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Primary Oxalosis (An Autopsy Case)

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= Abstract =Primary oxalosis is a rare genetic disorder of glyoxylic acid metabolism. In a $3\frac{1}{2}$ year old girl who presented with convulsion and uremia, we found severe nephrolithiasis, numerous calcium oxalate crystals in the kidneys. They were found also in the bone marrow, thymus, choroid plexus, and pituitary gland on postmortem examination.

We believe this is the first proven primary oxalosis case, probably Type I, in the Korean literature.

Key Words: ***Nephrolithiasis, Renal Failure, Primary Oxalosis***

INTRODUCTION

Primary oxalosis or hyperoxaluria is a rare genetic disorder clinically characterized by recurrent calcium oxalate nephrolithiasis, and nephrocalcinosis leading to chronic renal failure usually in early ages (Enger *et al.* 1965, Williams 1978, Godwin *et al.* 1958).

Pathologically oxalosis, the term first used by Chou and Donohue (1952), refers to the disseminated deposition of oxalate crystals in various organs includng kidney, brain, bone, myocardium, *etc.* (Hughes 1959).

Two variants (Type I and Type II) of primary hyperoxaluria have been described and both of them are thought to be inherited as autosomal recessive traits (Smith and Williams 1968, Willams and Smith 1968).

We had a $3\frac{1}{2}$ year old girl who came to our Emergency service for convulsion associated with uremia, and died soon after admission. Postmortem examination revealed severe nephrolithiasis and numerous calcium oxalate crystals in the kidney and other tissues which led us to make the diagnosis of oxalosis, probably Type I. The case is reported for rarity of the disease, so far unreported in the Korean literature, and for prominent pathological findings.

CASE REPORT

A 3 year and 6 month old Korean girl was admitted to Seoul National University Hospital on November 20, 1979. The neonatal and developmental history was normal. Her parents were not consaguinous and family history was not eventful. She had been relatively healthy until 1 month prior to admission, when anorexia and fatigability developed insidiously without specific signs or symptoms. For the previous 2 weeks she had suffered from intermittent fever, nasal obstruction, and frequent epistaxis. On November 28, 1979, she had a seizure lasting several minutes, followed by 5 attacks thereafter.

On admission, physical examination revealed a moderately well developed and nourished girl who appeared lethargic. The blood pressure was 100/60 mmHg, the temperature 36°C, the pulse 104/min. The respiration was deep with the rate of 24/min. The face was edematous. The conjunctivae were anemic but sclera was not icteric. The pupils were isocoric, but were slightly dilated with sluggish light reflex. Epistaxis was noted in the both nostrils. Breath sounds were coarse but no definite rales were audible. The abdomen was slightly distended and the liver was palpable about 2 cm below the right costal margin. No pathological reflexes were elicited.

The laboraory investigations are listed as follows; Blood studies: Hb 7.7 gm/dl, WBC 15,500/mm^3

with 75% neutrophil. Urine: S.G. 1.015, pH 6.0, albumin 1+, sugar 1+. RBC 4-5, WBC 0-1/HPF. Serum : Na 126 (Nov. 30), 118 (Dec. 1) mEq/L, K 5.5, 6.4 (Dec. 1) mEq/L, Cl 89,86 mEq/L, Ca 4.0 mg/dl, phosphorus 13.5 mg/dl, magnesium 3.8 mEq/dl. Coagulation profile; prothrombin time 15 sec. (60%). PTT 44 sec. Blood ammonia 298.5 ug/dl. CSF studies; color-clear, pressure-over 30cm H_2O, cell count-normal, glucose 100 mg/dl, protein 67 mg/dl. Blood gas analysis; pH 7.302, PaO_2 100.1 mmHg, $PaCO_2$ 47.7 mmHg, standard bicarbonate 12.3 mEq/L.

Chest X-ray showed a pleural effusion on the right, and a plain film of the abdomen revealed numerous patchy areas of calcification on both sides overlying the kidney shadows. After admission her clinical condition rapidly deteriorated and on December 1, 1979, one day after admission, she expired despite all subsequent efforts.

POSTMORTEM EXAMINATION

General development and nourishment were fairly good. There were 30 ml of pleural effusion, a few ml of pericardial effusion and 50 ml of straw colored ascites. The right and left kidneys weighed 50 gm and 45 gm respectively. The right kidney was larger than the left, and was slightly distorted because of dilated calyces and stone formation. Both kidneys were firm and gritty on palpation. The capsules were stripped off with ease to reveal a slightly granular gray tan cortical surface. Cut sections revealed that the renal pelvis was filled with numerous pale grayish stones measuring up to 0.5 cm in diameter. They were roundish and not faceted. They were crumbled with some difficulty. Larger stones were in the pelvis, but sandy stones were also seen in the calyces and in the medulla of the renal parenchyma (Plate 1). A mild degree of hydronephrosis was present bilterally. X-ray films of the kidney specimen (Plate 2) showed disseminated fine granular radio-opaque material throughout the parenchyma. Chemical analysis of stones from the renal pelvis consisted entirely of calcium oxalate. Microscopically diffuse interstitial fibrosis and inflammation were the most prominent findings. Refractile crystals of various sizes were seen, primarily in the proximal convoluted tubules (Plate 3), but they were also seen in the interstitium. The tubular epithelia were often compressed and destroyed or atrophied together with fibrosis. Some tubules were dilated. The crystals in general appeared slightly yellowish globular or rhomboidal and were characteristically arranged in rosettes and were doubly refractile under polarized light (Plate 3 & 4). In the cortex, foreign body reaction around these crystals in interstitium was frequently seen.

Fibrosis was intensified in those areas. Blood vessels were thickened but no crystals were detected in the walls. The glomeruli were spared from crystal deposit, although periglomerular fibrosis and hyalinization were seen not infrequently. In addition, occasional intratubular laminated calcium precipitates were also seen. Extrarenal deposits of oxalate were found in bone marrow, thymus (Plate 5), choroid plexus and the pituitary gand. However, the degree of deposit was minimal in comparison with that of kidneys. The lungs showed features of uremic pneumonitis. Other organs did not show any specific abnormalities. The parathyroid glands were slightly enlarged and showed microscopically chief cell hyperplasia. The brain showed no specific changes.

DISCUSSION

According to the etiolgy, hyperoxaluria is divided into primary or secondary. Secondary hyperoxaluria occasionally results from excessive ingestion of oxalate or its metabolic precursors such as ethylene glycol (Berman *et al.* 1957), and methoxyflurance (Mazz *et al.* 1971). Excessive absorption of the oxalate from the bowel, so called "enteric hyperoxaluria", was also reported in conditions such as small bowel resection and chronic gastrointestinal disorders (Smith *et al.* 1972). Our patient didn't have any history listed above suggesting secondary oxalosis. Since the kidney is the only organ to excrete absorbed oxalate, oxalosis can be noted in chronic renal failure from any cause. Marked elevation of oxalate in blood up to 80 times of normal with a positive correlation with blood urea level was reported in renal failure due to decreased urinary excretion of oxalate (Zarembski *et al.* 1966, Constable *et al.* 1979). But oxalosis has been reported only in prolonged renal failure and mostly in adult patients (Chaplin 1977). Although our patient showed anemia and mild parathyroid hyperplasia with renal failure, it seemed likely that she didn't have renal failure long enough to induce secondary oxalosis, for her physical development was not affected. Also the extent of oxalosis was too remarkable to think that she might have had oxalosis secondary to renal failure.

Primary hyperoxaluria is a rare inherited disorder and now is classified as Type I and Type II (Wil-

liams and Smith 1968). In Type I, which is by far the more common variant, there is an absence of the soluble thiamine pyrophosphate dependent carboligase leading to increased synthesis of oxalate. Thus, excessive amounts of glyoxylic and glycolic acids, as well as oxalate are excreted in the urine. The resultant hyperoxaluria then leads to excessive saturation of urine with respect to calcium oxalates, and recurrent nephrolithiasis results. Tissue oxalate deposition (oxalosis) eventually occurs, particularly after renal failure ensues.

In Type II, the enzyme defect is thought to be in the gluconeogenic pathway of serine metabolism. There is excessive excretion of oxalic acid and L-glyceric acid (also L-glyceric called aciduria) in the urine. Clinically Type I and II cannot be differentiated, but oxalosis has never been reported in Type II. Since our patient showed diffuse oxalate deposition in various tissues, she seemed to have Type I hyperoxaluria leading to oxalosis.

Phenotypically, primary hyperoxaluria (Type I) can be variable (Williams 1978). The most severe form, although rarely reported, is oxalosis in infancy which is characterized by early onset of renal failure in infancy and progression to death usually within 3 months (Gilboa *et al.* 1983, Zegher *et al.* 1984).

On the other hand in a small number of patients, stone disease did not develop until the age of 20 years (Boquist *et al.* 1973). Most of the cases are characterized by the appearance of recurrent calcium oxalate renal calculi typically before the age of six years and by eventual deposition of calcium oxalate in a variety of extrarenal tissue.

Our patient is a typical case which showed nephrocalcinosis on KUB, birefringent calcium oxalate crystals in most of the reported sites including most prominently the kidneys, then bone marrow, thymus, choroid plexus and pituitary gland. Pathologically our case is different in terms of deposition of the crystals in the choroid plexus which was mentioned by Dunn (1954) and was not observed in his cases.

Mild parathyroid chief cell hyperplasia as seen in our case seemed to be secondary to renal failure. Seizures which are not infrequently encountered in primary oxalosis were believed to be secondary to the deposition of oxalate in CNS (Dunn 1954). But because our patient didn't show deposition of oxalate crystals in the CNS itself, the cause of the seizures in this case seemed more likely due to the low serum calcium level, probably secondary to renal failure or others. Treatment of oxalosis is limited, and mostly general supportive care such as increased fluid intake, large amount of phosphate intake and pyridoxine administration has been tried.

Pyridoxine therapy, even with physiologic dose (Yendt and Cohanim 1985), is reported to be effective in some cases of both in adult and infantile Type I hyperoxaluria probably by enhancing the metabolism of glyoxylate to glycine (Gibbs and Watts 1967). However once oxalosis develops which accelerates renal failure, then more oxalate crystal deposition occurs by renal failure itself. Because of the inborn nature of the disease, dialysis and transplantation are not usually justified (Zegher *et al.* 1984).

In summary, we report a typical primary oxalosis case, probably Type I, in a 3 and half year old girl who presented with renal failure and died soon after admission. This is the Ist case with primary oxalosis reported in the Korean literature.

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LEGENDS FOR FIGURES

Fig. 1. Gross specimen of bisected right kidney. Numerous light-colored and various sized stones are seen in the pelvocalyceal system.

Fig. 2. A cut section of the left kidney seen grossly (left) and radiographically (right). Note innumerable finely granular radioopaque densities throughout the cortex and medulla.

Fig. 3. Photomicrograph of the kidney showing abnormal glomerulus, tubular atrophy with interstitial fibrosis and disseminated refractile oxalate crystals forming rosettes. This picture was taken partially polarized light. H&E, ×100

Fig. 4. Higher magnification of oxalate crystal deposited in renal interstitium. Rectangular or rhomboid crystals are provoking foreign body reaction. H&E, ×400

Fig. 5. Photomicrograph of thymus showing refractile oxalate crystals in Hassall's corpuscles. H&E, ×100

= 국문초록 =

일차성 수산증 (부검예)

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일차성 수산증은 드문 유전성 질환으로서, glyoxylic 산 대사 이상에 기인한다. 경련과 뇨독증으로 입원 사망한 3년 6개월된 여아에서, 부검을 시행한 결과 심한 신장 결석, 그리고 신장을 포함한 골수, 흉선, 맥락총, 뇌하수체 등에서 수많은 칼슘·수산결정체를 발견하여 일차성 수산증으로 진단하였다. 본 예는 우리나라 문헌에 보고된 최초의 일차성 수산증이라고 믿어진다.


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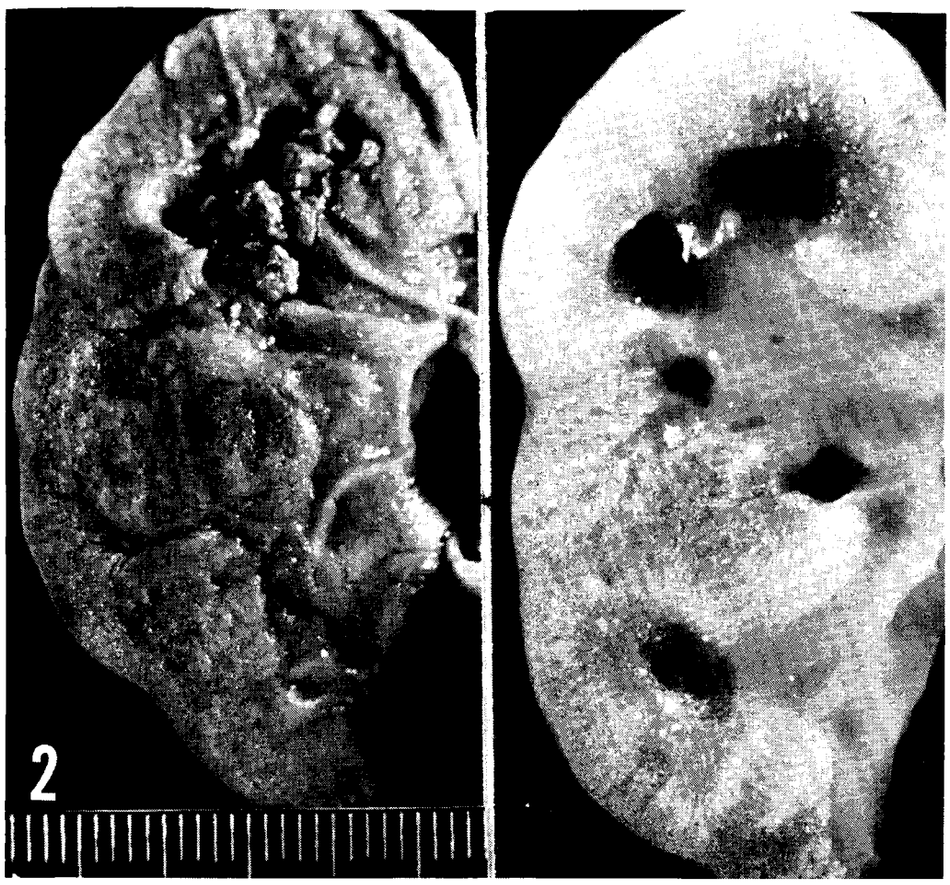
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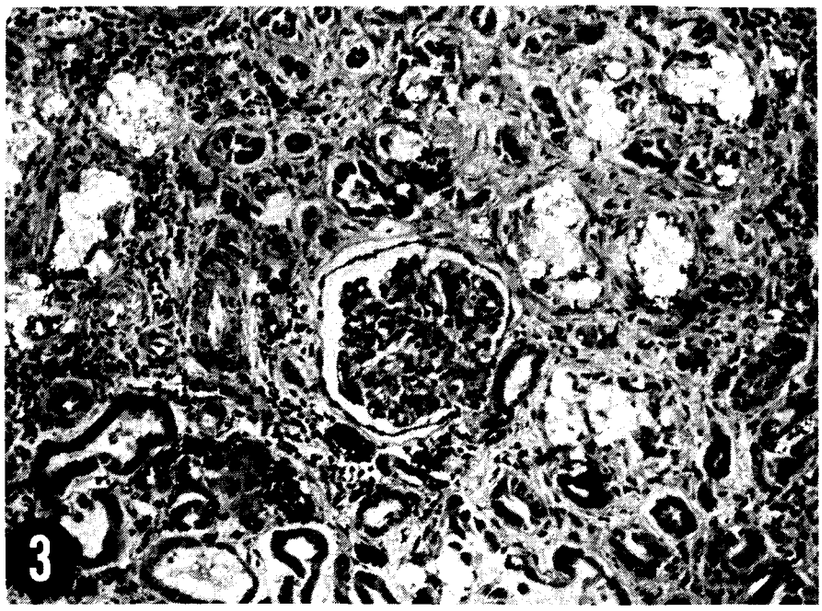

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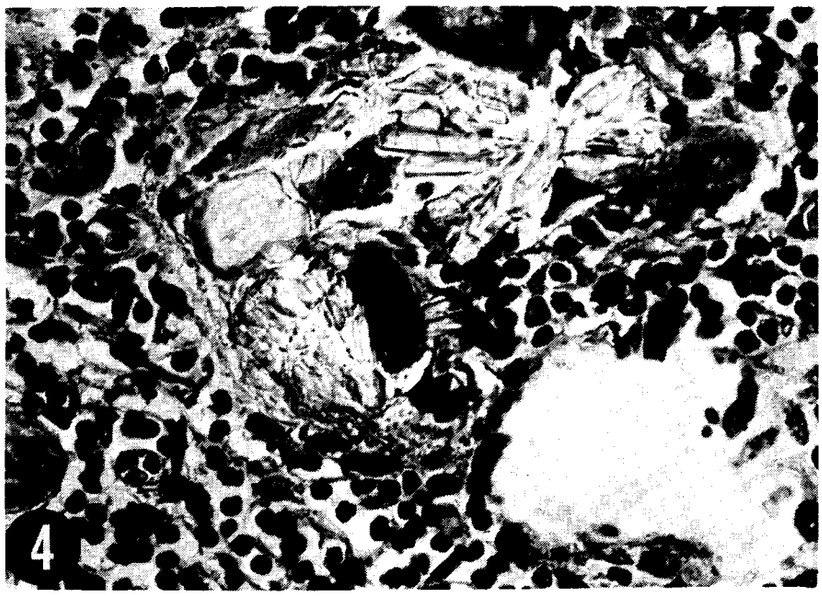

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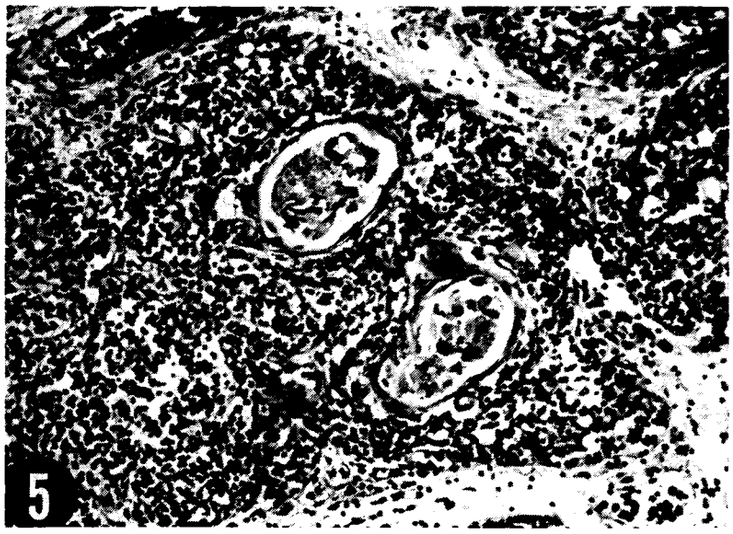

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