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A Case of Primary Hyperparathyroidism with Hypercalcemic Nephropathy in Children

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Primary hyperparathyroidism is a rare disease in children and is characterized by conspicuous skeletal and renal changes. A 12 year old male patient presented with symptoms of polydipsia, polyuria, general weakness, nausea, and vomiting which had begun 3 months earlier, and showed typical laboratory findings of primary hyperparathyroidism. Confirmatory diagnosis was made by elevated parathyroid hormone concentration in serum, technetium-thallium subtraction scan imaging method and histopathologic finding of chief cell hyperplasia. The laboratory findings revealed elevated levels of BUN, creatinine and decreased GFR. Kidney biopsy showed typical calcium deposits in tubules with marked tubulointerstitial infiltration. After subtotal parathyroidectomy, clinical findings improved remarkably.

Key Words : *Primary hyperparathyroidism, Hypercalcemic nephropathy, Parathyroid hyperplasia, Children.*

INTRODUCTION

Primary hyperparathyroidism is rare in children. Since the introduction of automated biochemical determinations of serum calcium and the increasing availability of parathyroid hormone radioimmunoassay, the prevalence of primary hyperparathyroidism has been much higher than was recognized previously. However, reports on children with primary hyperparathyroidism are still uncommon.

Until 1982, only 86 cases had been described in the literature (Girard et al., 1982), and only two cases of primary hyperparathyroidism in children had been reported in Korea (Kim et al., 1988; Park et al., 1992). Children with primary hyperparathyroidism have a high frequency of detectable bone changes, but renal lesions seem to be less common in children than in adults (Bjernulf et al., 1970).

In the present paper, we report a case of primary hyperparathyroidism with hypercalcemic nephropathy in a 12 year old boy in Korea.

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CASE REPORT

A 12 year old boy visited our hospital because of general weakness, vomiting, polyuria and polydipsia of 3 month duration. In the outpatient clinic, routine electrolyte measurement revealed a high serum calcium level of 13.7mg/dl. There was no specific past or family history.

On admission, his body temperature was 36.6℃, pulse rate 95 beats/min, respiratory rate 24 times/min and blood pressure 100/70mmHg. He was 127cm tall and weighed 22kg.

On examination, he appeared weak and chronically ill. Although consciousness was clear, his

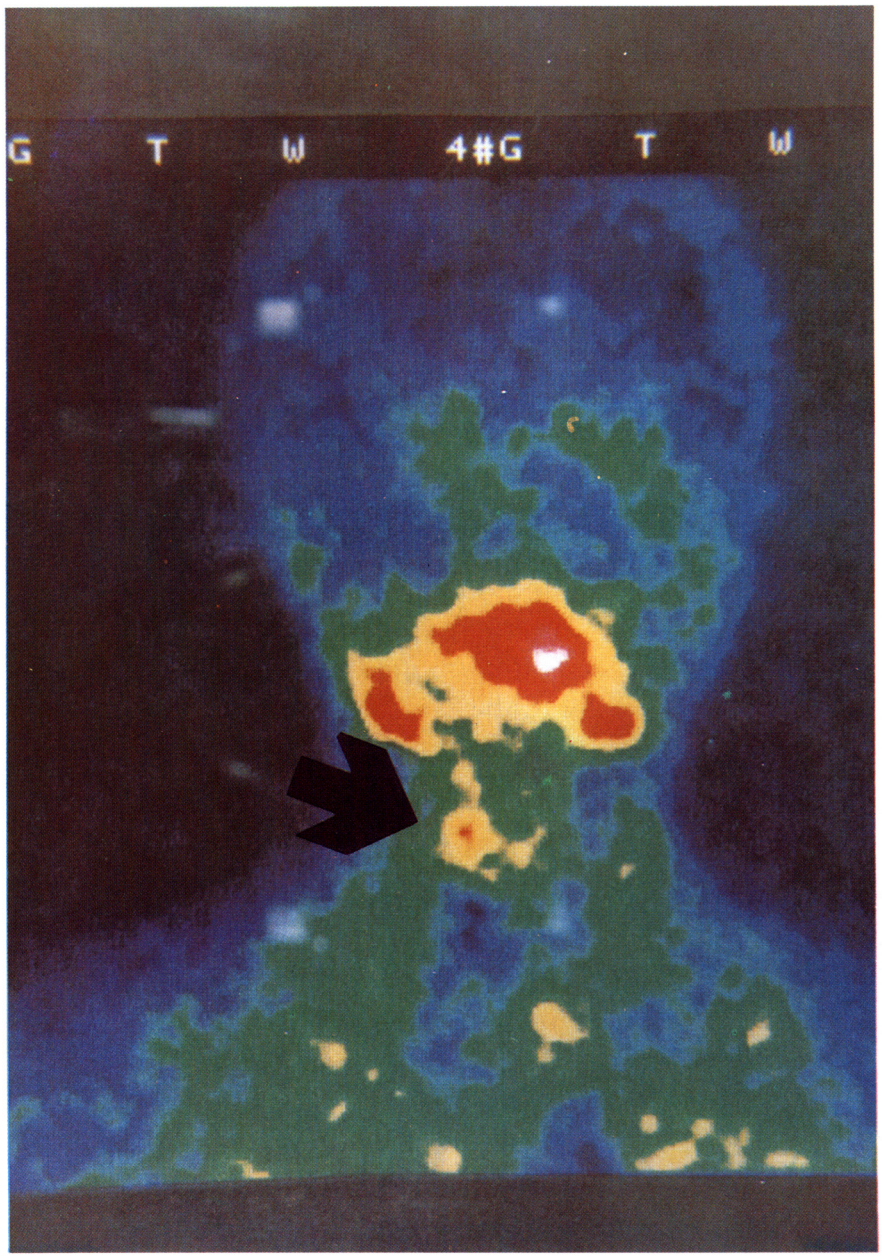

Fig. 1. Technetium-thallium subtraction scan shows hot uptake on the lower part of right parathyroid gland(arrow marking).

general appearance and nutritional condition were not good. The head and neck were normal and no mass was palpated in the cervical area. The lungs were clear and the heart was normal. The abdomen and extremities were normal. No abnormal neurological findings were found.

Laboratory data on admission were as follows: Hemoglobin and hematocrit were 11.4g/dl and 32.6%; white cell count was 8,600/mm^3; serum electrolytes were 138mEq/L for sodium, 4.0mEq/L for potassium, 111mEq/L for chloride, 13.7mg/dl for calcium (Ca^{++} 5.4mg/dl) and 5.3mg/dl for phosphorous; BUN 38mg/dl; creatinine 4.2mg/dl; alkaline phosphatase 142U/L (normal for the age: 20-150U/L); liver function tests were normal; urine analysis was normal except for specific gravity 1.010; 24 hours urine study showed volume 2,300ml, osmolality 122mOsmol/kg H_2O, creatinine 437mg/day, calcium 246mg/day (8.8mg/kg, normal<4mg/kg) phosphorus 265mg/day (normal: 300-1,300mg/day), creatinine clearance 12.6ml/min/1.73m^2; Serum parathyroid hormone(PTH) by RIA was 2.8ng/ml (normal : 0-0.5ng/ml), serum Vit-D_3 by RIA 12.1ng/ml (normal : 24.3±14ng/ml).

Roentgenograms of the skull, long bones, and hands were normal. Ultrasonograms of the neck and kidneys were normal. Bone scan was normal, and technetium-thallium parathyroid subtraction scan showed hot uptake on the lower part of the right parathyroid gland (Fig. 1).

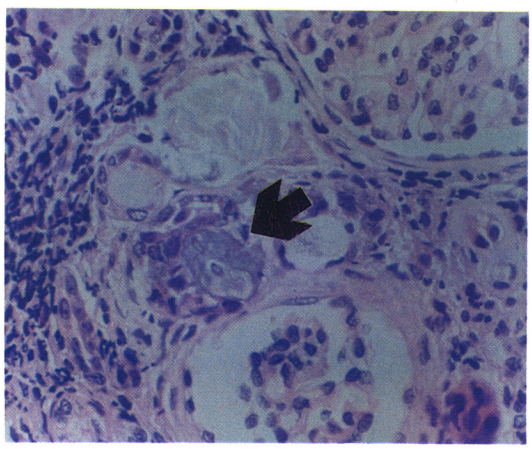

Fig. 2. Kidney biopsy finding shows calcium deposit in tubule(arrow marking) with marked cellular infiltration in tubulointerstitium(H & E,×200).

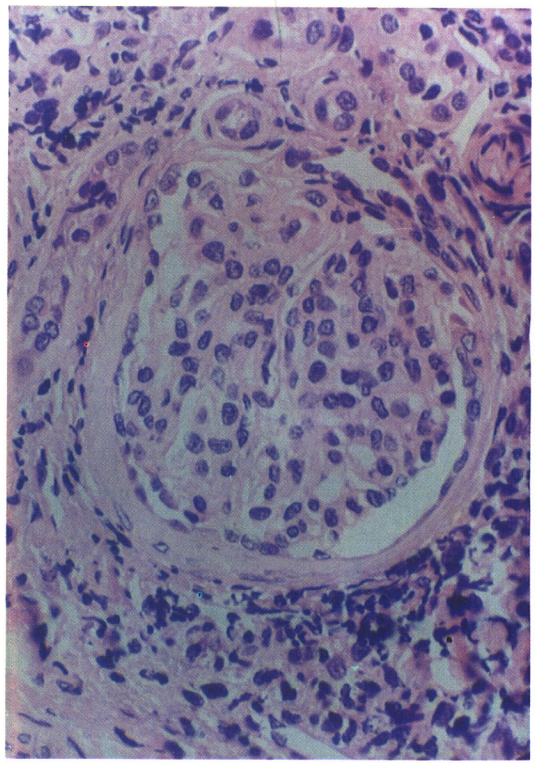

Fig. 3. Kidney biopsy finding shows fibrotic capsular change(H & E,×200).

A kidney biopsy was done on the 4th hospital day, and the findings were as follows; Tubules revealed marked atrophy and occasional calcium deposits were present in tubular walls and lumens with marked cellular infiltration in tubulointerstitium (Fig. 2). Interstitial fibrosis and pericapsular fibrotic change were also noted (Fig. 3).

On the 21th hospital day, a subtotal parathyroidectomy was performed under general anesthesia. Histologic examination showed parathyroid hyperplasia constituted mainly of chief cells(Fig. 4). After the operation, symptoms of polyuria and polydipsia disappeared and on the 28th day after the operation, serum calcium level decreased to 9.7mg/dl, serum phosphorus 4.3mg/dl, serum PTH 1.6ng/ml, serum creatinine 2.3 mg/dl and creatinine clearance slightly increased to 30.4ml/mim/1.73m^2(Table 1).

Table 1. Laboratory findings

	on admission	hospital 21th day	postop. 28th day
Calcium/Ca^{++}(mg/dl)	13.7/5.4	11.2/4.7	9.7/4.0
phosphorus(mg/dl)	5.3	4.1	4.3
AP(U/L)	142	98	85
Ca in 24hrs urine(mg)	246	342	148
P in 24hrs urine(mg)	265	445	337
PTH(ng/ml)(N : 0-0.5)	2.8	4.5	1.6
ADH(ng/ml)(N : 0.3-12)	17.7		
Vit$-D_3$(ng/ml)(N : 24±14)	12.1		
BUN/Cr(mg/dl)	38/4.0	23/2.2	17/2.3
Ccr(ml/min/1.73m^2)	12.6	25	30.4

AP : alkaline phosphatase, PTH : parathyroid hormone, ADH : antidiuretic hormone

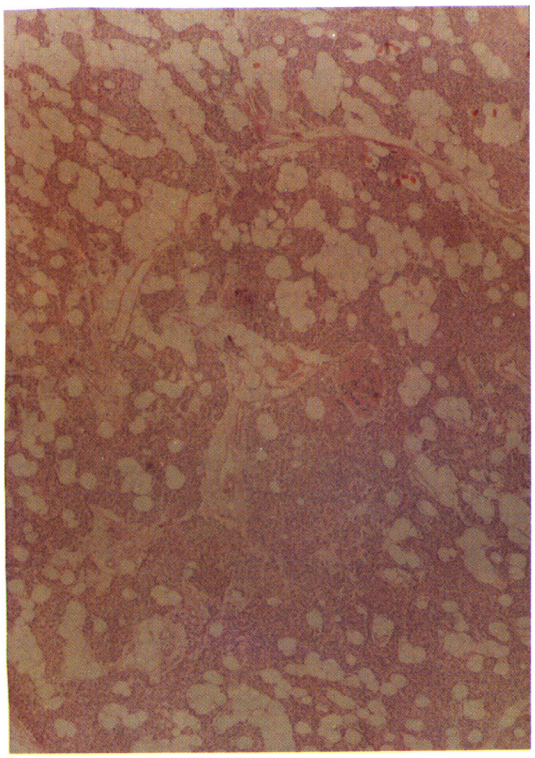

Fig. 4. Parathyroid gland shows parathyroid hyperplasia constituted mainly of chief cells with fat tissues(H & E,× 100).

DISCUSSION

Primary hyperparathyroidism can occur at any age, but it is rare in children. Since the first review of primary hyperparathyroidism in children was published in 1960 by Nolan and associates who found 23 cases, until 1982, only 86 cases had been described in the literature (Girard et al., 1982).

Two types of primay hyperparathyroidism are recognized in children, one occurring in neonates and the other during childhood. Those children who develop primary hyperparathyroidism prior to three months of age (neonatal hyperparathyroidism) present with a devastating spectrum of metabolic abnormalities, often resulting in death. These patients are also classified as having hereditary parathyroid hyperplasia or neonatal familial hyperparathyroidism because the disease is often genetically transmitted as an autosomal dominant trait and the characteristic pathology is chief cell hyperplasia of the parathyroid glands.

Distinct from this type of neonatal hyperparathyroidism, in children older than one year of age, hyperparathyroidism usually does not have any known genetic inheritance and is caused by parathyroid adenomas. These patients generally present with non-life threatening symptoms and signs similar to those of adults. Thus the disease should be considered merely an early onset of adult-acquired primary hyperparathyroidism (Norwood and Andrassy, 1983).

However, the symptoms in children seem to be somewhat different from those in adults. Incidences of anorexia, weight loss, and personality changes are all more striking in children (Mannix, 1975).

Children with primary hyperparathyroidism have a high frequency of detectable bone diseases. 25 of 43 pediatric patients reported by Bjernulf and colleagues (Bjernulf et al., 1970) had skeletal changes demonstrated radiologically while overt skeletal changes are identified in only approximately 10% of

the adults with primary hyperparathyroidism (Habener and Potts, 1989). But our patient did not show any signs of bone disease. Otherwise, renal lesions seem to be less common in children than in adults, probably because of the shorter duration of the disease (Bjernulf et al., 1970), but this case showed the typical clinical and laboratory findings of renal disease. However, we cannot explain these findings in our case.

The effects of calcium on the kidneys in patients with primary hyperparathyroidism are well described. The pathophysiological effects of excessive calcium on the kidneys in these patients can be considered in two broad categories : anatomical and functional. The anatomical defects include the occurrence of nephrolithiasis or nephrocalcinosis; The functional defects are included a spectrum of tubular and glomerular disorders (Habener and Potts, 1989).

A variety of renal functional abnormalities in hyperparathyroidism include elevation of blood urea nitrogen and serum creatinine, reflecting a modest to marked reduction in glomerular filtration rate (GFR), and numerous renal tubular defects (Habener and Potts, 1989). Hypercalcemia may cause either an acute and reversible decrement in GFR or a chronic irreversible nephropathy. Hypercalcemia may lead to vasoconstriction of the afferent arteriols and decreased renal blood flow. It can decrease ultrafiltration across glomerular capillaries. In addition, acute hypercalcemia may produce natriuresis and ECF volume contraction. In chronic hypercalcemic nephropathy, there is a fall GFR and a decrease in the maximum concentrating capacity, and the urine is free of cells or casts, although mild proteinuria may be observed. The findings are similar to those seen in patients with interstitial nephritis (Slatopolsky et al., 1993).

The most common feature of hypercalcemic nephropathy, although not invariably present, is hyposthenuria. Concentrating ability is impaired out of proportion to the general reduction in renal function, and polyuria and polydipsia are frequent presenting complaints (Epstein, 1968; Benabe and Martinez-Maldonado, 1978). In this case the diagnosis of hypercalcemic nephropathy was made on the kidney biopsy findings, clinical symptoms such as polyuria and polydipsia, and a fall in GFR.

Although hypercalcemia can be caused by tertiary hyperparathyroidism due to chronic renal failure (Slatopolsky et al., 1993), in this case we could exclude tertiary hyperparathyroidism because of the finding of a normal serum phosphorus level and the absence of renal osteodystrophy.

In this paper, we report a case of primary hyperparathyroidism with hypercalcemic nephropathy in a 12 year old boy with review of literatures.

REFERENCES

Benabe JE, Martinez-Maldonado M : *Hypercalcemic nephropathy. Arch Intern Med 138 : 777-9, 1978.*

Bjernulf A, Hall K, Sjogren I, Werner I : *Primary hyperparathyroidism in children. Brief review of the literature and a case report. Acta Paediatr Scand 59 : 249-58, 1970.*

Epstein FH : *Calcium and the kidney. Am J Med 45 : 700-14, 1968.*

Girard RM, Belanger A, Bernard B : *Review article. Primary hyperparathyroidism in children. Can J Surg 25 : 11-3, 1982.*

Habener JF, Potts JT : *Primary hyperparathyroidism. In : Degroot LJ, eds. Endocrinology. 2nd ed., W.B. Saunders Co., Philadelphia, 954, 1989.*

Kim DS, Lee SJ, Lee KI, Lee BC : *A case of primary hyperparathyroidism in children. J Kor Pediatr Soc 31 : 1350-6, 1988.*

Mannix H : *Primary hyperparathyroidism in children. Am J Surg 129 : 528-31, 1975.*

Nolan RB, Hayles AB, Woolner LB : *Adenoma of the parathyroid gland in children. Report of case and brief review of the literature. Am J Dis Child 99 : 622-7, 1960.*

Norwood S, Andrassy R : *Primary hyperparathyroidism in children : A review. Military Med 148 : 812-4, 1983.*

Park MJ, Kim HS, Kim DH : *A case of primary hyperparathyroidism in infancy. J Kor Pediatr Soc 35 : 1008-13, 1992.*

Slatopolsky E, Hruska K, Klahr S : *Disorders of phosphorus, calcium, and magnesium metabolism. In : Schrier RW, Gottschalk CW, eds. Diseases of the kidney. 5th ed., Boston, Little, Brown and Co., 2627, 1993.*