A Case of Cutaneous Ossification occurring in Pseudohypoparathyroidism

Hyohyun Ahn, M.D., Ki Sung Kim, M.D., Il Hwan Kim, M.D., Hae Jun Song, M.D., Hae Won Cheon, M.D.*, Joo Won Lee, M.D.*, Chil Hwan Oh, M.D.

Department of Dermatology, Department of Pediatrics, College of Medicine, Korea University*

In Albright's hereditary osteodystrophy (AHO) including the syndromes of pseudohypoparathyroidism (PHP) and pseudopseudohypoparathyroidism (PPHP), multiple areas of intracutaneous ossification are often encountered. The characteristic features are short stature, round face, short neck, obesity, cutaneous ossifications, and various skeletal anomalies including short metacarpal and metatarsal bones, curve of radius, and brachydactyly.

The patient was a 10-month-old male infant. He presented slightly depressed erythematous hard plaques on the left upper chest and left thigh. We had taken biopsies from both skin lesions, confirming cutaneous ossification or bone formation. He also had the characteristic features of AHO. He had a history of admission due to patent ductus arteriosus and atrial septal defect. The laboratory results showed slightly decreased calcium, increased phosphorus and PTH levels. The patient received no specific corrective measures because his calcium and phosphorus levels were not far from normal values until newly developed similar skin lesions appeared.

(Ann Dermatol 11(4) 263~266, 1999).

Key Words : Cutaneous ossification, Pseudohypoparathyroidism.

In Albright's hereditary osteodystrophy (AHO) including the syndromes of pseudohypoparathyroidism (PHP) and pseudopseudohypoparathyroidism (PPHP), multiple areas of intracutaneous ossification are often encountered[1,2,3]. The characteristic features are short stature, round face, short neck, obesity, cutaneous ossifications, and various skeletal anomalies including short metacarpal and metatarsal bones, curve of radius, and brachydactyly[1-5]. There would be a member of family with a similar phenotype[3,4].

PHP is a pathologic condition of which a basic defect is an end organ resistance to parathyroid hormone (PTH). So it mimics hypoparathyroidism, manifesting as lower calcium and higher phosphorus. But, in contrast to hypoparathyroidism, it has a higher PTH level. PPHP is thought as a variant of PHP with AHO phenotype, but has no end organ resistance to PTH as in PHP, resulting in normal calcium and phosphorus level, and normal PTH level[2]. But, because there is a wide variability in this disorder, the term AHO is preferred rather than dividing it into PHP, PPHP[3].

The cutaneous bone formation is either primary or secondary. The formers are AHO and osteoma cutis, and the latter are those from metaplasia of previous skin lesions[6].

REPORT OF A CASE

The patient was a 10 month-old male infant. He presented slightly depressed erythematous hard plaques on the left upper chest and left thigh from birth (Fig. 1,2). He had a history of admission due to a patent ductus arteriosus and an atrial septal defect. The initial body weight was within normal limits. His mother also had similar skin lesions, and he was an only child. The physical examination showed obesity, weighing 15-kilo gram when he

Received October 14, 1998.
Accepted for publication January 11, 1999.
Reprint request to : Hyohyun Ahn, M.D., Department of Dermatology, College of Medicine, Korea University

Table 1. Laboratory findings

	96.11.18.	96.12.18.	97.12.18.	97.3.25.
Total Ca (9~11mg/dl)	10.2	9.4	9.5	9.4
ionized Ca (4.4~4.9mg/dl)	4.6	3.8 ↓	4.5	4.3 ↓
Phosphorus (4.0~7.0mg/dl)	7.1 ↑	6.3	7.2 ↑	7.5 ↑
Magnesium (1.6~2.6mmol/l)	*	1.92	*	*
Alkaline phosphatase (145-420IU/l)	185	151	175	205

*: Not performed

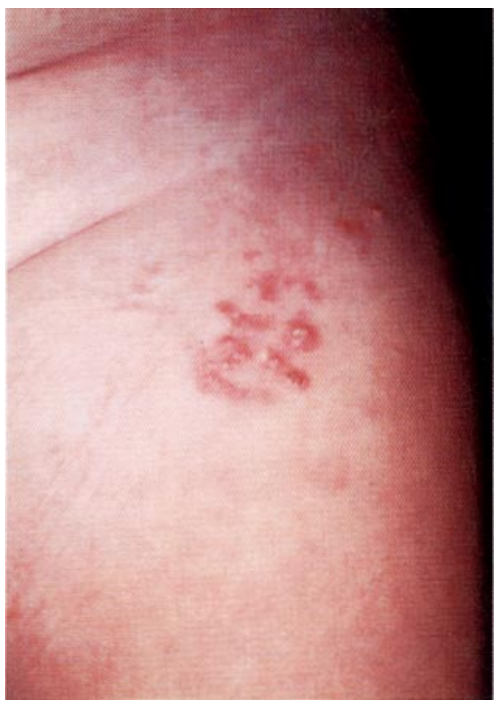

Fig. 1. Irregularly surfaced hard plaque on the left thigh.

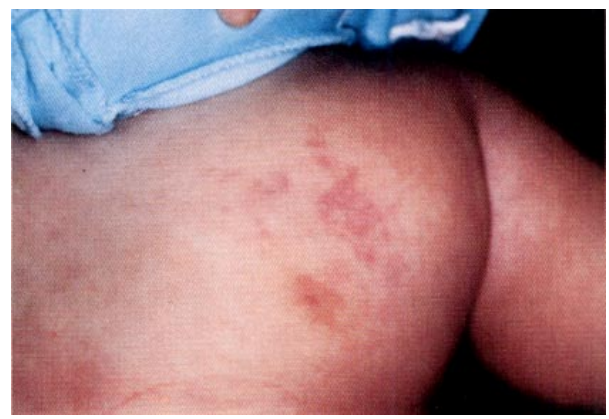

Fig. 2. Similar skin lesions on the left upper chest.

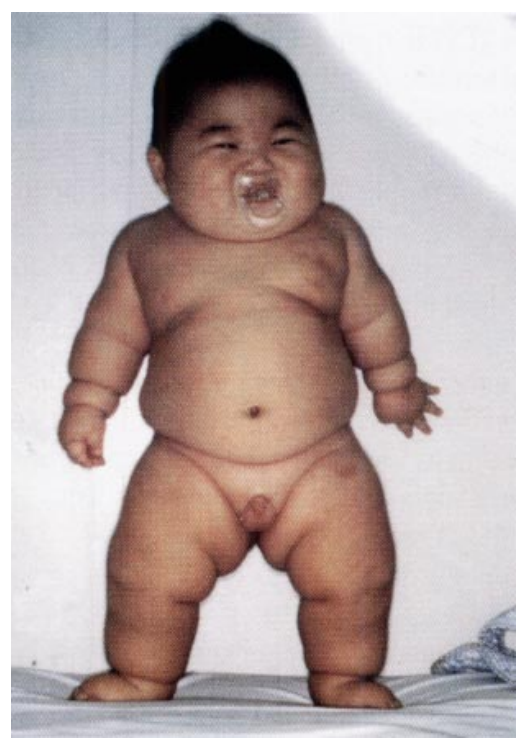

Fig. 3. Whole body view showing short stature, round face, short neck and obesity.

was 10 month old, round face, short neck, and short stature (Fig. 3). Those suggested the characteristic features of AHO.

We had taken biopsies from both lesions, confirming cutaneous ossifications or bone formations (Fig. 4). The laboratory results serially taken from him showed slightly decreased calcium, and increased phosphorus (Table 1). Parathyroid hormone was increased to 395 pg/ml (normal 9~55 pg/ml), and urinary cyclic AMP was decreased down to 2.8 μmol/day (normal 4.4~14.5 μmol/day). The other laboratory results such as complete blood cell count, serology, thyroid function test, cortisol, corticotropin, 1,25-(OH)2 vitamine D3, chromosomal analysis, and electroencephalogram were normal. The radiologic evaluations

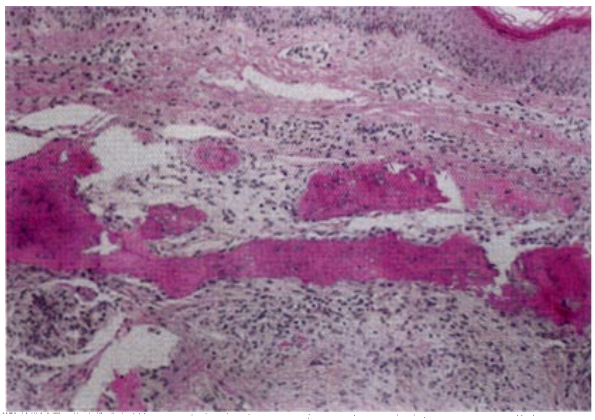

Fig. 4. The photomicrograph showing irregular bony spicules and osteocytes.

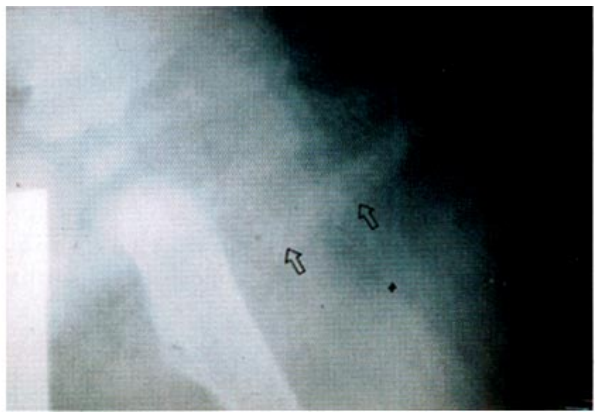

Fig. 5. The part of femur AP view showing soft tissue calcification (indicated by the arrows).

showed soft tissue calcifications on the identical sites perceived by palpation (Fig. 5).

Diagnosed as normocalcemic PHP evolved from PHP type Ia, he didn't show any symptoms and signs from overt hypocalcemia, so 5 months had elapsed without specific corrective measures. But, recently, finding a few newly developed similar skin lesions, we subscribed vitamin D preparations.

DISCUSSION

The cutaneous ossification is composed of the primary and the secondary. The former consists of AHO having their characteristics of itself, and osteoma cutis without those, and the latter are those developed from metaplasia within preexisting lesions, namely, cutaneous tumors, cicatrices, chronic venous insufficiency, and inflammatory conditions[6,7].

As a phenotype of the PHP and PPHP, our patient showed abnormal cutaneous ossifications and peculiar characteristics such as a short stature, round face, short neck, and obesity. AHO may be characterized by other calcifications such as intracranial calcification, especially basal ganglia, and lenticular calcification leading to cataracts. The additional characteristic features include curvature of radius, brachydactyly, short broad nail and shortening of metatarsal and metacarpal bone of especially 4th and 5th fingers presenting as 'knuckle sign' or 'Albright dimple sign'. The other characteristics are abnormal dentitions, moderate degree of mental retardation, and seizure. It is known to inherit as an autosomal dominant disorder[1,2,3,7].

Normocalcemic pseudohypoparathyroidism is thought as a compensated state in a patient with PTH resistance, so the patient is able to maintain a normal serum calcium level without treatments[1]. PTH-mediated osteoclastic bone resorption, enhanced phosphate clearance, and a normal distal tubular calcium reabsorption may contribute to the maintenance of serum calcium level[8].

The pathophysiologic mechanism involved in PHP is uncertain, and research into this has carried on for decades. Considering the variability of this disorder, one can expect the multiple defects in PHP. One report showed that three different pathophysiologic mechanisms are probably responsible for PHP[9].

In an ordinary setting, the diagnosis of PHP can be considered if one sees a patient with biochemical hypoparathyroidism i.e. hypocalcemia and hyperphosphatemia, and an elevated PTH level. Because the reduced magnesium level can blunt the response of end organ to PTH, it is important to exclude hypomagnesemia. Finding the unique anomalies mentioned above including cutaneous ossifications provides additional evidences. But, to confirm the diagnosis and to distinguish the variants, additional tests are indicated. The Ellsworth-Howard test and Gs α subunit assay are those[1,2]. The former test is seeing a urinary cyclic AMP response to PTH given exogenously. It differentiates PHP type I from PHP type II and other equivocal cases.

In our case, these tests were not performed, because his baseline urinary cyclic AMP level was lower than normal even though he had abnormally high

endogenous PTH, presenting his resistance to PTH. Gsα subunit assay is indicated in the case of difficulty of differentiating clinically between PHP type Ia and Ib, unlike this case.

In conclusion, because it is one of the systemic diseases with cutaneous manifestations, we, as dermatologists, seeing a cutaneous lesion of bone formation, must keep an eye out for the characteristic features of AHO, because systemic disease like this may be overlooked.

REFERENCES

1. Moore WT, Eastman RC: Laboratory evaluation of calciotropic hormones and minerals. In Diagnostic endocrinology. 2nd edition. Mosby-Year Book Inc, St. Louis, 1996, pp 425~426
2. DiGeorge AM: Pseudohypoparathyroidism. In Behrman RE, Behrman RE, Kliegman RM, Nelson WE: In Nelson textbook of pediatrics. 15th edition. WB Saunders Company, Philadelphia, 1995, pp1608~1609
3. Eyre WG: Albright's hereditary osteodystrophy with cutaneous bone formation. Arch Dermatol 104:635~642, 1971.
4. Kwon SW, Lee HJ, Choi SY, Yoon UK: Two cases of pseudohypoparathyroidism in siblings. Journal of the Korean pediatric society 36:882~886, 1993.
5. Kim TW, Oh ES, Ko KW: A case of pseudohypoparathyroidism. Journal of the Korean pediatric society 17:293~298, 1970.
6. Barranco VP:Cutaneous ossification in pseudohypoparathyrodism. Arch Dermatol 104:643~647, 1971.
7. Na GY, Kim YH, Min PK, Hwang SJ: A case of cutaneous ossification in pseudohypoparathyroidism. Kor J Dermatol 34:842~846, 1996.
8. Breslau NA: Pseudohypoparathyrodism: Current concepts. Am J Med Sci 298:130~140, 1989.
9. Radeke HH, Aufmkolk B, Juppner H, Krohn H, Keck E, Hesch R: Multiple pre- and postreceptor defects in pseudohypoparathyroidism(a multicenter study with twelve four patients) J Clin Endocrinol Metab 162:393~402, 1986.