-
mary hypothyroidism which had been adequately treated 
with thyroid extract or 1-thyroxine since the age of 5.5 
years. In the other patients thyroid function was normal. 
The children were followed in the outpatient department 
until adult height was reached. The period of observa-
tion included puberty and varied from 7 to 13 years.

Methods

Height was measured to the nearest 0.1 cm at least once 
every year and usually more often with a Harpenden 
stadiometer. From the recorded measurements of height a 
growth curve was constructed by hand (Tanner et al. 
1966). Prepubertal height at age 8.0 years was found by 
extrapolation from this curve. For purposes of calculation 
and comparison height was expressed as the standard 
deviation score (SDS), i.e. the difference between the 
height of the patient and the mean value for height of 
normal children of the same age and sex, divided by the 
standard deviation of height for age and sex. Normal 
values for height and physical maturation of Dutch 
children were taken from van Wieringen et al. (1971). 
Skeletal age was determined several times in each patient 
according to the method of Tanner & Whitehouse (TW2) 
(Tanner et al. 1975). All 3 scoring systems of this method 
were applied: the radius-ulna-short bone score (RUS) to 
determine the state of development of the tubular bones 
of the hand; the carpal bone score (CB) to estimate the 
state of development of the round bones; and the 20 
bone score (20 bones) combining the 2 previous scores in 
a general value for skeletal age.

Results

Height at the age of 8.0 years was within the 
normal range (2SD > height > -2SD) in all patients 
and in 2 patients it was above the mean for 
normal children (Table 1). Adult height was below 
the mean in all cases however and abnormally low 
(< -2SD) in 3 patients. Average adult height was 
2.25 SD less than average height at the age of 8.0 
years.

Physical maturation was enhanced in all patients, 
although it was still within the normal range and the 
acceleration was insufficient to warrant a diag-
nosis of precocious puberty (Bierich 1975). In 
the 4 girls menarche occurred early (average normal 
age for Dutch girls: 13.4 years) and in the boy 
genital development began at the age of 10.0 years 
(average normal for Dutch boys: 11.0 years). Apart 
from its early onset pubertal development was 
entirely normal; there were no signs which might 
indicate a disorder of the hypothalamic-hypo-
physal-gonadal system.

Skeletal age was markedly advanced in all pa-
patients, the RUS-score being more advanced than the 
CB-score. The difference between these 2 scores was 
1.6–2.9 years in the first 4 patients (Table 1). 
Since the CB-score had reached its adult value in 
the X-rays of the 5th patient the difference be-
tween the 2 scores could not be calculated in this 
case. In normal children of comparable age the 
difference between the RUS- and CB-scores has a 
mean of 0 years and a standard deviation of 
0.7–0.8 years (Tanner et al. 1975).

Table 1.

Data on growth and development in 5 patients with pseudo-hypoparathyroidism.

<table>
<thead>
<tr>
<th>Patient</th>
<th>Sex</th>
<th>Height at age 8.0 years (SDS)</th>
<th>Adult height (SDS)</th>
<th>Age at menarche (years)</th>
<th>Skeletal age (years)</th>
<th>at chronological age</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>20 bones</td>
<td>RUS</td>
</tr>
<tr>
<td>1</td>
<td>M</td>
<td>-1.61</td>
<td>-2.79</td>
<td>-</td>
<td>13.8</td>
<td>15.1</td>
</tr>
<tr>
<td>2*</td>
<td>F</td>
<td>+0.45</td>
<td>-2.79</td>
<td>11.8</td>
<td>11.6</td>
<td>13.3</td>
</tr>
<tr>
<td>3**</td>
<td>F</td>
<td>+0.18</td>
<td>-1.29</td>
<td>11.5</td>
<td>10.3</td>
<td>11.4</td>
</tr>
<tr>
<td>4</td>
<td>F</td>
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<td>-1.82</td>
<td>12.8</td>
<td>11.8</td>
<td>12.9</td>
</tr>
<tr>
<td>5</td>
<td>F</td>
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<td>-4.21</td>
<td>12.2</td>
<td>14.0</td>
<td>14.6</td>
</tr>
<tr>
<td>Average</td>
<td></td>
<td>-0.33</td>
<td>-2.58</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

* Hypothyroidism, treated since age 5.5 years. ** No short metacarpals.
Discussion

As a result of early puberty and subsequent epiphyseal fusion all patients were relatively taller before puberty (at the age of 8.0 years) than at the end of growth. The pubertal growth spurt was of insufficient magnitude to compensate for the effect of early maturation on adult height. As an example the growth curve of one of the patients is shown in Fig. 1. Our data offer an explanation for the finding that in PHP short stature appears to occur more often in adults than in children. It must be emphasized however that the pattern of growth and development as seen in our 5 patients is not invariably found in this disease. Werder (1979) has shown that some children grow and mature at a normal rate and do not end up as small adults. The reason why early puberty occurs more often in patients with PHP than in normal adults is unknown. To our knowledge this question has never been studied.

The accelerated skeletal maturation found by all 3 scoring systems in all patients is in agreement with the early onset of puberty. The observed remarkable discrepancy between the RUS- and CB-scores is rarely encountered in normal skeletal development (Tanner et al. 1975) and its occurrence here in the 4 patients in whom it could be determined suggests the presence of a special factor to account for it. First of all it is possible that inappropriately early fusion of the epiphysis to the metaphysis in disproportionally short metacarpals and phalanges, as described by Steinbach & Young (1966), constitutes this factor. Additional evidence in support of untimely fusion has been found in X-ray photographs of the hand of patient No. 2 and has been reported elsewhere (de Wijn & Steendijk (1982). Abnormally early closure of the epiphysial disc of a number of metacarpals and phalanges would imply that skeletal age, as determined by the RUS- and 20 bone-scores is overestimated in such cases. Perhaps this could account for the observation (Table 1) that the RUS- and 20 bone-scores were more advanced than the age at menarche, whereas the CB-score and the age at menarche were approximately equally enhanced.

In the second place Vejvoda & Grant (1981) recently found a similar discrepancy between the RUS- and CB-scores in 10 children with idiopathic precocious puberty and in 10 children with early puberty resulting from congenital adrenal hyperplasia. So, alternatively, it is possible that the discrepancy between the maturation of the tubular bones and the round bones of the hand is an aspecific phenomenon of advanced physical maturation. The observation that the discrepancy between the RUS- and CB-scores was also present in the patient with normally shaped bones of the hand (No. 3) is in agreement with this.

![Growth chart of patient No. 1. The grey area represents the normal range for Dutch children (3rd–97th percentile)](image)
Acknowledgments

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References


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