NOTE

A Patient of Short Stature with Idiopathic Hypoparathyroidism
Round Face and Metacarpal Signs

OSAMU ISOZAKI*, KANJI SATO*, TOSHIo TSUSHIMA*, KAZUO SHIZUME* AND JUNTA TAKAMATSU**

* The Second Department of Internal Medicine, Tokyo Women’s Medical College, Ichigaya-Kawada-cho 10, Shinjuku-ku, Tokyo 162
** The First Department of Internal Medicine, Osaka Medical College, Takatsuki, Osaka

Abstract

A 16-year old girl of short stature, with round face, mental retardation, and Albright’s dimple sign was admitted for evaluation of hypocalcemia. Her serum calcium levels were 6.3–8.0 mg/dl, and phosphorus 6.9–7.8 mg/dl. Although a diagnosis of pseudohypoparathyroidism was initially suggested, her serum iPTH concentration was low (0.1 ng/ml). Furthermore, an injection of synthetic human parathyroid hormone (100 U, hPTH (1-34)) was followed by a marked increase in urinary excretion of cyclic AMP and phosphorus. This case suggests that a shortened metacarpal is not a reliable guide in distinguishing between idiopathic hypoparathyroidism and pseudohypoparathyroidism and that a standard Ellsworth-Howard test is a prerequisite to differential diagnosis.

Patients with pseudohypoparathyroidism are usually associated with obesity, short stature, a stocky build, round face, brachydactyly, and subcutaneous calcification, termed Albright’s osteodystrophy (AOD; Breslau and Pak, 1979; Fitch, 1982). However, patients with pseudohypoparathyroidism without such somatic features were reported in the recent literature (Nusynowitz et al., 1976; Werder et al., 1978). It is confusing, however, that a patient with idiopathic hypoparathyroidism with AOD was reported by Moses et al. (1974) although this patient had only a short 4th metatarsal without other skeletal abnormalities. More recently, a patient with idiopathic hypoparathyroidism with short metacarpals was reported by Le Roith et al. (1979). We report here an additional case of idiopathic hypoparathyroidism involving short stature, round face, and short metacarpals.

Case presentation

A 16-year old girl (Y. T.) was referred to the Tokyo Women’s Medical College Hospital because of short stature and mental retardation in August, 1981. She was born in the 7th month of gestation and weighed
1200 g at birth. Her mental and physical development were retarded from infancy. In schooldays, she was always the smallest in her class and was in a special class for mentally handicapped children. She started menstruation at the age of 16. She had no history of tetany or convulsions. Her parents and an older brother are mentally and physically normal. No consanguineous marriage was noted in the family pedigree.

She was 134.2 cm tall and weighed 37 kg. Her pulse was 88/min and blood pressure 100/70 mmHg. Her face was relatively round. Her neck was short and of webbed type. Her fourth and fifth fingers looked short: when the hands were closed, the knuckles of the affected fingers were replaced by dimples. Ophthalmologic examination disclosed congenital type cataracts in both eyes and a blurred disc margin in the right fundus, indicating pseudo-optic nerve neuritis. She had poorly developed teeth and jaws. No Chvostek's or Trousseau's signs were elicited. There was no abnormality in the chest, the heart, abdomen, or external genitalia except for a small anal fistula. Her memory and calculating ability were very poor. Neurological examination was normal except for decreased grasping power in both hands.

Her serum calcium was 6.3–8.0 mg/dl, phosphorus 6.9–7.8 mg/dl, magnesium 1.7 mEq/L, and total protein was 7.0 g/dl with 3.8 g/dl albumin. Ionized calcium was 1.99 mEq/L (normal range: 2.1–2.4 mEq/L). Other laboratory data such as urinalysis, blood cell count, creatinine, and alkaline phosphatase were in the normal range. An electrocardiogram showed no abnormality. EEG examination revealed sporadic slow wave bursts but no spikes.

Fig. 1. X-ray of the patient’s hands, demonstrating short fourth metacarpals. The metacapal sign is positive in the right, and borderline in the left hand.
Radiological examination revealed no subcutaneous calcification. CT scan of the brain disclosed no calcification of the basal ganglia. Radiography of the hands showed shortening of the 4th and 5th metacarpals of both hands with a positive metacarpal sign on the right hand and a borderline metacarpal sign on the left (Fig. 1). However, no shortness of the distal phalanx was found.

Serum parathyroid hormone concentration, determined by radioimmunoassay specific for the C-terminal region, was less than 0.1 ng/ml (normal range 0.1–0.6 ng/ml). An Ellsworth-Howard test was performed by infusing 100 U (30 μg) of synthetic hPTH (1–34) according to the guideline of the Hormone Receptor Disease Research Committee, the Ministry of Health and Welfare of Japan (Yamamoto, M., et al. 1982). As shown in Table 1, the basal urinary excretion of cyclic AMP was 264 nmoles/h, which increased to 16,800 nmoles/h. The basal urinary excretion of phosphorus was 58.2 mg/2 h, which increased to 116.0 mg/2 h after the infusion.

Serum 25-hydroxyvitamin D₃ was 74.8 ng/ml and 1,25-dihydroxyvitamin D₃ was 27.8 pg/ml (normal range 20–80 pg/ml). Serum calcitonin was 72 pg/ml. Thyroid function test results were all normal; T₄: 7.9 μg/dl, T₃: 183 ng/dl, and TSH 4.9 μU/ml. TSH response to TRH was also normal. The basal prolactin level was normal (6.7 ng/ml) with normal response to TRH. The serum GH level was normal with normal response to an insulin-infusion test. Serum estrogens were normal and LH and FSH responded normally to an LH–RH administration test. Analysis of the chromosomes showed a normal female karyotype of 46 XX.

After discharge, she was prescribed 1α-hydroxycholecalciferol (2–3 μg/day; Alfarol, Chugai Pharmaceutical Co.), and her serum calcium and phosphorus levels have gradually returned to normal in the last 13 months.

Discussion

The differential diagnosis of idiopathic hypoparathyroidism and pseudohypoparathyroidism is of great importance since the etiology, clinical course (especially subcutaneous calcification), and response to therapy are different: an average dose of 1α-hydroxycholecalciferol sufficient to maintain the normal calcium concentration in patients with pseudohypoparathyroidism is about 2 μg/day, but should be doubled in treating patients with idiopathic hypoparathyroidism (Okano et al., 1982).

Traditionally, patients with pseudohypoparathyroidism, or PTH-resistant hypoparathyroidism, are associated with short stature, a stocky build, round face, brachydactyly, obesity, and subcutaneous calcification, and, in most instances, are easily distinguished from those with idiopathic

<table>
<thead>
<tr>
<th>Time</th>
<th>11:00</th>
<th>12:00</th>
<th>13:00</th>
<th>14:00</th>
<th>15:00</th>
</tr>
</thead>
<tbody>
<tr>
<td>Urine</td>
<td>(1)</td>
<td>(2)</td>
<td>(3)</td>
<td>(4)</td>
<td></td>
</tr>
<tr>
<td>Urine volume (ml/h)</td>
<td>285</td>
<td>110</td>
<td>205</td>
<td>180</td>
<td></td>
</tr>
<tr>
<td>Phosphorus (mg/h)</td>
<td>35.9</td>
<td>22.3</td>
<td>58.8</td>
<td>57.2</td>
<td></td>
</tr>
<tr>
<td>creatinine (mg/h)</td>
<td>59.6</td>
<td>43.1</td>
<td>46.1</td>
<td>45.0</td>
<td></td>
</tr>
<tr>
<td>cyclic AMP (nmol/h)</td>
<td>---</td>
<td>264</td>
<td>---</td>
<td>16,000</td>
<td>---</td>
</tr>
</tbody>
</table>

The patient was asked to drink 200 ml water every hour throughout the test, and urine was collected. At 1:00 P. M., 100 U of hPTH (1–34) (30 μg) was injected intravenously.
hypoparathyroidism, since the latter entirely lack such somatic features. However, a number of patients with pseudohypoparathyroidism without AOD were recently reported (Nusynowitz et al., 1975; Werder et al., 1978), but, to our knowledge, no patient with idiopathic hypoparathyroidism with full-blown features of AOD has been so far reported. Since the present case showed several features compatible with AOD, i.e., short stature, round face, and short metacarpals in addition to mental retardation, we initially suspected pseudohypoparathyroidism. However, her serum PTH concentration was low and the kidneys responded very well to exogenous PTH, resulting in a marked increase in urinary excretion of cyclic AMP and phosphorus, as found in patients with idiopathic hypoparathyroidism (Werder et al., 1978). It should be pointed out that borderline or positive metacarpal signs can be found in 10% of normal male hands and 13% of normal female hands (Slater, 1970; Bloom, 1970), so that skeletal abnormality of a short 4th or 5th metacarpal or metatarsal alone is not sufficient to warrant a diagnosis of AOD (Fitch 1982; Yamamoto, 1982). In view of a number of case reports of pseudohypoparathyroidism and pseudo-pseudohypoparathyroidism, criteria for AOD are not strict and the diagnosis of AOD is made quite arbitrarily in some cases. According to a recent review of Fitch (1982), Moses' case with idiopathic hypoparathyroidism with only a short metatarsal was erroneously identified as AOD. We presume that our present case had a sporadic form of idiopathic hypoparathyroidism, and had short metacarpals, but this did not have any relation to AOD, since the distal phalanx of the digits is not shortened (Poznanski, 1979).

As pointed out by Le Roith et al. (1979), it is essential to measure both the serum PTH level and the response of urinary cyclic AMP and phosphorus to exogenous PTH especially in such a hypoparathyroid patient with Albright's sign. Furthermore, since the metacarpal sign is not rare, patients with only a shortened 4th or 5th metacarpal or metatarsal should not be made an over diagnosis of AOD (Fitch, 1982).

Acknowledgment

The authors thank the Pseudohypoparathyroidism Study Group, Hormone Receptor Disease Research Committee, the Ministry of Health and Welfare of Japan, for supplying hPTH (1–34), Dr. Michiko Yamamoto, the Fourth Department of Internal Medicine, University of Tokyo, for advice in preparing the manuscript, and Mrs. K. Matsumoto for typing the manuscript. We are also indebted to Drs. Y. Nishi and M. Fukushima, Chugai Pharmaceutical Co., for measuring vitamin D metabolites in the serum.

References

