Case Report

Primary Hyperoxaluria

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A 5-month-old female infant who had chronic diarrhea and acute renal failure was referred to Chulalongkorn Hospital for further investigation and management. Laboratory investigation revealed elevated blood urea nitrogen and creatinine level, hypocalcemia, hyperphosphatemia, and hyponatremia. Ultrasonography of the kidneys showed normal size with bilateral hyperechoic kidneys. Eyes examination was compatible with oxalosis maculopathy. Urine organic acid analysis revealed peak of oxalate and glycolate. Clinical impression concluded acute renal failure from hyperoxaluria. The patient underwent continuous venovenous hemodiafiltration (CVVH-DF) with regional citrate anticoagulation and expired on day 13 after admission. Pathological examination of kidney necropsy revealed diffuse intraluminal deposition of oxalate crystals within the renal parenchyma. Primary hyperoxaluria is a very rare disease and has rarely been reported in Thailand. In the presented case, the diagnosis was delayed due to uncommon presentation and unavailability of diagnostic laboratory.

Keywords: *Primary hyperoxaluria, Oxalosis, Oxalate*

J Med Assoc Thai 2007; 90 (8): 1669-72
Full text. e-Journal: *http://www.medassocthai.org/journal*

Primary hyperoxalurias (PH) are rare diseases characterized by overproduction and accumulation of oxalate in the body. The main target organ is the kidney, as oxalate cannot be metabolized and is excreted in the urine, leading to nephrocalcinosis, recurrent urolithiasis, and subsequent renal impairment[1]. Once renal function declines, oxalate, which is only excreted by the kidney, accumulates and calcium oxalate gets deposited in various tissues - a condition called 'systemic oxalosis'[2].

The two forms of primary hyperoxalurias with a significant epidemiological impact and better characterized are the type 1 (PH1) and type 2 (PH2), both caused by a recessively transmitted genetic defect of glyoxylate metabolism. PH1 is caused by a defect or an absence of liver-specific peroxisomal alanine: glyoxylate aminotransferase. PH2 results from absent glycoxylate reductase activity. Clinically, PH is very heterogeneous, with the spectrum ranging from early end-stage renal failure, due to infantile oxalosis, to occasional kidney stones in adults[3].

The prevalence and incidence of PHs among the general population are difficult to define and often underestimated due to the rare availability of adequate diagnostic tools[4]. The reported incidence rates range from one in 5-15 million to 0.15 per million per year[5-7]. However, a case of primary hyperoxaluria has rarely been reported in Thailand. The pathological findings of the kidney in the case of a Thai female infant, whose first clinical manifestation was chronic diarrhea followed by renal failure and convulsions, are documented in the present report.

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Case Report

A 5-month-old female had the history of chronic diarrhea for one month. One day prior to admission, she developed oliguria and generalized tonic clonic convulsion. At Prapokklao Hospital, blood chemistry examination revealed elevated blood urea nitrogen and creatinine level, hypocalcemia, hyperphosphatemia,

hyponatremia, and acidosis. The patient was treated until clinical status was stable, and then, was referred to King Chulalongkorn Memorial Hospital.

The patient is the first-born. She was delivered by vaginal delivery, with birth weight of 3,200 grams, and was healthy prior to this illness. The mother was 18 years old and had no underlying disease. She had two sisters and four brothers. One of her 13-year-old brothers had an underlying renal disease, but did not know the definite diagnosis, and a sister's daughter died at 7 months old of unknown cause. The father was a healthy 28 years old. He did not have any history of renal disease in his family. History of consanguineous marriage in both families was denied.

Physical examination on admission revealed pulse rate at 120 beats per minute, respiratory rate at 28 per minute and blood pressure at 138/92 mmHg. There was systolic ejection murmur grade 2/6 at left middle parasternal border. Liver was palpable at 2 cm below right costal margin.

Abnormal laboratory investigation revealed the following findings: Complete blood count showed mild anemia, blood urea nitrogen 93 mg/dL, creatinine 8.4 mg/dL, calcium 4.7 mg/dL, phosphate 7.8 mg/dL, and hyponatremia. Urine analysis showed proteinuria and glucosuria. Stool examination revealed no parasite, and neither red nor white blood cells were identified. Echocardiogram demonstrated mild tricuspid regurgitation. Ultrasonography of the kidneys showed normal size with bilateral hyperechoic kidneys (Fig. 1). Eye examination revealed bilateral submacula yellowish deposits, compatible with oxalosis maculopathy. Urine organic acid analysis revealed peak of oxalate and glycolate. Plasma oxalate concentration was not measured.

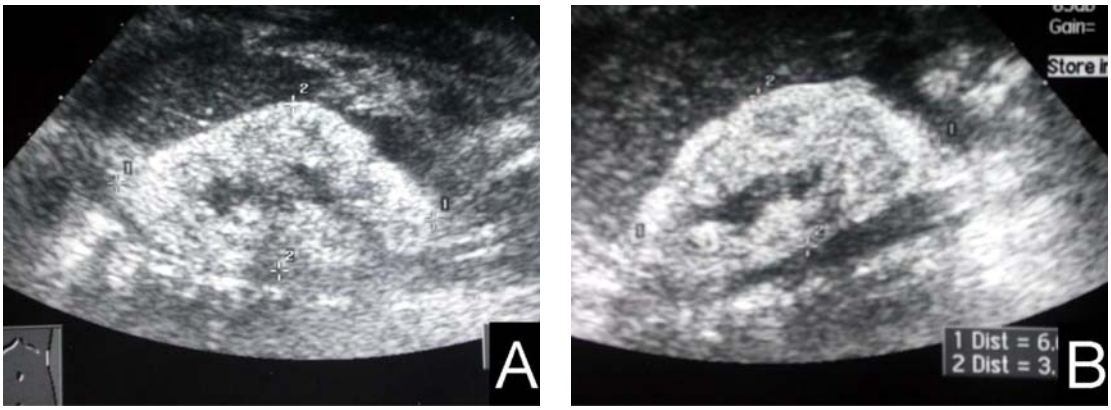

Fig. 1 (A) Ultrasonogram of the left kidney and (B) the right kidney demonstrates normal sized with bilateral hyperechoic kidneys

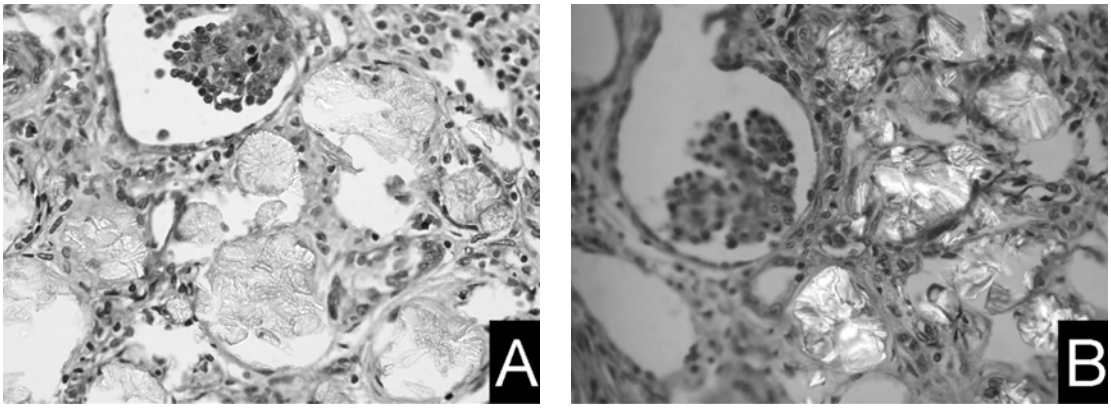

Fig. 2 Microscopic examination reveals diffuse intraluminal deposition of oxalate crystals within the renal cortex Magnification x 400 of (A) H&E staining and (B) polarizing microscopy

Clinical impression concluded acute renal failure from hyperoxaluria. She was treated with sodium and calcium supplement, intravenous administration of dopamine, antihypertensive drugs, and intermittent diuretics administration. Peritoneal dialysis was carried out but failed. The patient underwent continuous veno-venous hemodiafiltration (CVVH-DF) with regional citrate anticoagulation on the 7th day of admission. She remained stable for a few days. On the 4th day of CVVH-DF, she developed pneumonia, which was complicated by bilateral pneumothorax. She died 13 days after admission.

Opened kidney necropsy was performed with permission of the parents. Microscopic examination revealed diffuse intraluminal deposition of oxalate crystals mostly within the renal cortex, which were irregular or fan-shaped, laminated, and birefringent by polarizing microscopy (Fig. 2). The interstitium showed minimal fibrosis and mild mononuclear inflammatory cell infiltration.

Discussion

According to several authors, the disease is highly variable in clinical presentation[8-11]. In fact, the clinical setting of the disease, including age at onset, type of presentation, severity of hyperoxaluria, residual enzymatic activity, and progression to renal failure is extremely heterogeneous[11]. The majority of patients suffer from recurrent episodes of nephrolithiasis in childhood or adolescence. Up to 10% of patients are diagnosed with infantile oxalosis and often die from renal failure during the first months of life[4].

Diagnosis of PH is often missed or delayed, and the reported cases represent only a small number[3]. The first step in diagnosing a suspected case of PH is to find high oxalate levels in urine and plasma. A distinction between PH1 and PH2 should be made by finding elevated urine and plasma concentrations of glycolate and L-glycerate[4]. In the presented case, the diagnosis was delayed due to uncommon presentation and unavailability of diagnostic laboratory. The patient presented with chronic diarrhea, which mislead the attending physician. Unfortunately, no further investigation was performed, including genetic study, because the patient passed away during the period when the laboratory test was unavailable.

Treatment of PH is aimed at reducing oxalate biosynthesis and calcium oxalate supersaturation, and preventing systemic oxalosis. Oxalosis is not preventable with current dialysis techniques. In the last few years, combined liver-kidney transplantation has become an elected procedure in the majority of patients and appears to give excellent results. Although, the results are poor when transplantation is delayed, advanced systemic oxalosis has developed[12,13]. However, the management of infants presenting with severe oxalosis is still controversial, as a high mortality rate has been reported[4].

In summary, the presented case reminds us that primary hyperoxaluria may have clinical expression rather than urological manifestation or renal failure. Early detection is the key to improving the clinical outcome. Hyperoxaluria should be a differential diagnosis in all childhood renal insufficiency cases.

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ภาวะออกซาเลทสูงแบบปฐมภูมิ

พฐู ตัณฑ์ไพโรจน์, วิภาวี กิตติโกวิท, พรชัย กิ่งวัฒนกุล

ภาวะออกซาเลทสูงแบบปฐมภูมิเป็นโรคที่พบได้น้อยและแทบไม่มีรายงานในประเทศไทย คณะผู้เขียนได้รายงานภาวะนี้ในผู้ป่วยเด็กหญิงไทยอายุ 5 เดือน ที่ถูกส่งมารับการรักษาต่อที่โรงพยาบาลจุฬาลงกรณ์ เนื่องจากอาการอุจจาระร่วงเรื้อรัง และไตวายเฉียบพลัน ผลตรวจทางห้องปฏิบัติการพบว่ามีการเพิ่มขึ้นของระดับไนโตรเจนในเลือด และครีตินิน ร่วมกับแคลเซียมต่ำ ฟอสเฟตสูง และโซเดียมต่ำ การตรวจคลื่นเสียงความถี่สูงของไตทั้งสองข้างพบมีความหนาแน่นสูงขึ้น ผลการตรวจตาเข้าได้กับภาวะผลึกออกซาเลทสะสมในจอประสาทตา การตรวจสารอินทรีย์ในปัสสาวะพบมีการเพิ่มขึ้นของออกซาเลทและไกลโคเลท ผู้ป่วยจึงได้รับการวินิจฉัยว่าเป็นไตวายเฉียบพลัน เนื่องจากภาวะออกซาเลทสูงในปัสสาวะ จากนั้นได้รับการรักษาด้วยการล้างไตโดยวิธีฟอกเลือด และได้เสียชีวิตลงในวันที่ 13 หลังจากเข้ารับการรักษา การตรวจทางพยาธิวิทยาของชิ้นเนื้อเยื่อไตหลังเสียชีวิตพบมีการสะสมของผลึกออกซาเลทจำนวนมาก การวินิจฉัยที่ล่าช้าในผู้ป่วยรายนี้เกิดจากอาการแสดงของโรคที่ไม่เด่นชัด ร่วมกับขาดแคลนอุปกรณ์การตรวจทางห้องปฏิบัติการที่ใช้ในการวินิจฉัยโรคนี้