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End stage renal disease due to primary hyperoxaluria in a 7-month infant; a case report

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ABSTRACT

Primary hyperoxaluria (PH) is a rare genetic metabolic disease presented severely in infants with end-stage renal disease (ESRD). Promoting diagnosis with aggressive management is essential in these patients. Here we presented a rare case of primary hyperoxaluria type 1 (PH1) in a seven-month infant girl who underwent dialysis with prospective kidney transplantation in the future.

Keywords: Primary hyperoxaluria, Dialysis, End-stage renal disease

Case Report

Implication for health policy/practice/research/medical education:
Using available methods for diagnosis and intensive management in infants with PH is essential for reducing mortality at this age.

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Introduction

Oxalate is a normal harmless metabolism byproduct excreted in the urine. Hyperoxaluria, depositions of calcium oxalate crystals in the kidney and other organs, is divided into primary and secondary causes (1). Primary hyperoxaluria (PH) is a rare autosomal recessive categorized into three subgroups according to different gene mutations that impair glyoxylate metabolism. It is considerable that, these rare disorders account for approximately 2% of kidney replacement requirements before the age of 15 years. Additionally, however, the prevalence reported 1-3 cases/million, in countries with common consanguinity marriage is more (2,3).

In primary hyperoxaluria type 1 (PH1), alanine glyoxylate aminotransferase enzyme defect, involves most patients with more severe phenotypes than other types (4). Progressive nephrocalcinosis, nephrolithiasis, and early end-stage renal disease (ESRD) are presented in infantile PH1; therefore, promoting the diagnosis of PH1 is important to prevent complications (5). Here we reported a rare case of PH1 with ESRD, which was diagnosed based on pathologic findings.

Case Presentation

A 7-month infant girl from a consanguine parent with a history of ESRD was referred to our hospital due to unstable hemodynamics followed by diarrhea, vomiting, and respiratory distress. She was a term baby with a dead twin who passed away during infancy because of an unknown reason.

On her physical exams, severe edema with hypertension was considerable. Moreover, primary laboratory data revealed severe acidosis, uremia, and hyperkalemia which took under treatment with adequate liquid and symptomatic management (Table 1).

During hospitalization diarrhea, vomiting, and respiratory distress were controlled, however, low urinary output and serum high creatinine levels were noticeable. According to the patient's uremia, hypertension, edema, acid-base, and electrolyte disturbance with no adequate response to treatment, permanent peritoneal dialysis was inserted. Then, voiding of the cyst urethrogram (VCUG)

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Table 1. Laboratory study

Test	Result
WBC (mg/dL)	23.6-15.3-11.5-5.6
Hemoglobin (mg/dL)	7.3-9.3-11.3
PLT (mg/dL)	263-157-100-43
ESR (mg/dL)	35
CRP (mg/dL)	20
Uric Acid (mg/dL)	9.3-3.8-1.7
BUN (mg/dL)	70.1
PT	15
PTT	40
INR	1.5
Fluid analysis	
Glucose	638
Protein	100
WBC	70
RBC	160
Creatinine (mg/dL)	5.16-4.85-3.72
Calcium (mg/dL)	7.5
Phosphorus (mg/dL)	9.6
Magnesium (mg/dL)	2.7
Sodium (mEq/L)	137
Potassium (mEq/L)	4.3
Albumin (mg/dL)	2.2

WBC; White blood cells, PLT; Platelet, ESR; Erythrocyte sedimentation rate, CRP; C-reactive protein, BUN; Blood urea nitrogen, RBC; Red blood cells, PT; Prothrombin time test, PTT; Partial thromboplastin time, INR; International normalized ratio.

and renal biopsy was conducted. VCUG was reported normal (Figure 1). However, her renal biopsy was reported three months later. Finally, she discharged symptoms free with considering regular follow-ups and dialysis.

Three months later she was re-admitted to our hospital due to peritoneal dialysis caterer's malfunction, severe edema, and lethargy. In addition, primary hyperoxalosis as partial effacement of visceral foot processes (50-70%), and expression of GBM-like mesangial matrix, with all negative immune tests, were reported in the renal biopsy. Figure 2 identifies that our patient is a case of PH.

During hospitalization, sepsis and catheter infection were recognized, and underwent treatment. Despite the initiation of lasix and enalapril and albumin infusion, the edema did not control. We presumed that calcium-oxalate depositions could be a cause of catheter malfunctions along with her kidney biopsy. Thus, catheter was fixed and reinserted again. Unfortunately, despite generalized edema, our patient was discharged by her parent's self-consent.

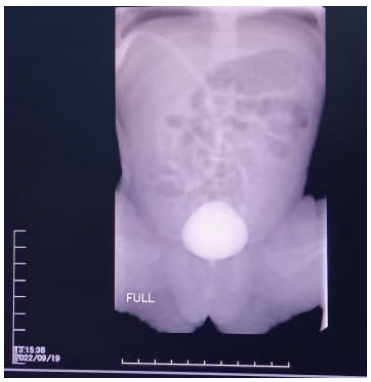

Figure 1. Voiding the cyst urethrogram: after catheterization urinary bladder is filled with contrast, media bladder is distensible with regular and normal wall thickness. No filling defect or outpouching is seen. No residue is seen after voiding

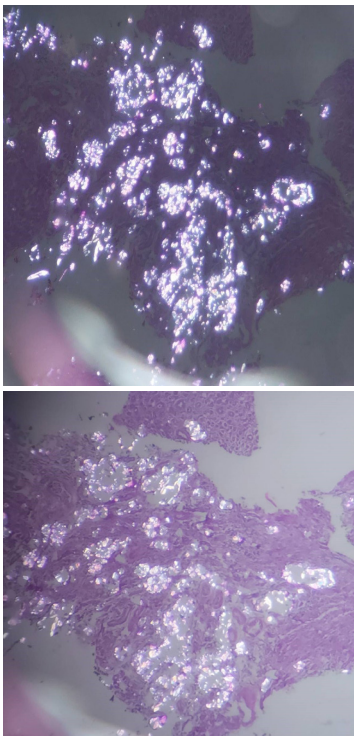

Figure 2. Renal biopsy specimen under polarized light; calcium oxalate crystals depict a characteristic birefringence

Discussion

Primary hyperoxaluria type 1 is an autosomal recessive disorder with a prevalence of 1-3 cases/million population/year more than other PH (6). However, this inherited metabolic disease is rare, while the frequency is highly reported in regions where consanguinity marriage is common. These children account for 10% of ESRD (7). Moreover half of the infantile hyperoxaluria reported a most severe form of PH with having already ESRD (8). In our study, we reported a rare case of PH1 consequent to a consanguinity marriage.

Clinical manifestations of PH are heterogeneous from death PH1 in infancy to asymptomatic in childhood considering the age of presentation, severity, and rate of renal insufficiency (2). Significant manifestations in our patients were hemodynamic instability with respiratory distress which is similar to a case report from Nieto-Vega et al (9) up to the fact that the kidney is the first organ affected by oxalate depositions, edema, electrolyte disturbances with low urinary output predicted.

To prevent downstream complications of PH, promoting diagnosis is essential therefore, several studies showed the diagnostic clinic-laboratory in PH (10). Fresh urine sample for measuring the oxalate/creatinine ratio is the first step. Patients with PH1 usually have a high urinary oxalate excretion (>100 mg/d >1.0 mmol/1.73 m^2/d, or 1000 µmol/d) without any history of vitamin C supplement as ascorbic acid ingestion (5). Another important evaluation is using pelvic-abdominal ultrasonography and plain urinary tract study to find radio-opaque renal stones. The definite diagnosis made by gene sequencing detecting the gene defects (11). Due to laboratory limitations, we couldn't measure the urine oxalate level. Although the VCUG was reported normal, the definite diagnosis was conducted based on pathology findings.

Oxalate, a metabolic end product, is filtered at the glomerulus and transported bi-directional in the renal tubules. Several studies on animal models demonstrated that epithelial cell injury is due to oxalate or calcium oxalate crystals (12). These injuries may have contributed to cells death following the change in gene expression or improper inflammation handling leading to glomerulonephritis, chronic kidney disease, and ESRD(1, 12). On light microscopy, the oxalate crystals have a clear appearance, and under polarized light bright birefringence particularly abundant crystals easily could detect (4).

Non-stop oxalate production by the liver causes other organs damages, thereby there is no curative treatment unless transplantation for PH1 with ESRD (10). A study on six infants with PH1, reported 100% long-term kidney allograft survival after combined liver-kidney transplantation (13). Moreover, based on several studies, conservative therapy in patients with PH includes massive fluid intake (tube or gastrostomy feeding in infants) calcium oxalate inhibitors, and vitamin b6 (pyridoxine) (7). In our case, liquid therapy considering acid-base and electrolyte disturbance was conducted to stabilize her hemodynamics. Due to difficult transplantation circumstances, we used peritoneal dialysis as a bridge with future kidney transplantation considerations. However, hemodialysis is preferred over peritoneal dialysis, as difficult center catheter insertion and patients' changeable hemodynamics we used peritoneal dialysis. The dialysis frequencies were evaluated in several studies, hence, five to six times per week, sometimes in combination with peritoneal dialysis is required (14). Complications related to intensive dialysis regimens, such as dialysis-associated infections, and extreme stress for family's concomitant with financial and psychological issues make the infants' PH1 treatment tremendously complex than other age groups.

Conclusion

Here we reported a rare case of PH1 diagnosed based on pathologic findings for avoiding expensive genetic tests. The phenotype divergence together with the rarity of the disease may cause a delay in diagnosis. Therefore, using the best available diagnostic test instead of expensive facilities could help practitioners manage the disease.

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Author's contribution

Conceptualization: PP, ZP, FN, AZ, FK.
Validation: ZP, FN.
Investigation: PP, ZP, FK.
Resource: PP, ZP, FN.
Data correction: PP, AZ.
Writing-original draft : PP, AZ.
Writing review and editing: AZ.
Visualization: PP, ZP.
Supervision: PP, ZP.
Project administration: AZ.

Conflicts of interest

The authors declare that they have no conflict of interest.

Ethical issues

This case report was conducted in accordance with the World Medical Association Declaration of Helsinki. Written informed consent was obtained from the parents of patients for publication of this report. Ethical issues (including plagiarism, data fabrication, double publication) have been completely observed by the authors.

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