ELEVATED PTH LEVEL IN THE FLUID OF A SOLITARY BONE CYST

—— A Case Report ——

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INTRODUCTION

Solitary bone cyst is a common benign lesion in children. The lesion is nearly always located in the long tubular bone[1].

The pathological entity was established about seventy years ago[2]. However, considerable confusion still exists concerning the pathogenesis of this disease.

Solitary bone cyst was once thought to be a "healing form of giant-cell tumor or osteitis fibrosa", or "encapsulation and alteration of a focus of intramedullary hemorrhage". It has also been postulated that an abnormality of development and maturation of the long bone or a circulatory disturbance may be a pathogenic mechanism.

The chemical composition of the fluid in solitary bone cysts has been investigated by Cohen[3,4] and Neer[5] precisely. Cohen notes that the chemical constituents of the fluid in simple bone cysts are similar to those of serum[3]. Neer shows the elevation of bilirubin, lactic dehydrogenase, and alkaline phosphatase[4]. To our knowledge no one reports the value of the calcium regulating hormones in the fluid in a solitary bone cyst. Parathyroid homone (PTH), 1,25-$(OH)_2$ vitamin D_3 (cholecalciferol), calcitonin are essential hormones affecting bone metabolism. The investigation of such hormones might yield information about the etiology of this disease. This case report records such data.

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CLINICAL MATERIAL

The patient is an eleven year-old boy. The birth was normal. He grew up without any diseases till 5 years old. He was found to have a cyst in the proximal metaphysis of his right femur with a limping gait persisting for 2 months after contusion when he was 5 years old. X-ray films (Fig. 1) showed a large expansil radiolucent area in the intertrochanteric region and very thin cortical bone especially in the calcar. Pathological fracture through cyst was noticed in the lateral view film. He underwent operation on the 19th, November, 1976. Curettage and heterogenous bone graft with Kiel bone were carried out (Fig. 2). Solitary bone cyst was proven pathologically. He was discharged a month later. Recurrence was noticed 1 year later (Fig. 3). Bone cyst somewhat enlarged 5

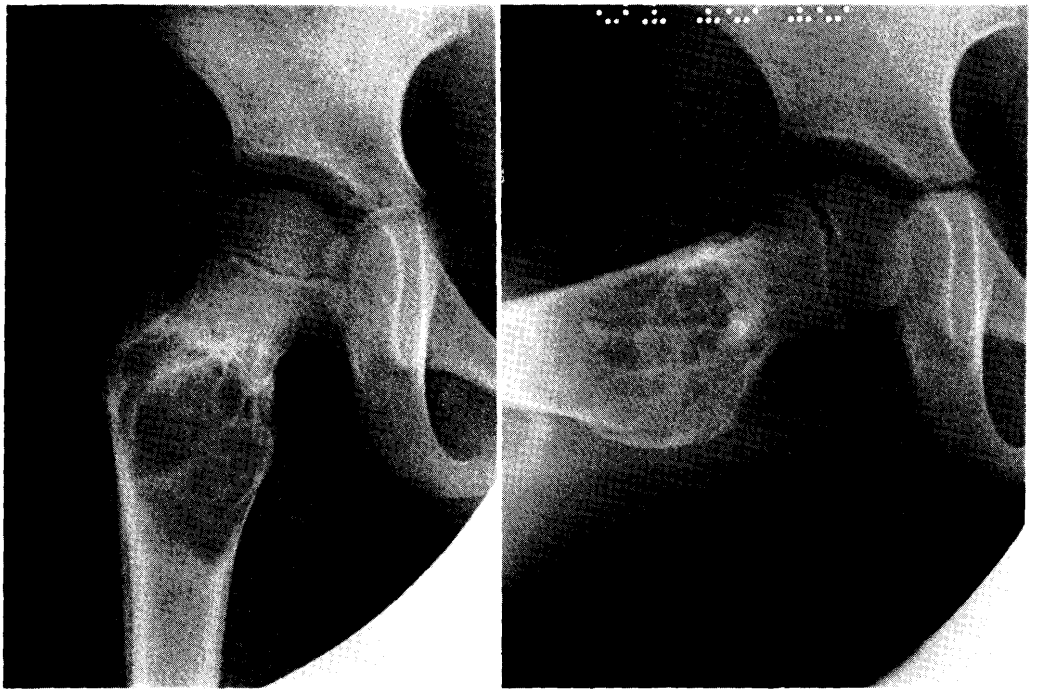

Fig. 1 Preoperative radiograph, 5 years old.

Fig. 2 Postoperative radiograph.

years after operation. He was admitted again on the 29th, June, 1983. X-ray films showed coxa valga and the deformity of the greater trochanter on the right side. The radiolucent area was obvious and the cortical bone of the calcar became thin again (Fig. 4).

Computed tomogram was taken. The femoral neck and shaft were cut at every 1 cm slice. Fig. 5 shows multilocular cyst with thin cortex near to the lesser trochanter which may be fractured.

Physical examination revealed muscle atrophy in the right thigh. Measurement of limb length from the anterior superior iliac spine to the tip of the medial malleolus was equal. The hips and knees showed a full range of painless motion. There was no redness or swelling of the right lower extremity and no tenderness to deep palpation or pain on percussion of the heel or trochanter.

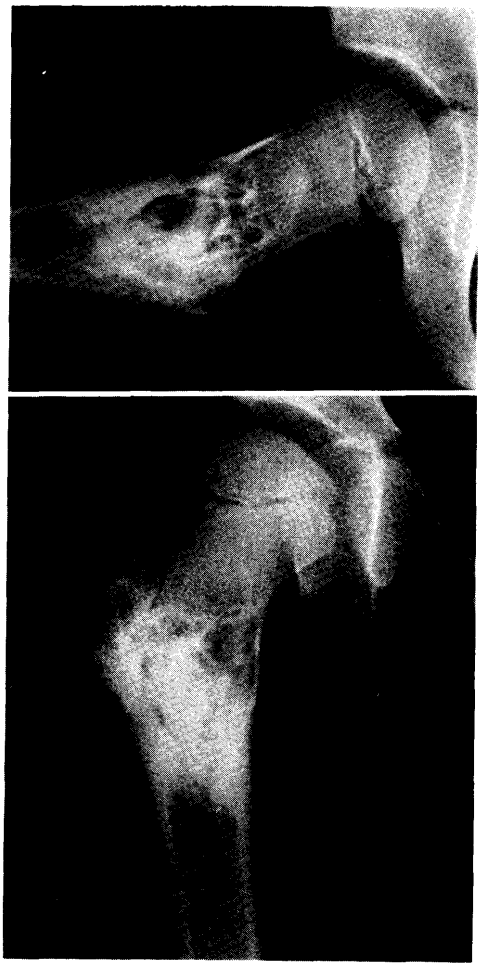

Fig. 3 One year later after the operation.

Fig. 4 Six years later after the operation.

Serum biochemistry is shown in Table 1. The values of alkaline phosphatase and acid phosphatase had increased. GOT, GPT, LDH, total protein, albumin, total bilirubin, total cholesterol, creatinine, uric acid, BUN, glucose, Mg, Ca, P, Na, K, Cl were all normal. LDH isozyme and protein electrophoresis were also normal. CRP and RA were negative. Blood cell count, hemogram and urinalysis were normal.

INJECTION OF METHYLPREDNISOLONE ACETATE AND NATURE OF THE FLUID

Direct puncture and injection of microcrystalline corticosteroid was carried out under local anaesthesia on the 16th, July, 1983. An 18-gauge needle was inserted under fluoroscopic guidance. Intracystic pressure was 90 mm H_2O. Pulsation was noticed. The hydrostatic pressure was increased by Valsalva maneuver. Eleven ml of intracystic fluid were removed. It was serous mixed with a small amount of blood. Then a radiopaque contrast medium (Amipaque) was injected into the cyst, and an X-ray picture was taken (Fig. 6-A). A trocar was inserted and used for irrigation with 100 ml of normal saline (Fig. 6-B). The patient complained of severe pain when the pressure of the injection was

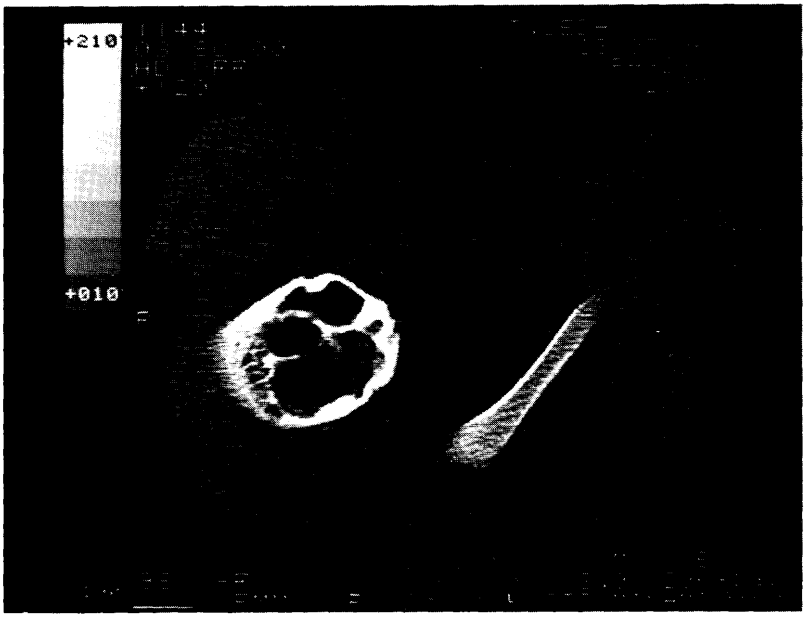

Fig. 5 CT-scan.

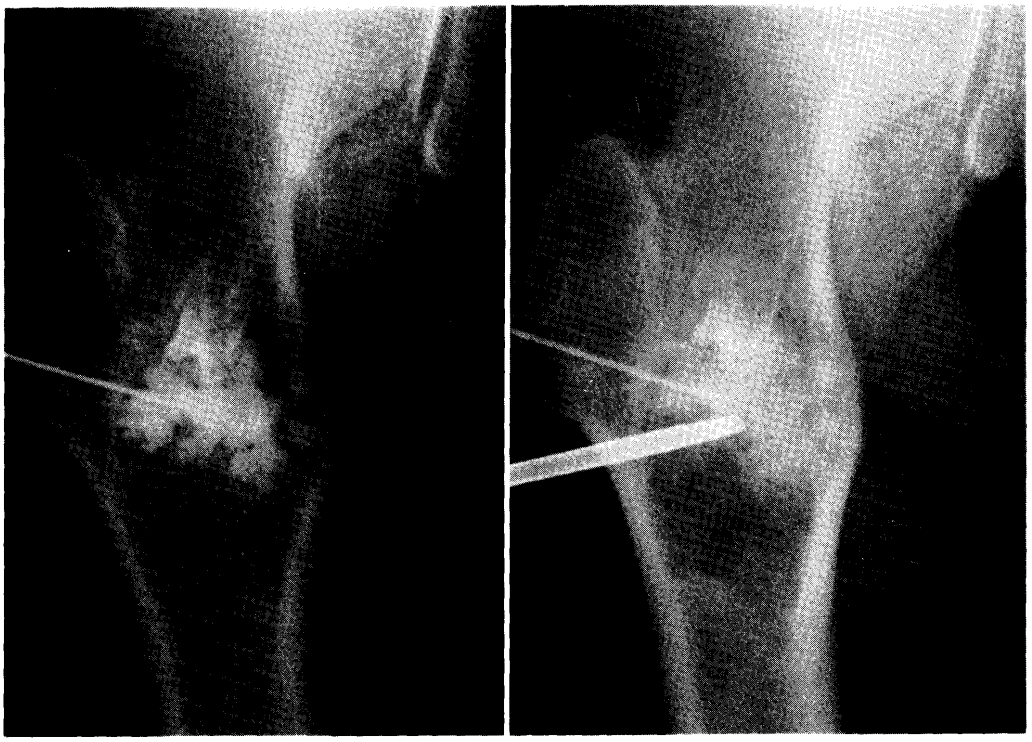

Fig. 6-A **Fig. 6-B**

Fig. 6-A (left) Intracystic injection of Amipaque.
Fig. 6-B (right) Irrigation with normal saline.

Table 1 Laboratory findings

GOT	16	(12～ 32)	IU/L
GPT	9	(5～ 26)	〃
LDH	443	(228～ 475)	〃
ALP	219H	(15～ 70)	〃
Acid P	6.5H	(1.0～ 4.0)	〃
T.P.	7.5	(6.8～ 8.5)	g/dl
ALB	4.5	(4.0～ 5.1)	〃
T-Bil	0.7	(0.1～ 0.9)	mg/dl
T-Cho	134	(120～ 260)	〃
Cre	1.0	(0.6～ 1.3)	〃
U.A.	5.3	(3.0～ 7.6)	〃
BUN	17	(8～ 22)	〃
Glu	78	(70～ 110)	〃
Mg	2.7	(2.2～ 3.1)	〃
Ca	9.3	(8.2～ 9.8)	〃
P	4.9	(2.9～ 4.7)	〃
Na	143	(136～ 146)	mEq/L
K	4.2	(3.6～ 4.9)	〃
Cl	106	(100～ 110)	〃
WBC	4.9 $\times 10^9$/L		
RBC	4.67$\times 10^{12}$/L		
PLT	278 $\times 10^9$/L		
CRP	(−)		
RA	(−)		
LDH I	28.4	(17.6～34.0)	%
II	31.2	(32.4～41.6)	〃
III	30.2	(21.2～29.6)	〃
IV	7.5	(1.7～11.7)	〃
V	2.4	(0.7～ 8.3)	〃
ALP II	(+)		
ALP III	(+)		
Protein electrophoresis			
Alb	59.4	(58～ 68)	%
α_1-G	3.1	(2～ 5)	〃
α_2-G	10.1	(6～ 11)	〃
β-G	10.5	(7～ 12)	〃
γ-G	16.6	(12～ 17)	〃

raised or the cyst fluid was sucked forcefully. Eighty mg of methylprednisolone acetate (Depo-Medrol) was injected into the solitary bone cyst through an 18-gauge needle after removal of the trocar.

The chemical data of the fluid contents of bone cyst is shown in table 2 and compared with those of the plasma. Acid phosphatase value in the cyst fluid was as much as 5.5 times that of venous blood. Alkaline phosphatase, about twice. Total bilirubin, more than 11 times. However, total protein content of the cyst fluid was about three quarters of plasma protein level.

Table 2 Biochemical data of the fluid contents of bone cyst compared with the plasma in venous blood

		Plasma	Bone cyst
ALP	(15～70 IU/L)	175 H	375 H
Acid P	(1～4 K.A.)	6.0 H	33.0 H
T.P	(6.8～8.5 g/dl)	7.6	5.7 L
ALB	(410～511 g/dl)	4.4	3.5 L
T-Bil	(0.1～0.9 mg/dl)	0.4	4.6 H
T-Cho	(120～260 mg/dl)	138	115
GOT	(12～32 IU/L)	20	16
GPT	(5～26 IU/L)	22	8
LDH	(228～475 IU/L)	344	398
UA	(3.0～7.6 mg/dl)	4.5	3.9
BUN	(8～22 mg/dl)	11	11
GLU	(70～110 mg/dl)	80	86
Mg	(2.2～3.1 mg/dl)	2.2	2.0
Ca	(8.2～9.8 mg/dl)	9.9	9.1
P	(2.9～4.7 mg/dl)	4.1	3.7
Na	(136～146 mEq/L)	136	139
K	(3.6～4.9 mEq/L)	4.8	4.1
Cl	(100～110 mEq/L)	99	101

H: High L: Low

Table 3 shows the value of calcium regulating hormones in the plasma, cyst fluid and the plasma of normal bone marrow

Table 3 Calcium regulating hormones in the fluid of bone cyst compared with the plasma in venous blood and bone marrow blood

		Plasma	Bone cyst	Bone marrow
PTH	(0.6>ng/ml)	0.24	0.61	0.26
CT	(0.3>ng/ml)	0.014	0.020	0.030
25-OH D_3	(7～25 ng/ml)	15.0	13.6	27.6
1, 25-$(OH)_2D_3$	(18～68 pg/ml)	50	67	—

aspirated from the left greater trochanter.

PTH(C-terminal) value in the cyst fluid was 0.61 ng/ml, which was much higher than that in plasma (0.24 ng/ml) or in the normal bone marrow plasma (0.26 ng/ml).

The value of calcitonin was highest in the normal bone marrow plasma (0.030 ng/ml), next in the cyst fluid (0.020 ng/ml), and lowest in plasma (0.014 ng/ml).

Concerning 25-OH Vit. D_3, the value in the normal bone marrow plasma was highest (27.6 ng/ml) and the value in the cyst fluid was lowest (13.6 ng/ml).

The 1,25-$(OH)_2$ Vit. D_3 level of the cyst fluid (67 pg/ml) was slightly higher than in that of plasma (50 pg/ml).

DISCUSSION

This may be the first report to mention the calcium regulating hormones in the fluid of the solitary bone cyst. These hormones seem to be an important factor concerning the behavior of the cyst. The recurrence rate following surgery was reported as 40-50% (Jaffe[1]), 50% (Wilber and Hyatt[6]), 45% (Spence et al.[7]), humeral; 30%, femoral; 17% (Neer et al.[5,8]) and 5% (Fahey and O'Brien[9]). Hypothetical factors in recurrence summarized by Neer[5] are sinusoidal obstruction (Cohen[3]), hydrostatic pressure (Cohen[4]), osmotic pressures of the cyst fluid (Neer[5]), and acid phosphatase activity. The difference in the recurrence rate between the active phase and latent phase was not significant[10].

The main calcium regulating hormones are parathyroid hormone, calcitonin and 1,25-$(OH)_2$ vitamin D_3 (cholecalciferol). The action of PTH on bone tissue is the mobilization of calcium from bone through osteocytic and osteoclastic bone resorption[11]. It stimulates osteocytic osteolysis[12] and the formation of osteoclast[13]. Calcitonin has a protective effect against osteolysis and decreases the resorption of calcium from the bone[14]. 1,25-$(OH)_2$ Vit. D_3 may have a role in mobilizing calcium from bone[15,16]. A high-affinity receptor for 1,25-$(OH)_2$ Vit.D_3 has been detected in bone[17]. A vitamin D-dependent Ca-binding protein has also been observed in an extract of chick bone[18].

The PTH level in the cyst fluid was as much as 3 times higher than that of plasma and normal bone marrow plasma. Two mechanisms were proposed concerning the high value of PTH in the cyst fluid. One is that PTH might be produced by the lining membrane of the bone cyst wall. Another is that the elevated value of C-terminal PTH might be caused by the congestion of the cyst fluid.

The calcitonin levels were all within normal range.

The value of 25-OH Vit. D_3 in cyst fluid was lower than in normal bone marrow plasma. But the value of 1,25-$(OH)_2$ Vit. D_3 in the cyst fluid was higher than in plasma. It is difficult to explain this phenomenon. One hypothesis is that 1-hydroxylation of 25-OH Vit. D_3 might happen in the bone cyst. 1-hydroxylation by macrophage has been proposed in sarcoidosis[19], and macrophages are rich in bone marrow. Another hypothesis is that blood-cyst membrane-barrier might actively transport 1,25-$(OH)_2$ Vit. D_3 from blood to cyst.

We consider that local environment is more important rather than systemic condition in solitary bone cyst. Such local factors as prostaglandin or osteoclast activating factor (OAF), shall be investigated.

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